Section A7.1.1.1.1 **BPD Annex Point IIA, VII.7.6.2.1**	**Hydrolysis as a function of pH and identification of breakdown products** 7.1.1.1.1. Hydrolysis (Flufenoxuron)

0. Justification of the choice of the key study	**RMS Comment (01/02/05):** Two studies are submitted for this endpoint and are summarized in Document IIIA. The notifier did not provide any justification for the choice of a key study. RMS recommend the study of Hassink J (2003) (reference 2, page 15) as "key study" for the following reasons: - Contrary to Reference 1, Reference 2 is GLP study conducted according to OECD Guideline 211; - Metabolites were identified in reference 2 ; DT_{50} derived in comparable temperature and pH conditions were higher than in reference 1.

			Official use only
		1 REFERENCE	
1.1	**Reference**	**1) Langner EJ, Camilleri P (1987)** Hydrolysis of WL 115110 in aqueous media. XXXX unpublished XXXX	
1.2	**Data protection**	No	
1.2.1	Data owner	BASF	
1.2.2	Companies with letter of access	XXXX	
1.2.3	Criteria for data protection	No data protection claimed	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	The study is not conducted according to GLP or a specific guideline, however the study is scientifically valid and provides more complete characterization of the pH and temperature effects on hydrolysis rate than studies meeting guideline minimums.	
2.2	**GLP**	No, GLP was not compulsory at the time the study was performed	
2.3	**Deviations**	No	
		3 MATERIALS AND METHODS	
3.1	**Test material**		
3.1.1	Lot/Batch number	XXXX	

Section A7.1.1.1.1 **BPD Annex Point IIA, VII.7.6.2.1**		**Hydrolysis as a function of pH and identification of breakdown products** 7.1.1.1.1. Hydrolysis (Flufenoxuron)	
3.1.2	Specification	Pure test substance	
3.1.3	Purity	99 ± 1%	
3.1.4	Further relevant properties	The solubility of Flufenoxuron in water is 186 µg/L at pH 4, 136 µ/L at pH 7 and 369 µg/L at pH 9	X
3.2	**Reference substance**	A WL115096 (CL 359882) standard was used to identify hydrolysis products; no details on lot no. and purity provided.	
3.2.1	Initial concentration of reference substance	Not applicable	
3.3	**Test solution**	The test substance was dissolved in acetone and diluted to a nominal concentration of 0.2 µg/mL. Aliquots of the solution were added to buffers to give a test substance concentration of ca 0.002 µg/mL in 1% acetone. See Table 7.1.1.1.1/2.	
3.4	**Testing procedure**		
3.4.1	Test system	Sterilized buffer solutions (see Table 7.1.1.1.1/1 and Table 7.1.1.1.1/3)	X
3.4.2	Temperature	Tests were run at 25, 40, 50, 60, 70, and 80ºC	X
3.4.3	pH	Tests were run at pH 5, 7, 9, 12, and 14	X
3.4.4	Duration of the test	2.2 to 112 days, depending on pH and temperature	
3.4.5	Number of replicates	2	
3.4.6	Sampling	200 mL aliquots were removed from the test flasks at intervals	
3.4.7	Analytical methods	The aliquots of buffer were extracted twice with 50 mL of 10% methyl -tert-butyl ether (MTBE) in hexane. The organic phases were concentrated to dryness and dissolved in 100 µL of MTBE with cyanazine internal standard and quantitated by HPLC (See Table 7.1.1.1.1/4). WL 115110 and WL 115096 standards at 5 concentrations (2 – 20 ppm) with cyanazine internal standard were used to determine response factors for quantitation of these compounds.	X
3.5	**Preliminary test**	No, tests covered a range of pH and temperatures	
		4 RESULTS	
4.1	**Concentration and hydrolysis**	See Table 7.1.1.1.1/5, Table 7.1.1.1.1/6, Table 7.1.1.1.1/7, Table 7.1.1.1.1/8, Table 7.1.1.1.1/9	

Section A7.1.1.1.1 **BPD Annex Point IIA, VII.7.6.2.1**		**Hydrolysis as a function of pH and identification of breakdown products** 7.1.1.1.1. Hydrolysis (Flufenoxuron)	
	values		
4.2	**Hydrolysis rate constant (k_h)**	See Table 7.1.1.1.1/5, Table 7.1.1.1.1/6, Table 7.1.1.1.1/7, Table 7.1.1.1.1/8, Table 7.1.1.1.1/9	
4.3	**Dissipation time**	See Table 7.1.1.1.1/5, Table 7.1.1.1.1/6, Table 7.1.1.1.1/7, Table 7.1.1.1.1/8, Table 7.1.1.1.1/9	
4.4	**Concentration – time data**	See Table 7.1.1.1.1/5, Table 7.1.1.1.1/6, Table 7.1.1.1.1/7, Table 7.1.1.1.1/8, Table 7.1.1.1.1/9	
		5 APPLICANT'S SUMMARY AND CONCLUSION	
5.1	**Materials and methods**	The hydrolysis of flufenoxuron was investigated over a range of temperatures (25 to 80ºC) and pHs (5 to 14). Solutions of ca 0.002 µg/mL of the test substance in buffers with 1% acetone were prepared and aliquots were analyzed by HPLC at intervals up to 122 days. The aliquots were extracted with hexane/MTBE and quantitated for WL 115110 and WL 115096 using cyanazine as internal standard.	X
5.2	**Results and discussion**	The hydrolysis rate generally increased with temperature and pH. WL 115096 was the only metabolite identified. Ahrrenius plots were linear for each pH (See Figure 2).	
5.2.1	k_H	Hydrolysis rate constants varied from 12.2 $days^{-1}$ (pH 9, 70ºC) to 0.0026 $days^{-1}$ (pH 7, 25ºC). See Table 7.1.1.1.1/5 through Table 7.1.1.1.1/9 and Figure 1.	
5.2.2	DT_{50}	Hydrolysis half-lives varied from 0.1 day (pH 14, 25ºC and pH 9, 70ºC) to 267 days (pH 7, 25ºC)	
5.2.3	r^2	The correlation coefficients varied from 0.994 to 0.755 with only three of seventeen below 0.900.	
5.3	**Conclusion**	The hydrolysis of flufenoxuron is very slow ($t_{1/2}$= 267days) at 25ºC and pH 7 but increases with pH and temperature to a very rapid degradation at pH 9 and 70ºC or pH 14 and 25ºC ($t_{1/2}$= 1 –3 hours). The major product is WL 115096.	
5.3.1	Reliability	2	
5.3.2	Deficiencies	No	

Section A7.1.1.1.1
BPD Annex Point IIA, VII.7.6.2.1

Hydrolysis as a function of pH and identification of breakdown products

7.1.1.1.1. Hydrolysis (Flufenoxuron)

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/02/2005
Materials and Methods	Applicant's version is acceptable except for: 3.1.7. Further relevant properties: The entry should be read as: "*The solubility of Flufenoxuron in water is* [1.86 µg/l] *at pH 4,* [1.36 µg/l] *at pH 7 and* [3.69 µg/l] *at pH 9,* [(see Doc IIIA, section 3.5)]. 3.4.1 Test system –Table 7.1.1.1.1/3: Glassware: change to *"2.5 L and 500 mL* [screw-capped brown] *bottles.* [No specific measures taken to avoid oxygen are reported.] ". 3.4.7 Analytical method: At the end of this paragraph, add [*Other degradation products were not investigated. The second degradation compound was not detected because of its polarity.*]".
Results and discussion	Applicant's version is acceptable.
Conclusion	Applicant's version is acceptable.
Reliability	2
Acceptability	Acceptable The study is not conducted according to GLP or a specific guideline but meet general scientific principles.
Remarks	This study brings out supplementary results (higher pH values and higher temperature tested) and compared to standard OECD guideline study and should be kept in the dossier. It should be noticed that the only metabolite WL 115096 (=Reg No. 241208) detected in this study at 70°C after 24h representing 23% and 91% of the parent compound at pH 7 and pH 9, respectively, is not identified as major metabolite in the second study.
IUCLID	Type: change "*biotic*" to "*abiotic*"
	COMMENTS FROM ...
Date	Give date of comments submitted
Materials and Methods	Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion. Discuss if deviating from view of rapporteur member state
Results and discussion	Discuss if deviating from view of rapporteur member state

Section A7.1.1.1.1 **BPD Annex Point IIA, VII.7.6.2.1**	**Hydrolysis as a function of pH and identification of breakdown products** 7.1.1.1.1. Hydrolysis (Flufenoxuron)

Conclusion	Discuss if deviating from view of rapporteur member state
Reliability	Discuss if deviating from view of rapporteur member state
Acceptability	Discuss if deviating from view of rapporteur member state
Remarks	

Table 7.1.1.1.1/1: Type and composition of buffer solutions

pH	**Composition**
5	22.6 mL 0.1 M NaOH and 50 mL of 0.1 M KH Phthalate per 100 mL of solution
7	29.1 mL 0.1 M NaOH and 50 mL 0.1 M KH_2PO_4 per 100 mL of solution
9	20.8 mL 0.1 M NaOH and 50 mL 0.1 M boric acid per 100 mL of solution
12	6.0 mL 0.2 M NaOH and 25 mL 0.2 M KCL per 100 mL of solution
14	1.0 M NaOH

Table 7.1.1.1.1/2: Description of test solution

Criteria	**Details**
Purity of water	Double-distilled
Preparation of test medium	Buffer solutions were transferred to 2.5 L or 500 mL bottles and autoclaved at 120ºC and 15 psi for 15 minutes then equilibrated at the test temperature for two hours before adding test substance and mixing thoroughly.
Test concentrations (mg a.i./L)	0.002 mg/L
Temperature (°C)	25 to 80 ºC
Controls	None
Identity and concentration of co-solvent	Acetone - 1%
Replicates	Two 200 mL aliquots were taken at each sampling interval

Table 7.1.1.1.1/3: Description of test system

Glassware	2.5 L and 500 mL glass bottles
Other equipment	No details given
Method of sterilization	autoclaving at 120ºC and 15 psi for 15 minutes

Table 7.1.1.1.1/4: HPLC Conditions

System	Cecil LC 212 with Rheodyne 100µL loop injector and 10 cm x 0.5 cm 5µm Amino column using 3% ethanol in hexane at 1.3 mL/min and UV detection at 254 nm
Retention Times	WL 115110 - 4.6 min. WL 115096 - 3.5 min Cyanazine (Internal Standard) - 8.6 min

Table 7.1.1.1.1/5: Results of hydrolysis of Flufenoxuron at pH 5 (40 to 70ºC)

	Concentration of test compound (µg/mLx 10^3)							
Sampling times (*days*) Rep	**40ºC**		**50ºC**		**60ºC**		**70ºC**	
	a	**b**	**a**	**b**	**a**	**b**	**a**	**b**
0	1.85	1.60	1.53	1.52	1.45	1.55	1.70	1.62
1					1.39	1.45		
2					1.24	1.30		
3			1.48	1.70				
6	1.63	1.65			1.58	1.63		
7							1.01	1.13
12	1.44	1.46	1.29	1.59				
13							1.00	1.12
14					1.10	1.08		
18	1.53	1.24						
20							0.97	0.87
21					1.15	1.12		
25	1.30	1.28					0.72	0.81
32	1.33	1.23						
33							0.60	0.41
34					1.07	1.04		
40	1.12	1.10						
45			1.12	1.32				
47	1.20	1.04						
50							0.47	0.41
60	1.19	0.96					0.32	0.36
63			1.07	1.07				
71			1.07	0.87				
$T_{1/2}$ (days)	83.7		105		67.1		27.7	
K_h (days^{-1} x10^3)	8.28		6.60		10.3		25.0	
Correlation	0.901		0.928		0.783		0.957	

Table 7.1.1.1.1/6: Results of hydrolysis of Flufenoxuron at pH 7 (40 to 80ºC)

	Concentration of test compound (µg/mLx 10^3)									
Sampling times (*days*) Rep	**40ºC**		**50ºC**		**60ºC**		**70ºC**		**80ºC**	
	a	**b**	**a**	**b**	**a**	**b**	**a**	**b**	**a**	**b**
0	2.30	1.99	1.70	1.80	1.89	1.85	1.82	1.78	2.23	2.24
0.9									1.25	1.38
1.0			1.43	1.73			1.40	1.33		
1.4									0.88	0.91
2.0					1.58	1.55			0.72	0.72
2.1									0.57	0.66
3.0							0.63	0.56		
3.2									0.37	0.29
4.0			1.26	1.60			0.40	0.39		
4.3									0.16	0.15
5.0			1.22	1.60			0.31	0.40		
5.2									0.09	0.06
6.0	1.94	1.88			1.36	1.22	0.24	0.27		
7.0					1.20	1.17	0.20	0.21		
8.0							0.13	0.12		
9.0					0.86	0.73				
12.0	1.44	1.46		1.28						
14.0					0.48	0.48				
21.0					0.22	0.22				
25.0	1.30	1.28								
29.0			0.92	0.77						
32.0	1.33	1.23								
40.0	1.12	1.10								
45.0			0.71	0.56						
47.0	1.20	1.04								
55.0			0.45	0.56						
60.0	0.97	0.70								
63.0			0.37	0.48						
$T_{1/2}$ (days)	50.8		32.5		6.65		2.14		1.07	
K_h (days^{-1} x10^3)	13.6		21.3		104		324		648	
Correlation	0.939		0.955		0.977		0.983		0.988	

Table 7.1.1.1.1/7: Results of hydrolysis of Flufenoxuron at pH 9 (50 to 70ºC)

	Concentration of test compound (µg/mLx 10^3)					
Sampling times (*days*) Rep	**50ºC**		**60ºC**		**70ºC**	
	a	**b**	**a**	**b**	**a**	**b**
0	1.84	1.72	1.77	1.79	1.51	1.65
0.021			1.49	1.49	1.42	1.41
0.042	1.62	1.66	1.41	1.34	0.73	1.10
0.063			1.31	1.31		
0.083			1.42	1.24	0.53	0.62
0.104	1.48	1.52				
0.125			1.01	1.52	0.32	0.35
0.167	1.70	1.71	0.82	0.85	0.22	0.22
0.208			0.85	0.66	0.12	0.14
0.229	1.53	1.45				
0.271			0.65	0.69		
0.333			0.49	0.54		
0.396			0.40	0.39		
0.958	0.93	0.91				
1.04	0.81	0.69				
1.15	0.69	0.68				
1.23	0.70	0.54				
1.96		0.27				
2.10	0.30	0.24				
2.19	0.25	0.23				
$T_{1/2}$ (days)	0.81		0.19		0.06	
K_h (days^{-1} x10^3)	858		3628		12160	
Correlation	0.992		0.975		0.992	

Table 7.1.1.1.1/8 Results of hydrolysis of Flufenoxuron at 25ºC (pH 5, 7, and 9)

	Concentration of test compound (µg/mLx 10^3)					
Sampling times (*days*) Rep	**pH 5**		**pH 7**		**pH 9**	
	a	**b**	**a**	**b**	**a**	**b**
0	2.02	2.10	1.99	1.94	1.88	1.88
6	2.14	2.07	2.07	2.08	2.25	2.23
14	1.70		1.93		1.54	
18	1.99		1.76		1.58	
26	1.57		1.77		1.07	
27					1.06	0.94
33	1.36		1.85		0.75	
34					0.86	0.88
40	1.38				0.72	
46	1.65				0.71	
49					0.74	
53	1.57		1.54		0.69	0.69
68	1.52		1.64	1.65	0.65	0.68
80					0.46	0.40
104	1.38	1.17	1.62	1.50		
112	1.48	1.50				
$T_{1/2}$ (days)	206		267		36.7	
K_h (days^{-1} x10^3)	3.36		2.60		18.9	
Correlation	0.755		0.879		0.943	

Table 7.1.1.1.1/9: Results of hydrolysis of Flufenoxuron at 25ºC (pH 12 and 14)

	Concentration of test compound (µg/mLx 10^3)			
Sampling times (*days*) Rep	**pH 12**		**pH 14**	
	a	**b**	**a**	**b**
0	2.66	2.45	1.78	1.69
0.021			1.48	1.41
0.063			1.17	1.14
0.125			0.70	0.71
0.167	2.29	2.33	0.63	0.60
0.208			0.40	0.45
0.875	1.55	1.30		
1.13	1.37	1.41		
2.88	1.07	1.02		
3.06	1.01	0.96		
3.88	0.84	0.81		
4.13	0.86	0.70		
$T_{1/2}$ (days)	2.68		0.11	
K_h (days^{-1} x10^3)	259		6540	
Correlation	0.955		0.994	

Table 7.1.1.1.1/10: Specification and amount of transformation products

CAS-Number	***CAS and/or IUPAC* Chemical Name*(s)***	**Amount [%] of parent compound measured at**	
		pH 7 24 Hr at 70ºC	**pH 9 24 Hr at 70ºC**
Not available	4-[2-chloro-4-(trifluoromethyl)phenoxy]-2-fluorobenzenamine (WL 115096, CL 359882)	23%	91%

Figure 1: Hydrolysis of Flufenoxuron as a function of pH and temperature

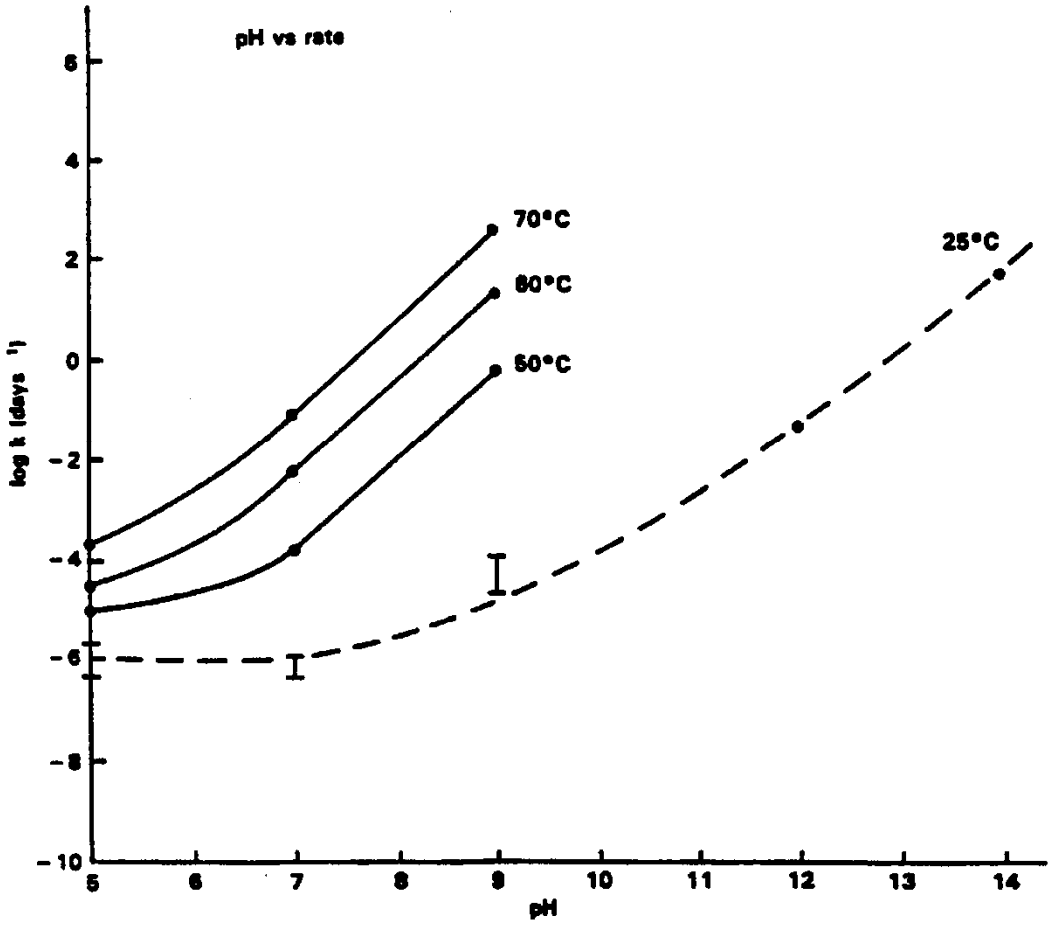
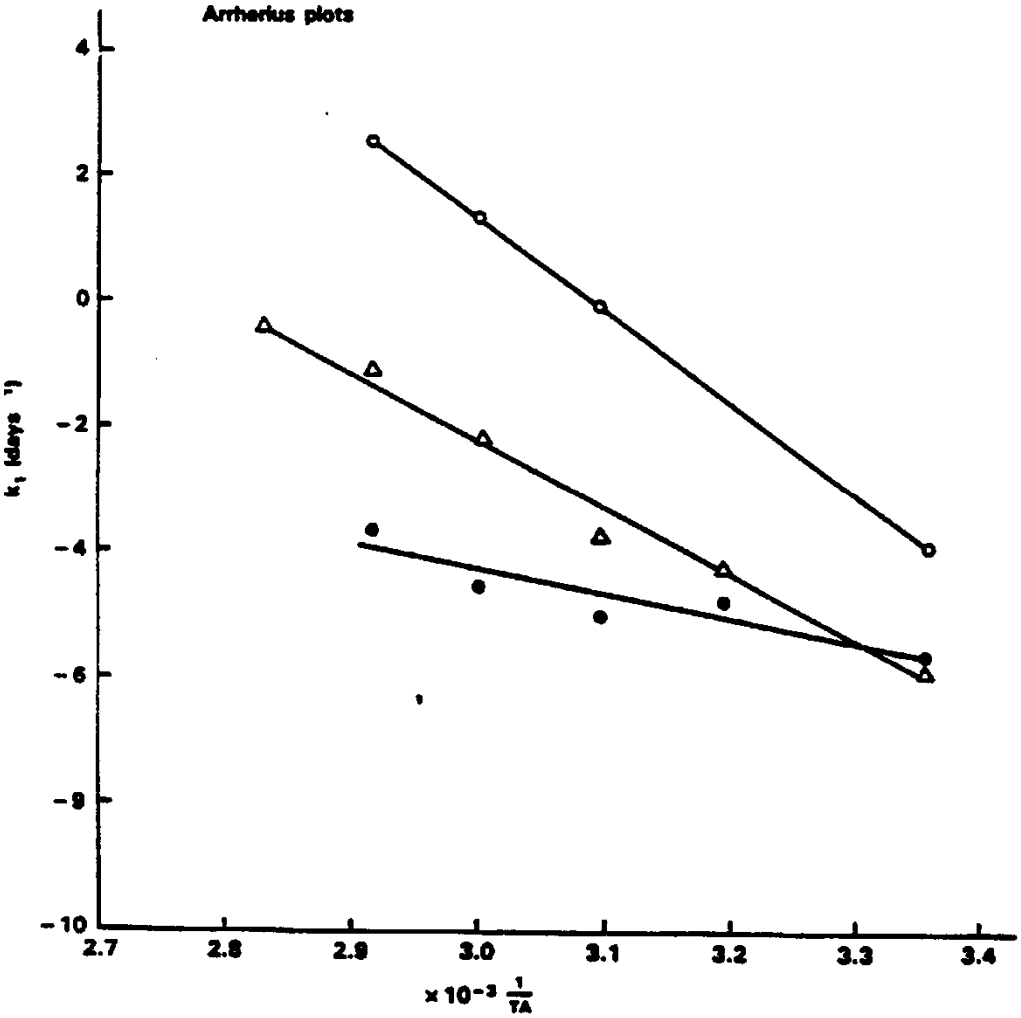


Figure 2 Ahrrenius plots for the hydrolysis of Flufenoxuron

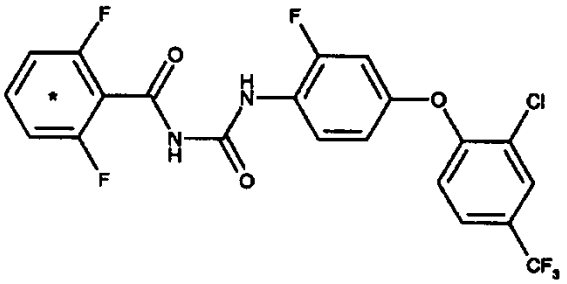
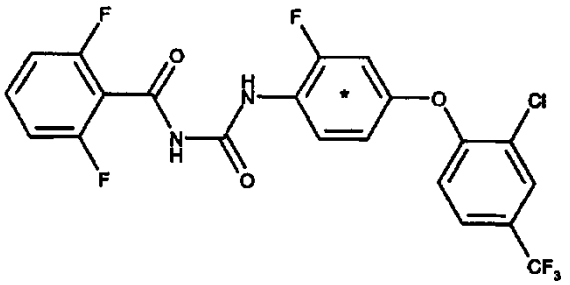


Section A7.1.1.1.1	**Hydrolysis as a function of pH and identification of breakdown products**
Annex Point IIIA7.1.1.1.1	7.1.1.1.1 Hydrolysis (Flufenoxuron)

Official use only

		1. REFERENCE
1.1	**Reference**	**2) Hassink J (2003)** Hydrolysis of BAS 307 I XXXX. unpublished XXXX
1.2	**Data protection**	Yes
1.1.1	Data owner	BASF
1.1.2	Companies with letter of access	XXXX
1.1.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I.
		2. GUIDELINES AND QUALITY ASSURANCE
2.3	**Guideline study**	Yes, Commission Directive 94/37/EG amending Council Directive 91/414/EEC, EC Method C7, EPA Subdivision N 161-1
2.4	**GLP**	Yes, (This laboratory certified by Landesamt fuer Umweltschutz und Gewerbeaufsicht, Mainz, Germany)
2.5	**Deviations**	No
		3. MATERIALS AND METHODS
3.1.	**Test material**	non-labelled and ^{14}C-labelled Flufenoxuron
3.1.1.	Lot/Batch number	XXXX
3.1.2.	Specification	Deviating from specification given in section 2 as follows
3.1.3.	Purity	XXXX
3.1.4.	Specific Activity	[XXXX

Section A7.1.1.1.1	**Hydrolysis as a function of pH and identification of breakdown products**
Annex Point IIIA7.1.1.1.1	7.1.1.1.1 Hydrolysis (Flufenoxuron)

3.1.5. Radiolabeling	 [XXXX]-Flufenoxuron  [XXXX]-Flufenoxuron	
3.1.6. Further relevant properties	The water solubility of flufenoxuron is 0.0043 ppm	X
3.2. Reference substance	Reference substances used to identify hydrolysis products are listed in Table 7.1.1.1.1/11	
3.2.1. Initial concentration of reference substance	Not Applicable	
3.3. Test solution	About 4 mg of [difluorobenzamide-ring-U-^{14}C] flufenoxuron and 2 mg of [fluoraniline-ring-U-^{14}C]-flufenoxuron were separately dissolved in acetone at about 1 mg/mL. Aliquots of 20 µL were evaporated and redissolved in 10.0 mL of acetonitrile. 240 to 670 µL of the acetonitrile solution was added to 1L of diluted (1:9 w/ distilled water) Titrisol buffer to give initial test substance concentrations of about 1, 1, 0.8, and 1.8 µg/L for pH 4, 5, 7, and 9, respectively.	
3.4. Testing procedure		
3.4.1. Test system	Sterile buffer solutions pH 4, 5, 7, 9. Sterility was checked by plate counts at each sampling time. The sterile samples (100 mL subsets) were stored in a climactic chamber at the required test temperature (25 or 50ºC).	

Section A7.1.1.1.1	**Hydrolysis as a function of pH and identification of breakdown products**
Annex Point IIIA7.1.1.1.1	7.1.1.1.1 Hydrolysis (Flufenoxuron)

3.4.2. Temperature	50ºC and 25ºC
3.4.3. pH	The initial pHs of 4, 5, 7, and 9 were verified at each sampling
3.4.4. Duration of the test	7 days for 50ºC and 30 days for 25ºC
3.4.5. Number of replicates	A single replicate was analyzed for each label, pH, and temperature at each interval.
3.4.6. Sampling	For the preliminary test at 50ºC, samples were taken at 0, 1, 2, 3, 4, and 7 (8 for pH 5) days. For the 25ºC study, samples were taken at 0, 1, 2, 7, 11, 16, 21, and 30 days.
3.4.7. Analytical methods	At each interval, samples (100 mL) were extracted three times with 60 mL of ethyl acetate (except for the pH 9, 50ºC, [difluorobenzamide-ring-U-14C] flufenoxuron samples which were assayed by LSC and HPLC directly). The combined extracts were quantitated by LSC, evaporated to dryness and redissolved in 250 µL of acetonitrile for HPLC analysis (See Table 7.1.1.1.1/12). [difluorobenzamide-ring-U-^{14}C], 25ºC, pH 9 samples with more than 5% TAR remaining in the extracted water were acidified to pH 1-2, re-extracted with ethyl acetate and analyzed by HPLC.
3.5. Preliminary test	Yes pH 4, 5, 7, and 9 at 50ºC

4. RESULTS

4.1	**Concentration and hydrolysis values**	See Table 7.1.1.1.1/13, Table 7.1.1.1.1/14, Table 7.1.1.1.1/15, Table 7.1.1.1.1/16, Table 7.1.1.1.1/17, Table 7.1.1.1.1/18, Table 7.1.1.1.1/19, Table 7.1.1.1.1/20, Table 7.1.1.1.1/21, Table 7.1.1.1.1/22
4.2	**Hydrolysis rate constant (k_h)**	See Table 7.1.1.1.1/23 and Table 7.1.1.1.1/25
4.3	**Dissipation time**	See Table 7.1.1.1.1/24 and Table 7.1.1.1.1/26
4.4	**Concentration – time data**	See Figure 3 to Figure 12
4.5	**Specification of the transformation products**	See Table 7.1.1.1.1/27

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	The hydrolysis of Fufenoxuron was investigated at pH 4, 5, 7, and 9 and at 25 and 50ºC using [difluorobenzamide-ring-U-^{14}C]-

Section A7.1.1.1.1	**Hydrolysis as a function of pH and identification of breakdown products**
Annex Point IIIA7.1.1.1.1	7.1.1.1.1 Hydrolysis (Flufenoxuron)

		flufenoxuron and [fluoraniline-ring-U-^{14}C]-flufenoxuron. The active substances, in acetonitrile solution, were added to sterile diluted Titrisol buffers at concentrations of 0.8 to 1.8 µg/L (Maximum cosolvent 0.06%). The buffers were stored at 25 or 50ºC and aliquots analyzed at intervals up to 8 days for the 50ºC samples and up to 30 days for the 25ºC samples. At each interval a 100 mL sample was extracted with ethyl acetate, which was analyzed by LSC and HPLC. Model Maker v.3 was used to analyze the data and derive rate constants.	
5.2	**Results and discussion**	No hydrolysis of Flufenoxuron was observed at pH 4, 5, or 7 at either 25 or 50ºC. Flufenoxuron was hydrolyzed at pH 9 with a half-life of about 90 days at 25ºC and about 1 day at 50ºC. The hydrolysis products detected are CL 932338, CL 245508, and CL 211558. The half-life of CL245508 at pH9 and 25ºC was about 60 days and the half-life of CL211558 at pH 9 and 50ºC was about 3 days.	
5.2.1	k_H	The hydrolysis rate constants for Flufenoxuron at 25 and 50ºC, respectively, varied from 0.001 and 0.007 at pH 5 to 0.0079 and 0.6773 at pH 9. See Table 7.1.1.1.1/23	
5.2.2	DT_{50}	The DT_{50} for flufenoxuron at 25 and 50ºC, respectively, varied from 682 and 99 days at pH 5 to 88 and 1.0 days at pH 9. See Table 7.1.1.1.1/24	
5.2.3	r^2	Correlation coefficients varied from 1.00 to 0.39. The lowest value was for the fit of the fluoroaniline label at pH 9 and 25ºC. The poor fit appears to be due to some low values, but the fitted result agrees well with the difluorobenzamide label under the same conditions.	
5.3	**Conclusion**	Flufenoxuron is hydrolytically stable at pH 4, 5, and 7, but is hydrolyzed rapidly at pH 9 with half-lives of about 90 days at 25ºC and about 1 day at 50ºC. The detected products are CL 932338, CL 245508, and CL 211558. The half-life of CL245508 at pH9 and 25ºC was about 60 days and the half-life of CL211558 at pH 9 and 50ºC was about 3 days. Hydrolysis of Flufenoxuron only occurs under alkaline conditions.	X
5.3.1	Reliability	1	X
5.3.2	Deficiencies	No	X

Section A7.1.1.1.1	**Hydrolysis as a function of pH and identification of breakdown products**
Annex Point IIIA7.1.1.1.1	7.1.1.1.1 Hydrolysis (Flufenoxuron)

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/02/2005
Materials and Methods	Applicant's version is acceptable providing the inclusion of the following ammendments: - 3.1.6 further relevant properties: According to the solubility assay (see Doc IIIA, section 3.5) the solubility of Flufenoxuron in water is 1.86 µg/L at pH 4, 1.36 µg/L at pH 7 and 3.69 µg/L at pH 9. The origin of the value of 4.3 µg/L was not found in the present study report.
Results and discussion	Applicant's version is acceptable providing the inclusion of the following ammendments: At the end of the paragraph, add [*Hydrolysis pathway for Flufenoxuron is proposed in Figure 13. At 25°C and pH 9, two major hydrolytic products (Reg.No 4064702 and Reg.No. 206925) were observed, the prefered pathway is the cleavage of the amid bound of the 2,6-difluorobenzamide (Reg.No. 102719) unit under formation of 2,6-difluorobenzoicacid (Reg.No. 206925)*.]
Conclusion	Applicant version is acceptable, with the following ammendments: - Add the range of DT_{50} values: [*Flufenoxuron is hydrolytically stable at pH 4, 5, and 7, but is hydrolyzed rapidly at pH 9 with half-lives of about 90 days* [(88-94 days)] *at 25ºC and about 1 day at 50ºC*.]. 5.3.2 deficiencies: - As one replicate is analysed (3.4.5.), the recovery rate, and the repeatability of the method cannot be evaluated according to OECD guideline 111, which defines the quality criteria of the method.
Reliability	2
Acceptability	Acceptable A statement on the validity of the study was not provided by the applicant in view of the quality criteria proposed in OECD Guideline 111 in line with the recommendations of the technical guidance document on dossier preparation (Part III-4, section A7.1.1.1.1, point 5.3). Nevertheless, results of this study is acceptable as they underline the stability of the molecule in the environmental conditions.
Remarks	No
IUCLID	Type: change "*biotic*" to "*abiotic*"

Section A7.1.1.1.1	**Hydrolysis as a function of pH and identification of breakdown products**
Annex Point IIIA7.1.1.1.1	7.1.1.1.1 Hydrolysis (Flufenoxuron)

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.1.1.1.1/11: Reference substances

Code	Name	Lot No.	Purity
XXXX	**XXXX**	**XXXX**	98.6%
XXXX	**XXXX**	**XXXX**	95%
XXXX	**XXXX**	**XXXX**	98%
XXXX	**XXXX**	**XXXX**	99%
XXXX	**XXXX**	**XXXX**	99%
XXXX	**XXXX**	**XXXX**	100%
XXXX	**XXXX**	**XXXX**	99.5%

Table 7.1.1.1.1/12: HPLC Conditions

Equipment	HPLC LC 176 Autosampler Midas, Spark Gykotek HPLC pump 580 Kontron HPLC/UV detector 535 HPLC radioactivity monitor Berthold LB 509 Data system Chromeleon V.6.11
Precolumn	ODS II, 4 x 3.0 mm
Column	Luna (Phenomenex) C18, 5µ, 250 x 4.6 mm
Eluent	A: water/formic acid (1000:1, v:v) B: acetonitrile formic acid (1000:1, v:v)
Gradient	0 min 5% B, 40 min 100% B45 min 100% B
Flow Rate	1 mL/min

Table 7.1.1.1.1/13: Hydrolysis of Flufenoxuron at pH 4 and 50ºC

DAT	difluorobenzamide label				fluoroaniline label			
	Flufenoxuron		others		Flufenoxuron		others	
	µg/kg	% TAR	µg/kg	% TAR	µg/kg	% TAR	µg/kg	% TAR
0	0.99	99.0	n.d.	n.d.	0.99	98.7	n.d.	n.d.
1	0.96	96.5	n.d.	n.d.	0.99	99.3	n.d.	n.d.
2	0.91	91.3	n.d.	n.d.	1.01	100.7	n.d.	n.d.
3	0.92	92.3	n.d.	n.d.	0.93	93.4	n.d.	n.d.
4	0.89	89.4	n.d.	n.d.	1.09	108.7	n.d.	n.d.
7	0.97	97.2	n.d.	n.d.	0.89	89.0	n.d.	n.d.

TAR = total applied radioactivity

Table 7.1.1.1.1/14: Hydrolysis of Flufenoxuron at pH 5 and 50ºC

DAT	difluorobenzamide label				fluoroaniline label			
	Flufenoxuron		others		Flufenoxuron		others	
	µg/kg	% TAR	µg/kg	% TAR	µg/kg	% TAR	µg/kg	% TAR
0	0.99	98.9	n.d.	n.d.	0.98	97.7	n.d.	n.d.
1	0.97	97.2	n.d.	n.d.	0.93	93.0	n.d.	n.d.
2	1.01	100.7	n.d.	n.d.	0.88	87.8	n.d.	n.d.
3	0.96	96.4	n.d.	n.d.	0.87	87.2	n.d.	n.d.
8	0.98	97.7	n.d.	n.d.	0.86	86.3	n.d.	n.d.

Table 7.1.1.1.1/15: Hydrolysis of Flufenoxuron at pH 7 and 50ºC

DAT	difluorobenzamide label				fluoroaniline label			
	Flufenoxuron		others		Flufenoxuron		others	
	µg/kg	% TAR	µg/kg	% TAR	µg/kg	% TAR	µg/kg	% TAR
0	0.80	99.7	n.d.	n.d.	0.77	96.3	n.d.	n.d.
1	0.81	100.9	n.d.	n.d.	0.65	81.6	n.d.	n.d.
2	0.68	84.8	n.d.	n.d.	0.79	98.8	n.d.	n.d.
3	0.68	84.7	n.d.	n.d.	0.70	87.7	n.d.	n.d.
4	0.68	85.6	n.d.	n.d.	0.73	91.5	n.d.	n.d.
7	0.68	84.8	n.d.	n.d.	0.67	84.2	n.d.	n.d.

Table 7.1.1.1.1/16: Hydrolysis of difluorobenzamide-labeled Flufenoxuron at pH 9 and 50ºC

DAT	Flufenoxuron		2,6-difluoro-benzoic acid CL 245508 Reg.No. 206925		2,6-difluoro-benzamide CL 211558 Reg.No. 102719		Others (not identified)	
	µg/kg	% TAR	µg/kg[1]	% TAR	µg/kg[1]	% TAR	µg/kg[1]	% TAR
0	1.80	100.0	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
1	1.51	83.9	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
2	n.d.	n.d.	1.21	67.4	0.47	26.3	n.d.	n.d.
3	n.d.	n.d.	1.29	71.4	0.69	38.5	n.d.	n.d.
4	n.d.	n.d.	1.32	73.1	0.52	29.0	0.12	6.7
7	n.d.	n.d.	1.75	97.2	0.27	15.2	n.d.	n.d.

[1] Parent equivalents

Table 7.1.1.1.1/17: Hydrolysis of fluoroaniline-labeled Flufenoxuron at pH 9 and 50ºC

DAT	Flufenoxuron		"urea" CL 932338 Reg.No. 4064702		Others	
	µg/kg	% TAR	µg/kg[1]	% TAR	µg/kg	% TAR
0	1.80	100.0	n.d.	n.d.	n.d.	n.d.
1	1.28	71.0	0.35	19.6	n.d.	n.d.
2	0.72	40.0	0.84	46.6	n.d.	n.d.
3	0.45	25.0	1.11	61.8	n.d.	n.d.
4	n.d.	n.d.	1.54	85.6	n.d.	n.d.
7[2]	--	--	--	--	--	--

[1] Parent equivalents

[2] Evaluation of HPLC chromatogram not possible

Table 7.1.1.1.1/18: Hydrolysis of Flufenoxuron at pH 4 and 25ºC

DAT	difluorobenzamide label				fluoroaniline label			
	Flufenoxuron		others		Flufenoxuron		others	
	µg/kg	% TAR	µg/kg	% TAR	µg/kg	% TAR	µg/kg	% TAR
0	0.99	98.7	n.d.	n.d.	0.97	96.8	n.d.	n.d.
1	0.83	83.0	n.d.	n.d.	0.92	92.1	n.d.	n.d.
2	0.86	85.9	n.d.	n.d.	0.93	92.5	n.d.	n.d.
7	0.97	97.3	n.d.	n.d.	0.93	93.4	n.d.	n.d.
11	0.99	98.7	n.d.	n.d.	1.02	101.6	n.d.	n.d.
16	0.94	93.8	n.d.	n.d.	0.86	85.9	n.d.	n.d.
21	0.86	86.0	n.d.	n.d.	0.82	81.7	n.d.	n.d.
30	0.89	89.2	n.d.	n.d.	0.93	92.7	n.d.	n.d.

Table 7.1.1.1.1/19: Hydrolysis of Flufenoxuron at pH 5 and 25ºC

DAT	difluorobenzamide label				fluoroaniline label			
	Flufenoxuron		others		Flufenoxuron		others	
	µg/kg	% TAR	µg/kg	% TAR	µg/kg	% TAR	µg/kg	% TAR
0	0.99	99.3	n.d.	n.d.	0.97	97.2	n.d.	n.d.
1	0.91	90.8	n.d.	n.d.	0.98	98.4	n.d.	n.d.
2	0.94	94.2	n.d.	n.d.	0.90	90.2	n.d.	n.d.
7	0.94	93.7	n.d.	n.d.	0.88	87.7	n.d.	n.d.
11	0.89	89.0	n.d.	n.d.	0.91	90.8	n.d.	n.d.
16	0.89	89.4	n.d.	n.d.	0.93	92.6	n.d.	n.d.
21	0.84	84.2	n.d.	n.d.	0.98	98.3	n.d.	n.d.
30	0.89	89.3	n.d.	n.d.	0.98	97.9	n.d.	n.d.

Table 7.1.1.1.1/20: Hydrolysis of Flufenoxuron at pH 7 and 25ºC

DAT	difluorobenzamide label				fluoroaniline label			
	Flufenoxuron		others		Flufenoxuron		others	
	µg/kg	% TAR	µg/kg	% TAR	µg/kg	% TAR	µg/kg	% TAR
0	0.80	99.4	n.d.	n.d.	0.77	96.3	n.d.	n.d.
1	0.80	99.9	0.01	1.0	0.80	99.5	n.d.	n.d.
2	0.80	100.1	n.d.	n.d.	0.69	85.9	n.d.	n.d.
7	0.78	97.5	n.d.	n.d.	0.75	93.2	n.d.	n.d.
11	0.77	96.1	n.d.	n.d.	0.74	92.6	n.d.	n.d.
16	0.79	98.2	n.d.	n.d.	0.64	80.5	n.d.	n.d.
21	0.76	95.5	n.d.	n.d.	0.74	92.1	n.d.	n.d.
30	0.75	93.7	n.d.	n.d.	0.67	83.6	n.d.	n.d.

Table 7.1.1.1.1/21: Hydrolysis of difluorobenzamide-labeled Flufenoxuron at pH 9 and 25ºC

DAT	Flufenoxuron		2,6-difluoro-benzoic acid CL 245508 Reg.No. 206925		2,6-difluoro-benzamide CL 211558 Reg.No. 102719		others		sum	
	µg/kg	% TAR	µg/kg[1]	% TAR	µg/kg[1]	% TAR	µg/kg[1]	% TAR	µg/kg	% TAR
0	1.78	98.7	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	1.78	98.7
1	1.56	86.9	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	1.56	86.9
2	1.51	83.8	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	1.51	83.8
7	1.56	86.4	0.12	6.6	n.d.	n.d.	n.d.	n.d.	1.68	93.0
11	1.40	77.5	0.14	7.6	n.d.	n.d.	n.d.	n.d.	1.54	85.1
16	1.41	78.2	0.16	9.1	n.d.	n.d.	n.d.	n.d.	1.57	87.3
21	1.39	77.3	0.17	9.4	n.d.	n.d.	n.d.	n.d.	1.56	86.7
30	1.36	75.3	0.28	15.6	n.d.	n.d.	n.d.	n.d.	1.64	90.9

[1] Parent equivalents

Table 7.1.1.1.1/22: Hydrolysis of fluoroaniline-labeled Flufenoxuron at pH 9 and 25ºC

Sample	**Flufenoxuron**		**"urea" CL 932338 Reg.No. 4064702**		**others**		**sum**	
	µg/kg	% TAR	µg/kg[1]	% TAR	µg/kg[1]	% TAR	µg/kg	% TAR
0	1.76	97.6	n.d.	n.d.	n.d.	n.d.	1.76	97.6
1 day	1.68	93.5	n.d.	n.d.	n.d.	n.d.	1.68	93.5
2 days	1.52	84.4	0.10	5.4	n.d.	n.d.	1.62	89.8
7 days	1.58	87.9	0.03	1.4	n.d.	n.d.	1.61	89.3
11 days	1.48	82.3	0.04	2.2	n.d.	n.d.	1.52	84.5
16 days	1.89	105.1	n.d.	n.d.	n.d.	n.d.	1.89	105.1
21 days	1.47	81.5	0.08	4.5	n.d.	n.d.	1.55	86.0
30 days	1.14	63.5	0.38	21.3	n.d.	n.d.	1.52	84.8

[1] Parent equivalents

Table 7.1.1.1.1/23: Hydrolysis Rate Constants for Flufenoxuron

	25ºC		50ºC	
pH	k_h ($days^{-1}$)	r^2	k_h ($days^{-1}$)	r^2
4[1]	0.0016	0.99	0.0105	0.99
5[1]	0.0010	1.00	0.007	0.99
7[1]	0.0030	0.99	0.0192	0.99
9 (fluoroaniline label)	0.0079	0.39	0.4642	0.94
9 (difluorobenzamide label)	0.0073	0.75	0.6773	0.82

[1] Average of both labels

Table 7.1.1.1.1/24: Hydrolysis DT_{50} and DT_{90} (days) for Flufenoxuron

pH	25ºC		50ºC	
	DT_{50}	DT_{90}	DT_{50}	DT_{90}
4[1]	434	1442	66	219
5[1]	682	2266	99	329
7[1]	234	778	36	120
9 (fluoroaniline label)	88.0	292.2	1.5	5.0
9 (difluorobenzamide label)	94.4	313.7	1.0	3.4

[1] Average of both labels

Table 7.1.1.1.1/25: Hydrolysis rate constants for Metabolites at pH 9

Metabolite	25ºC		50ºC	
	k_h ($days^{-1}$)	Std. Dev.	k_h ($days^{-1}$)	Std. Dev.
Reg. No. 206935	0.0117	0.0209	--[1]	--[1]
Reg. No. 102719	--[1]	--[1]	0.2300	0.99

[1] No evaluation possible

Table 7.1.1.1.1/26: Hydrolysis DT_{50}/DT_{90} (days) for Metabolites at pH 9

Metabolite	25ºC		50ºC	
	DT_{50}	DT_{90}	DT_{50}	DT_{90}
Reg. No. 206935	59.3	196.9	--[1]	--[1]
Reg. No. 102719	--[1]	--[1]	3.0	10.0

[1] No evaluation possible

Table 7.1.1.1.1/27: Specification and amount of transformation products

Code-Number	**Chemical Name**	**Amount [%] of parent compound measured at**		
		pH 4-7 25 or 50ºC	**pH 9 25ºC**	**pH 9 50ºC**
Reg. No. 4064702 CL932338	N-{4-[2-chloro-4-(trifluoromethyl)phenoxy]-2-fluorophenyl}urea	Not detected	21.3% at 30 days	85.6% at 4 days
Reg. No. 206925 CL245508 CAS No. 385-00-2	2,6-difluorobenzoic acid	Not detected	15.6% at 30 days	97.2% at 7 days
Reg. No. 102719 CL211558 CAS No. 18063-03-1	2,6-difluorobenzamide	Not detected	Not detected	38.5% at 3 days

Figure 3 Hydrolysis of Flufenoxuron at pH 4 and 25ºC

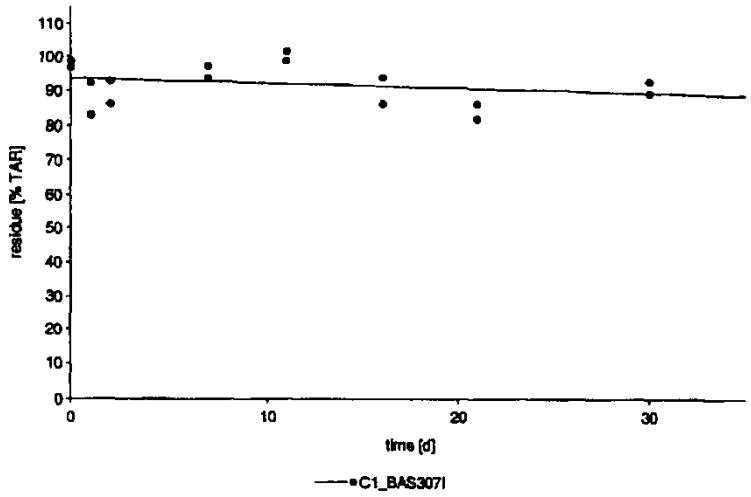


Figure 4 Hydrolysis of Flufenoxuron at pH 4 and 50ºC

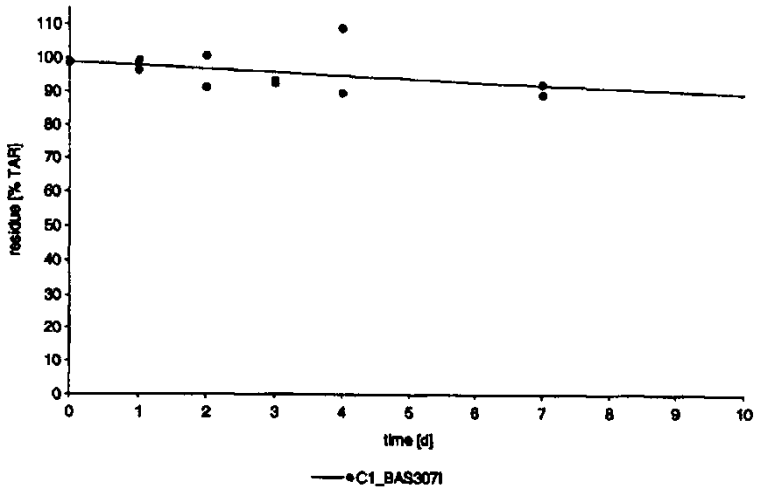


Figure 5 Hydrolysis of Flufenoxuron at pH 5 and 25ºC

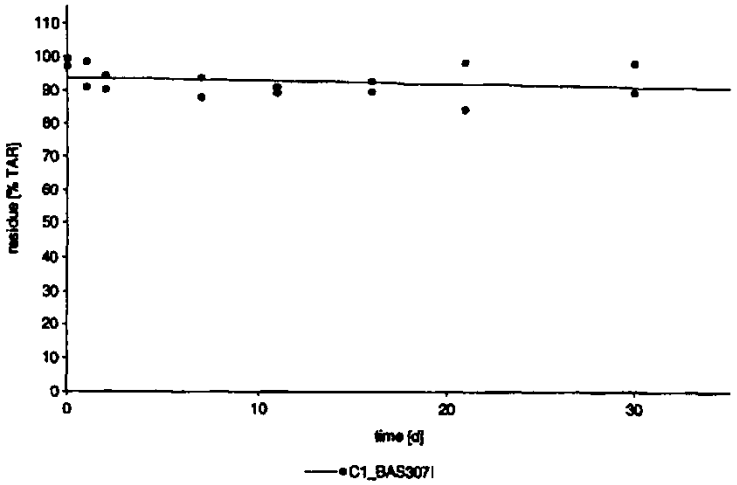


Figure 6 Hydrolysis of Flufenoxuron at pH 5 and 50ºC

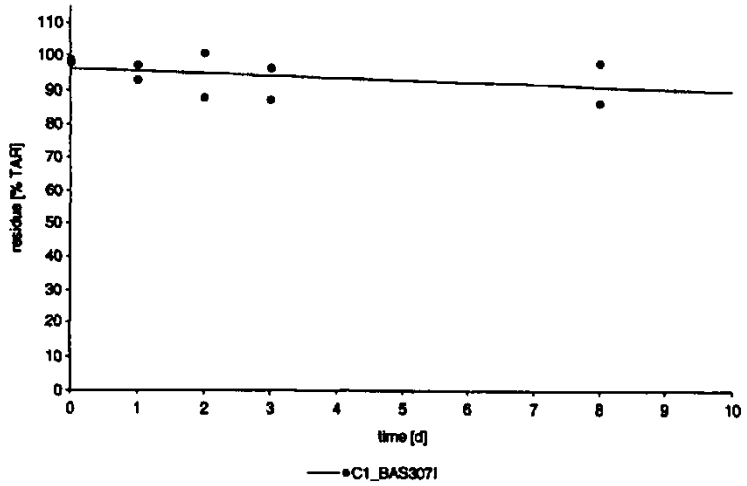


Figure 7 Hydrolysis of Flufenoxuron at pH 7 and 25ºC

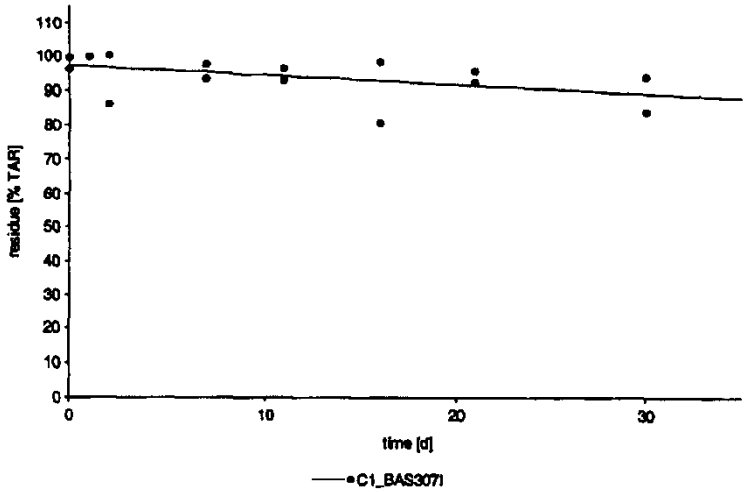


Figure 8 Hydrolysis of Flufenoxuron at pH 7 and 50ºC

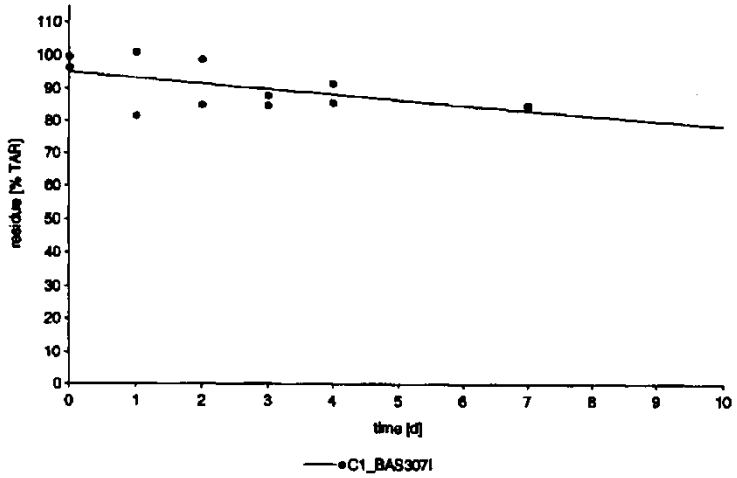


Figure 9 Hydrolysis of fluoroaniline-labeled Flufenoxuron at pH 9 and 25ºC

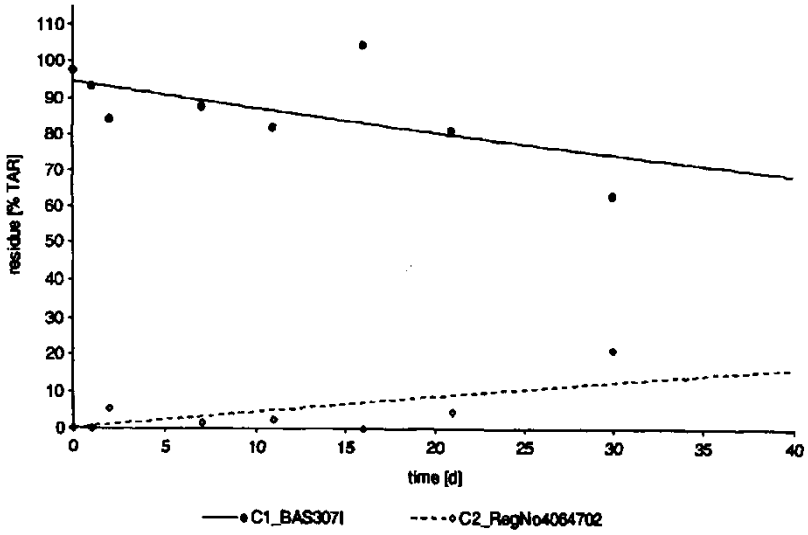


Figure 10 Hydrolysis of difluorobenzamide-labeled Flufenoxuron at pH 9 and 25ºC

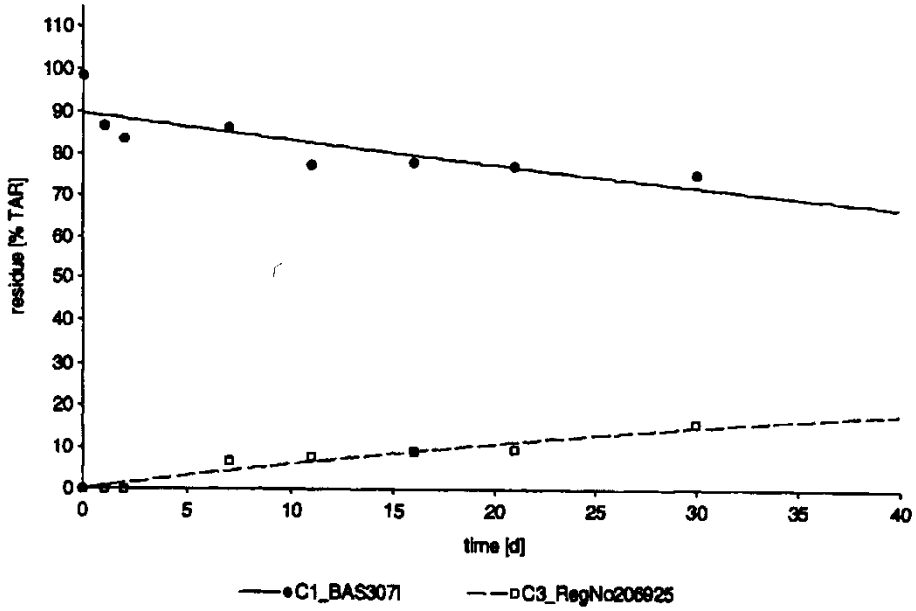


Figure 11 Hydrolysis of fluoroaniline-labeled Flufenoxuron at pH 9 and 50ºC

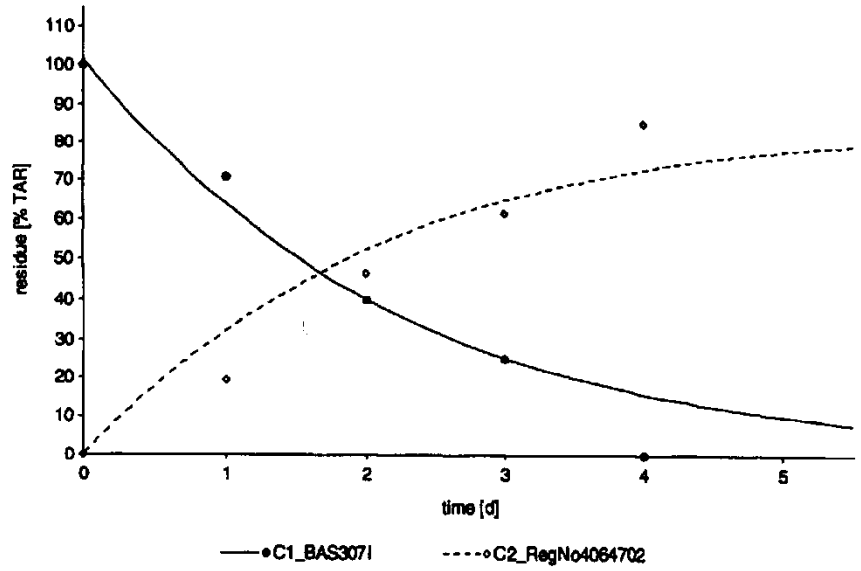


Figure 12 Hydrolysis of difluorobenzamide-labeled Flufenoxuron at pH 9 and 50ºC

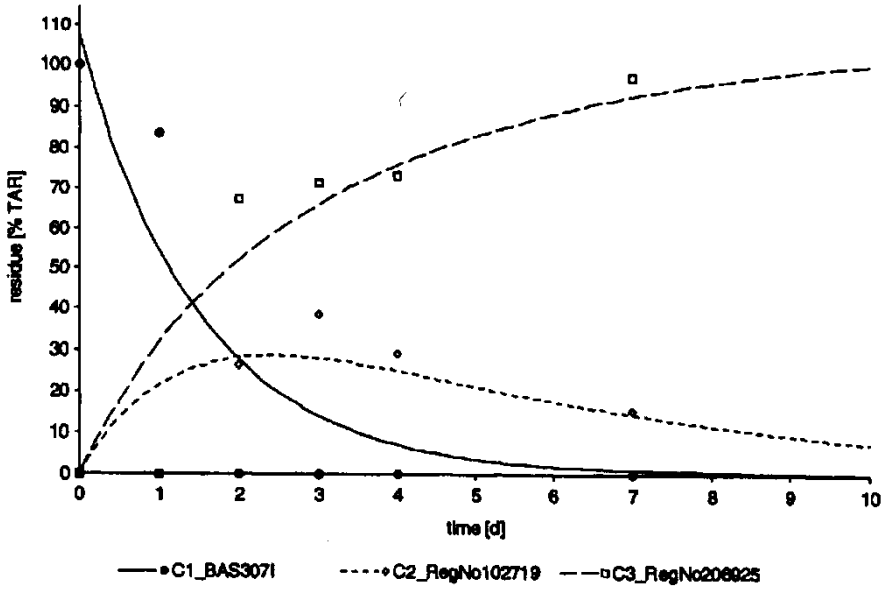
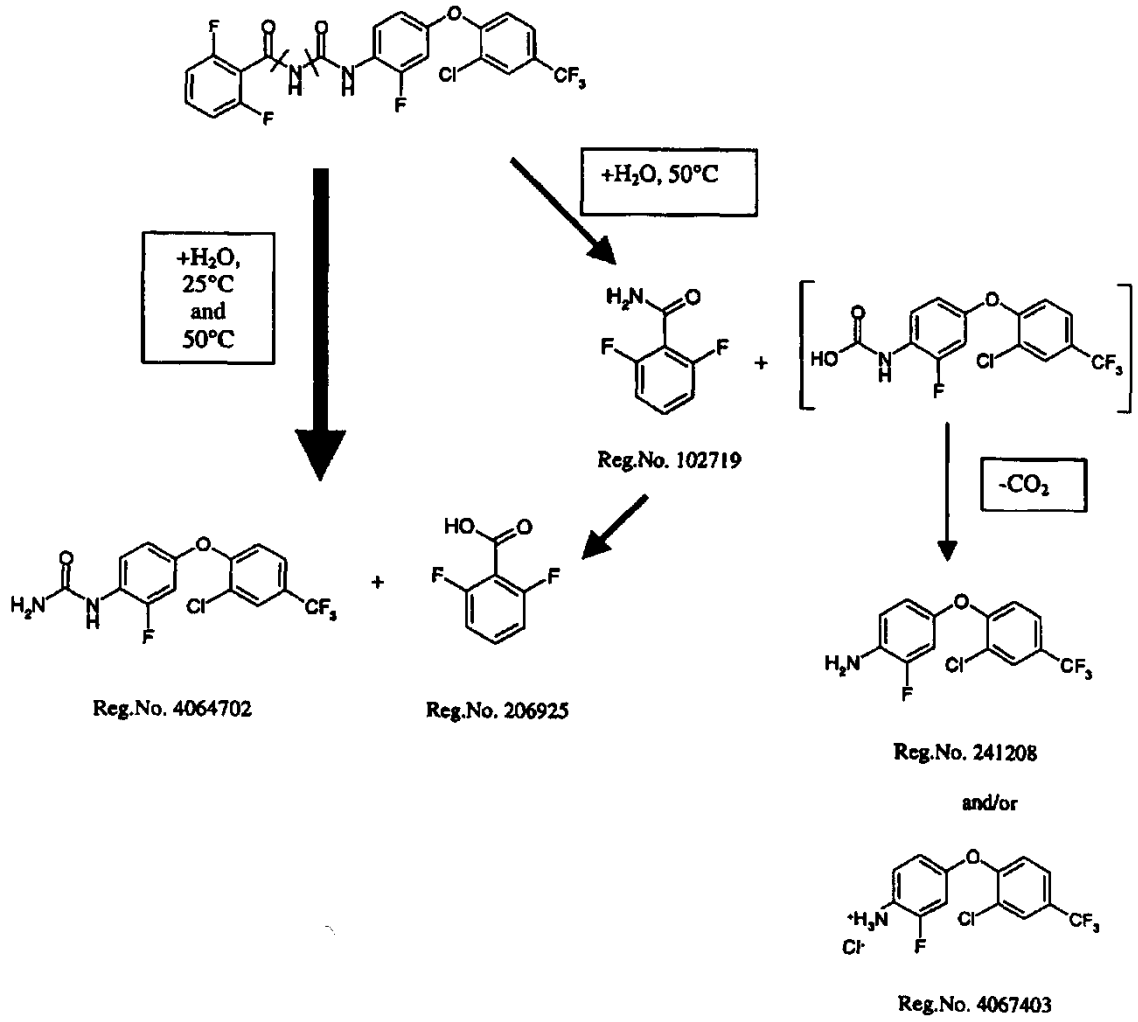


Figure 13 Hydrolysis pathway for Flufenoxuron



Section A7.1.1.1.2 **BPD Annex Point IIA, VII.7.6.2.2**	**Phototransformation in water including identity of transformation products** 7.1.1.1.2 Phototransformation (Flufenoxuron)
0. Justification of the choice of the key study	**RMS Comment (01/02/05):** Four studies are submitted for this endpoint and are summarized in Document IIIA: 1) Camilleri P, Langner E J (1987); 2) Langner E J (1991) see page 36 3) Burgener A (2001) see page 46 4) Hassink J (2003) see page 58 5) and 6) Mamouni A and van der Gaauw A (2001a and 2001b) see page 74 The notifier did not provide any justification for the choice of a key study but has identified in the IUCLID document Reference 4 (Hassink J, (2003)) with a "Risk assessment" flag. RMS agrees with this identification and recommend this study as "key study" for the following reasons: - two sites of radiolabelling were considered instead of one site in the other studies; - DT_{50} for metabolites are available; Actinometer data were included.

Section A7.1.1.1.2	**Phototransformation in water including identity of transformation products**
BPD Annex Point IIA, VII.7.6.2.2	7.1.1.1.2 Phototransformation (Flufenoxuron)

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**1) Camilleri P, Langner E J (1987)** Photodecomposition of aqueous solutions of Flufenoxuron by sunlight. XXXX unpublished XXXX **2) Langner E J (1991)** Corrigendum to SBGR.87.150: Photodecomposition of aqueous solutions of Flufenoxuron by sunlight. XXXXunpublished XXXX	
1.2.	**Data protection**	No	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	No data protection claimed	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	No, methods used comparable to SETAC Procedures for Assessing the Environmental Fate and Ecotoxicology of Pesticides, March 1995 and OECD/GD(97)21: Guidance Document on Direct Phototransformation of Chemicals in Water	
2.2.	**GLP**	No, GLP was not compulsory at the time the study was performed	
2.3.	**Deviations**	Not applicable	
		3. MATERIALS AND METHODS	
3.1.	**Test material**	^{14}C-labelled Flufenoxuron	
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	See below	
3.1.3.	Purity	99% radiopure	
3.1.4.	Radiolabeling	^{14}C in the carbonyl of the 2,6-difluorobenzoyl moiety.	
3.1.5.	Specific Activity	53.22 µCi/mg (1.97 MBq/mg)	
3.1.6.	UV/VIS absorption spectra and absorbance	Flufenoxuron showed a bathochromic shift in acetonitrile solutions. Spectra in acetonitrile and 5% acetonitrile in water are shown in Figure 7.1.1.1.2/ 14.	

Section A7.1.1.1.2 **BPD Annex Point IIA, VII.7.6.2.2**	**Phototransformation in water including identity of transformation products** 7.1.1.1.2 Phototransformation (Flufenoxuron)

	value		
3.1.7.	Further relevant properties	The solubility in water for Flufenoxuron at pH 4 is 1.9 ppb. Flufenoxuron is hydrolytically stable under neutral and acidic conditions.	X
3.2.	**Reference substances**	No reference chemicals for photometric and wavelength accuracy were used. Reference substances for identification of photolysis products are given in Table 7.1.1.1.2/ 28.	
3.3.	**Test solution**	See Table 7.1.1.1.2/ 29.	X
3.4.	**Testing procedure**		
3.4.1.	Test system	Quartz glass vessels containing sterilized buffer were purged with nitrogen and placed on the roof a building at the XXXX.	
3.4.2.	Properties of light source	The test was conducted under natural sunlight at XXXX (Longitude 0°44' east Latitude 51°20'). The daylight intensity, on a bright day and an overcast one, was measured at 12:00 Noon in 25 nm steps through the range 238-688 nm using a photomultiplier/ monochromator assembly. See Figure 7.1.1.1.2/ 14.	X
3.4.3.	Determination of irradiance	The daylight intensity was measured using a Blackray Ultraviolet intensity meter (Type J-221, Ultraviolet Products, Inc.) and a Photomultiplier-Monochromator assembly.	
3.4.4.	Temperature	The test was conducted outdoors at ambient temperature, which varied between 25 and 5ºC, with the higher temperatures occurring during the period of greater irradiation (noon to 2 pm) and lows in the morning.	
3.4.5.	pH	7 - $NaOH/KH_2PO_4$	
3.4.6.	Duration of the test	31 days	
3.4.7.	Number of replicates	A single aliquot of test solution was taken and analyzed at each sampling interval.	
3.4.8.	Sampling	Samples were taken from the quartz tubes at 0, 3, 7, 10, 14, 21, and 31 days.	
3.4.9.	Analytical methods	One mL aliquots of the photolysis solutions were also counted directly immediately after preparation to determine the initial dose. At each interval, a 50 mL aliquot of photolysis solution was removed from a quartz tube and reduced to dryness by rotary evaporation and redissolved in 1.0 mL of reference solution (2.5 pp each, flufenoxuron and its degradates in 50/50 acetonitrile/water). An aliquot (0.9 ml) was injected in a preparative HPLC (See Table 7.1.1.1.2/ 30). Fractions were collected and analyzed by LSC.	
3.5.	**Transformation products**	Transformation products tested: Yes	
3.5.1.	Method of	Metabolites were identified and quantitated by HPLC with reference	

Section A7.1.1.1.2	**Phototransformation in water including identity of transformation products**
BPD Annex Point IIA, VII.7.6.2.2	7.1.1.1.2 Phototransformation (Flufenoxuron)

	analysis for transformation products	standards described in Table 7.1.1.1.2/ 30.
		4. RESULTS
4.1.	**Screening test**	Not applicable
4.2.	**Actinometer data**	No actinometer was used
4.3.	**Controls**	The recovery of radiolabeled Flufenoxuron from the dark controls was greater than 95% throughout the study. The initial concentration was determined to be 0.0022 ppm or 4.5x 10^{-9} mole/L
4.4.	**Photolysis data**	
4.4.1.	Concentration values	See Table 7.1.1.1.2/ 32 and Figure 7.1.1.1.2/ 16.
4.4.2.	Mass balance	See Table 7.1.1.1.2/ 32.
4.4.3.	k^c_p	Not determined
4.4.4.	Kinetic order	Pseudo first order
4.4.5.	k^c_p / k^a_p	Not determined
4.4.6.	Reaction quantum yield (ϕ^c_E)	Not determined
4.4.7.	k_{pE}	Not determined
4.4.8.	Half-life ($t_{1/2}$)	The $t_{1/2E}$ of flufenoxuron at Latitude 51° 20' under June sunlight is approximated by the $t_{1/2}$ under the conditions of the study.
4.5.	**Specification of the transformation products**	See Table *7.1.1.1.2/ 33*.
		5. APPLICANT'S SUMMARY AND CONCLUSION
5.1.	**Materials and methods**	The photolysis of flufenoxuron was investigated under natural Spring-Summer sunlight and outdoor conditions at XXXX (Longitude 0°44' east Latitude 51°20'). Solutions of 2.2 ppb flufenoxuron, radiolabeled on the 2,6-difluorobenzoyl moiety, in pH 7 buffer were irradiated in quartz glass vessels. Aliquots were taken at intervals and either reduced by rotary evaporation and redissolved in water/acetonitrile or diluted with acetonitrile and analyzed by HPLC and fractions were analyzed by LSC.
5.2.	**Results and discussion**	The photolytic half-life of flufenoxuron under natural sunlight was 11 days in quartz vessels. The major photolysis product was 2,6 difluorobenzamide. The loss of 2,6-difluorobenzamide from Flufenoxuron would leave 4-[2-chloro-4-(trifluoromethyl)phenoxy]-2-fluorobenzenamine. This was not detected, as it had no radiolabel.

Section A7.1.1.1.2 **BPD Annex Point IIA, VII.7.6.2.2**	**Phototransformation in water including identity of transformation products** 7.1.1.1.2 Phototransformation (Flufenoxuron)	
5.2.1. k^c_p	Not determined	
5.2.2. K_{pE}	Not determined	
5.2.3. ϕ^c_E	Not determined	
5.2.4. $t_{1/2E}$	The $t_{1/2E}$ of Flufenoxuron at Latitude 51º 20' under June sunlight is approximated by the $t_{1/2}$ under the conditions of the study.	X
5.3. Conclusion	Although the study was not conducted under GLP, the study is scientifically valid and the results are given as supplementary information.	
5.3.1. Reliability	2	
5.3.2. Deficiencies	No	

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/02/2005
Materials and Methods	Applicant's version is acceptable providing the inclusion of the following amendments: - 3.1.6 further relevant properties: According to the solubility assay (see Doc IIIA, section 3.5) the solubility of Flufenoxuron in water is 1.86 µg/L at pH 4, 1.36 µg/L at pH 7 and 3.69 µg/L at pH 9. The origin of the value of 1.9 µg/L was not found in the present study report. The study report indicates the value of ca. 4 x 10^{-3} mg/L, based on the report SBGR.86.187 from Camilleri and Langner. - 3.3 Test solution, table 7.1.1.1.2/2, the entry in the field "Identity and concentration of co-solvent should be replaced with: [*Flufenoxuron: 0.05% acetonitrile* *WL115096: 10% acetonitrile* *2,5-difluorobenzamide: none*] -3.4.2 Properties of light source: the link to "*Figure 7.1.1.1.2/1*" should be change to "*Figure 7.1.1.1.2/2*". -3.4.9 Analytical methods: the link to "*Table 7.1.1.1.2/3*" should be change to " *Table 7.1.1.1.2/4*". -3.5.1 Methods of analysis for transformation products: the link to "*Table 7.1.1.1.2/3*" should be change to " *Table 7.1.1.1.2/1*".

Section A7.1.1.1.2	**Phototransformation in water including identity of transformation products**
BPD Annex Point IIA, VII.7.6.2.2	7.1.1.1.2 Phototransformation (Flufenoxuron)

Results and discussion	Applicant's version is acceptable providing the inclusion of the following amendments: - 4.1 Screening test: change "*not applicable*" to "*not performed*". - 4.4.8 Half-life: Add the sentence " *The photolytic half-life of flufenoxuron under natural sunlight was 11 days in quartz vessels."* at the end of the paragraph. - 4.5 specification of the transformation products: table 7.1.1.1.2/5 and table 7.1.1.1.2/6: in table 7.1.1.1.2/5, results obtained with metabolite WL129676 are given for 2,5 difluorobenzamide. WL129676 is identified in table 7.1.1.1.2/6 as 1-(2,6-difluorobenzoyl)-3-(4-hydroxyphenyl)urea, which is the correct identity.
Conclusion	Applicant's version is acceptable providing the inclusion of the following amendments: 5.2 results and discussion: add at the end of the paragraph: " *This moiety was tested separately as WL115096 under the same illumination condition as Flufenoxuron. It was found to be less stable to sunlight than flufenoxuron itself with a photochemical half-life of about 2.5 hours."* *5.2.4* $t_{1/2E}$: according to the TNG on data requirements, section 2, point 7.1.1.1.2 (p 44) "The results submitted should correspond to the light intensities and spectral distribution from northern to southern European regions, for example, in 40 and 65 degrees (proposed average 50 degrees) northern latitude during spring and autumn. This may be presented e.g. by extrapolation." 5.3.2 deficiencies: Add the following statements: *[- Only the carbonyl of the 2,6-difluorobenzoiyl moiety was radiolabelled. The second moiety was tested separately as WL115096 under the same illumination condition as Flufenoxuron.* *- The purity of the reference material for metabolites is not specified."* *- A variation of temperature of 20°C was observed during photolysis study (outdoor) instead of the maximum recommended 10° variation (laboratory).* *- 1 replicate was analysed instead of 2-3 replicates.]*
Reliability	3
Acceptability	acceptable Other studies are available. Despite the deficiencies, the results of this study may be kept into document III to reinforce the validated information.
Remarks	The degradation pathway could have been enclosed in doc IIIA.

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*

Section A7.1.1.1.2 Phototransformation in water including identity of transformation products

BPD Annex Point IIA, VII.7.6.2.2

7.1.1.1.2 Phototransformation (Flufenoxuron)

Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.1.1.1.2/ 28 Reference substances

Compound	**Batch, purity, source**
Flufenoxuron, WL 115110	XXXX, 99% pure
2,6-difluorobenzamide	Aldrich Chemical Co.
2-fluoroaniline	Aldrich Chemical Co.
1,2-benzenediol	Aldrich Chemical Co.
WL 129676 1-(2,6-difluorobenzoyl)-3-(4-hydroxyphenyl)urea	Unspecified
WL 115096 4-[2-chloro-4-(trifluoromethyl)phenoxy]-2-fluorobenzenamine	Organic Chemistry Division
2 chloro-4-trifluoromethyl phenol	Organic Chemistry Division

Table 7.1.1.1.2/ 29 Description of test solution and controls

Criteria	**Details**
Purity of water	Doubly distilled
Preparation of test chemical solution	A 5µL aliquot of test substance in acetonitrile was added to 1L of sterile (autoclaved 120ºC, 15 psi, 15 min) buffer (29.1 mL 0.1M NaOH and 50 mL 0.1 M KH2PO4/100 mL), mixed well and 150 mL transferred to each of 5 quartz tubes and one was wrapped with foil as control.
Test concentrations (mg a.s./L)	0.0022 ppm (by specific activity, radiopurity and initial LSC)
Controls	One tube was wrapped with foil as control.
Identity and concentration of co-solvent	Acetonitrile - 0.05% for Flufenoxuron - 10% for WL 115096

Table 7.1.1.1.2/ 30 Description of test system

Criteria	**Details**
Laboratory equipment	The photolysis was conducted in 150 mL quartz tubes. A Varian Cary 210 spectrometer was used to record UV-vis spectra.
Test apparatus	Blackray Ultraviolet intensity meter (Type J-221, Ultraviolet Products, Inc.) and a Photomultiplier-Monochromator assembly.
Properties of natural sunlight:	
Latitude	Latitude 51°20'
Hours of daylight	12 or more
Time of year	June
Light intensity	See Figure 7.1.1.1.2/15
Solar irradiance (L_λ)	Not Determined

Table 7.1.1.1.2/ 31 HPLC System and Conditions

Equipment		
Instrument:	Cecil LC212	
Injector	Rheodyne - 5 mL loop	
Column	25 cm x 20 mm id 5µm S5P-phenyl	
Eluent	42.5% Acetonitrile 57.5% (v/v) 0.1% H_3PO_4	
Flow Rate	8.4 mL/min	
Wavelength	210 nm	
Retention Times	WL 115110 Impurity in WL 115110 standard WL 129676 2,6-difluorobenzamide WL115096 2-chloro-4-trifluoromethylphenol 2-fluoroaniline 1,2-benzenediol	42.5 min 16 min 13.2 Min 9.6 min 19.4 min 13.5 min 10.7 min 9.4 min
Fraction Collector	LKB Multirac 2111; 0.4 min/fraction	

Table 7.1.1.1.2/ 32 Natural sunlight photolysis of Flufenoxuron in quartz vessels

Interval	% of applied radioactivity					
	Flufenoxuron	2,5 difluorobenzamide	2,6-difluorobenzamide	Polar components	Impurity[1]	Mass Balance
0 d	96	n.d.	n.d.	n.d.	4	100
3 d	84.6	2.1	6.3	2.1	4.9	100
7 d	68.4	3.3	18.8	4.5	5	100
10 d	51	4.4	30.7	9.9	4	100
14 d	37.9	5.4	37.7	11.7	4.3	97
21 d	29.4	5.5	46.3	15.7	3.1	100
31 d	23.7	3.2	42.1	29.2	1.8	100

[1] impurity originally present in test substance

Table 7.1.1.1.2/ 33 Specification and amount of transformation products

Code Number	Chemical Name	Amount [%] of parent compound
CL211558 (Reg No 102719)	2,6-difluorobenzamide	46.3% at 21 days
WL 129676	1-(2,6-difluorobenzoyl)-3-(4-hydroxyphenyl)urea	5.5% at 21 days

Figure 7.1.1.1.2/ 14: UV-Vis Absorption Spectrum of Flufenoxuron

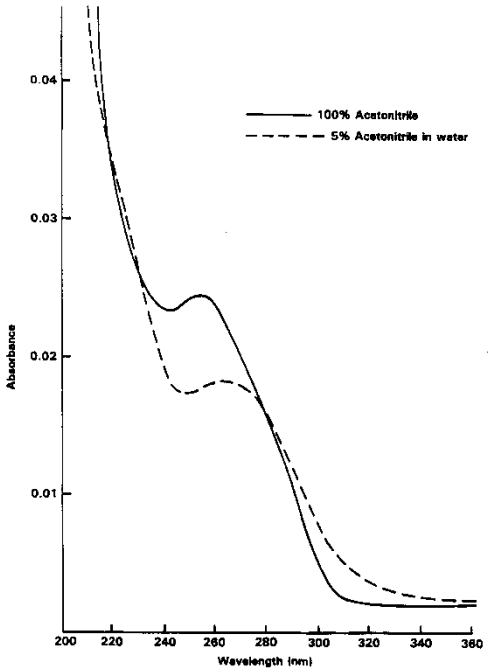

0.04
0.03
0.02
0.01
Absorbance
100% Acetonitrile
5% Acetonitrile in water
200
220
240
260
280
300
320
340
360
Wavelength (nm)

Figure 7.1.1.1.2/15 Sunlight Spectrum under various conditions

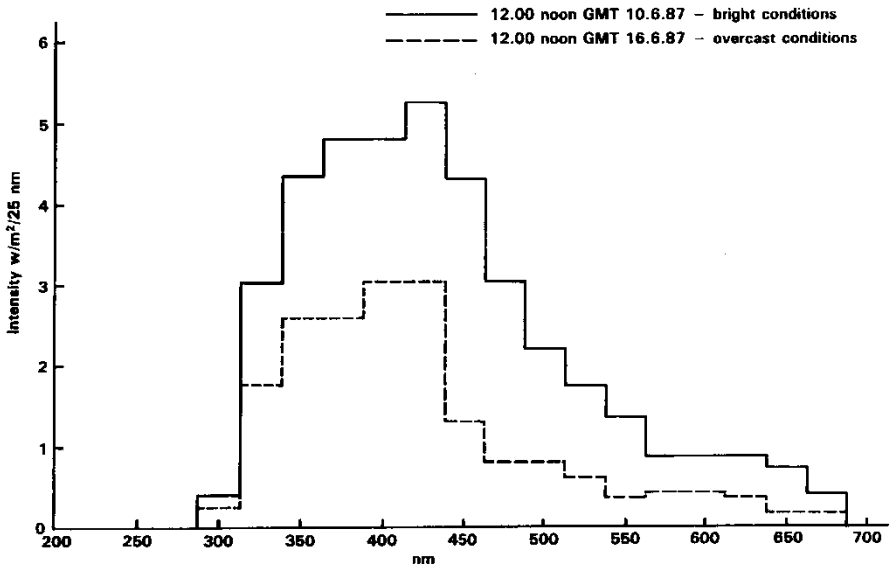
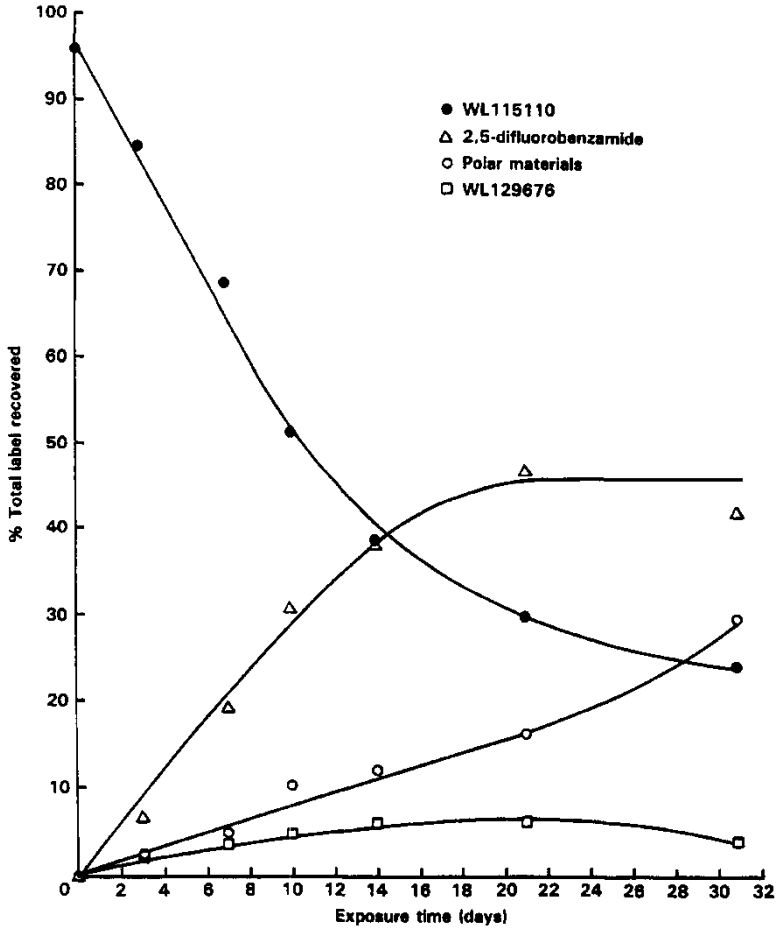


Figure 7.1.1.1.2/ 16 Photodegradation of Flufenoxuron in Quartz Vessels



Section A7.1.1.1.2 **Phototransformation in water including identity of transformation products**

BPD Annex Point IIA, VII.7.6.2.2 7.1.1.1.2 Quantum yield

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**3) Burgener A (2001)** 14C-Flufenoxuron (BAS 307 I): Quantum yield of direct phototransformation in water. RCC Ltd XXXX unpublished XXXX	
1.2.	**Data protection**	Yes	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing [a.s./b.p.] for the purpose of its entry into Annex I.	

Section A7.1.1.1.2	**Phototransformation in water including identity of transformation products**
BPD Annex Point IIA, VII.7.6.2.2	7.1.1.1.2 Quantum yield

		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Yes, SETAC Procedures for Assessing the Environmental Fate and Ecotoxicology of Pesticides, March 1995 and, OECD/GD(97)21: Guidance Document on Direct Phototransformation of Chemicals in Water	
2.2.	**GLP**	Yes, Swiss Agency for the environment, forests, and landscape; Berne, Switzerland	
2.3.	**Deviations**	No	
		3. MATERIALS AND METHODS	
3.1.	**Test material**	As given in section 2	
3.1.1.	Lot/Batch number	XXXX	X
3.1.2.	Specification	As given in section 2	
3.1.3.	Purity	97% radiopure, >99% chemically pure	
3.1.4.	Radiolabeling	[XXXX] -flufenoxuron	
3.1.5.	Specific Activity	1.2 MBq/mg	
3.1.6.	UV/VIS absorption spectra and absorbance value	See Figure 7.1.1.1.2/18.	
3.1.7.	Further relevant properties	The solubility of Flufenoxuron in water is 186 µg/l at pH 4, 136 µg/l at pH 7 and 369 µg/l at pH 9. Flufenoxuron is hydrolytically stable under neutral and acidic conditions.	X
3.2.	**Reference substances**	A uranyl oxalate actinometer was used to determine quantum yield. Unlabeled Flufenoxuron, Lot No. XXXX, 99.3% pure and 3,6-difluorobenzamide, Lot No. XXXX, 100% pure were used as reference standards for TLC.	X
3.3.	**Test solution**	An aliquot of 9.81 mg of ^{14}C-Flufenoxuron weighed into a 10 mL volumetric flask and brought to volume with acetone. The purity was checked by TLC before the start of the main experiment and LSC determined the initial concentration to be 0.9027 µg/µL. A 10 µL aliquot of the stock solution was evaporated and redissolved in 36 mL of acetonitrile. A 10 mL aliquot of this dilution was brought to 1.0 L with sterilized, pH 5 buffer (See Table 7.1.1.1.2/34). The concentration of the test solution was determined to be 1.975 µg/L by LSC and 22 mL aliquots were transferred to each test vessel.	X
3.4.	**Testing procedure**		
3.4.1.	Test system	Sterilized glass vessels with quartz glass coverings containing 22 ml test solution in sterilized buffer (pH 5) were irradiated in a thermostated	

Section A7.1.1.1.2	**Phototransformation in water including identity of transformation products**
BPD Annex Point IIA, VII.7.6.2.2	7.1.1.1.2 Quantum yield

		block using a xenon lamp. Each vessel had an air inlet and an air outlet. The incoming air was sterilized. No trapping system for volatiles was set up. In addition to the irradiated samples, aliquots were incubated under identical conditions in the dark using the same vessels as for the irradiated solution.	
3.4.2.	Properties of light source	A xenon lamp with UV filters was used. See Table 7.1.1.1.2/35	
3.4.3.	Determination of irradiance	A uranyl oxalate actinometer was used. See *Table 7.1.1.1.2/34*.	
3.4.4.	Temperature	20 ± 3ºC	
3.4.5.	pH	pH 5	
3.4.6.	Duration of the test	15 days continuous irradiation for test substance, 20 minutes for actinometer.	
3.4.7.	Number of replicates	Duplicate vessels were taken for analysis at each time interval If not analyzed immediately; samples were stored up to two days in the dark at 4ºC (dark control samples at 20ºC showed no degradation in 15 days).	
3.4.8.	Sampling	Samples were taken after 0, 0.166, 0.54, 1.0, 3.1, 4.8, 9.0, and 15.0 days of irradiation	
3.4.9.	Analytical methods	Samples (0-15 days) were concentrated using a rotary evaporator and analyzed by radio-TLC. The mean recovery values after evaporation were determined to be in the range of 79 % TAR to 98 % TAR. The amount of volatiles was not determined.	
3.5.	**Transformation products**	Transformation products tested: Yes	
3.5.1.	Method of analysis for transformation products	Transformation products were identified by radio-TLC with reference standards.	X
		4. RESULTS	
4.1.	**Screening test**	Not performed	
4.2.	**Actinometer data**	See Table 7.1.1.1.2/ 37.	
4.3.	**Controls**	The initial concentration in the dark controls was the same as the irradiated samples, 1.975 µg/L. After 4.8 and 15 days in the dark, the flufenoxuron was determined to be 92 and 95% of the original concentration, respectively.	
4.4.	**Photolysis data**		

Section A7.1.1.1.2	**Phototransformation in water including identity of transformation products**
BPD Annex Point IIA, VII.7.6.2.2	7.1.1.1.2 Quantum yield

4.4.1.	Concentration values	See Table 7.1.1.1.2/ 37 and Figure 7.1.1.1.2/20 and Figure 7.1.1.1.2/21.	
4.4.2.	Mass balance	Total recovery of radiolabeled test substance ranged from 72.4% to 110.2%.	
4.4.3.	k^c_p	The photolysis rate constant for flufenoxuron under the conditions of the test was 0.14645 $days^{-1}$.	X
4.4.4.	DT_{50}	The DT_{50} for flufenoxuron under the conditions of the test was 4.7 days. Analysis including only data from replicates with >80% recovery gave a DT_{50} of 4.57 days. See Figure 7.1.1.1.2/20 and Figure 7.1.1.1.2/21.	
4.4.5.	Kinetic order	Pseudo first order	
4.4.6.	ΔM	Using the DT_{50}, the number of reacted molecules of flufenoxuron was determined to be 3.561×10^{11} in 0.0477 days	
4.4.7.	P_{abs}	The number of photons absorbed by the test substance was determined to be 7.479×10^{16} in 0.0477 days	
4.4.8.	Reaction quantum yield (ϕ^c)	4.76×10^{-6}	
4.4.9.	Half-life ($t_{1/2E}$)	For the estimation of the environmental half-lives of Flufenoxuron, the program GCSOLAR from EPA (US EPA, GCSOLAR User's manual, Version 1.20, July 1999) was used. Direct photolysis at the surface of pure water was assumed at 30°N, 40°N and 50°N of latitude according to the geographical location of North America. In addition, the latitude of 50°N covers Central Europe. The obtained half-lives are given in Table 7.1.1.1.2/ 38. The absorption spectra of a river water sample were used to calculate the environmental half-life in natural water down to 30 cm depth. The calculations were performed for latitude 40°N, i.e. mid USA and southern Europe respectively (Table 7.1.1.1.2/ 39)	
4.5.	**Specification of the transformation products**	See Table 7.1.1.1.2/40	X

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1.	**Materials and methods**	The phototransformation of flufenoxuron in water was studied according to SETAC and OECD guidelines. Sterilized glass vessels with quartz glass coverings containing 22 ml of 1.975 µg/L flufenoxuron in sterilized buffer (pH 5) were irradiated at 20 ± 3ºC using a xenon lamp. Each vessel had an air inlet and an air outlet. The incoming air was sterilized. No trapping system for volatiles was set up. In addition to the irradiated samples, aliquots were incubated under identical conditions in the dark using the same vessels as for the irradiated solution. A uranyl oxalate

Section A7.1.1.1.2	**Phototransformation in water including identity of transformation products**
BPD Annex Point IIA, VII.7.6.2.2	7.1.1.1.2 Quantum yield

		actinometer was used to determine the total incident radiation, which was used to determine the quantum yield for flufenoxuron. The quantum yield was used to calculate the half-life under various environmental conditions.	
5.2.	**Results and discussion**	Flufenoxuron was photodegraded rapidly under the conditions of the test with a DT_{50} of 4.7 days. The only metabolite identified, 2,6-difluorobenzamide reached a maximum of 70% of the dose at 9 days and then declined	
5.2.1.	k^c_p	0.14645 $days^{-1}$.	X
5.2.2.	K_{pE}	Not determined	
5.2.3.	ϕ^c	4.76 x 10^{-6}	
5.2.4.	$t_{1/2E}$	Calculated environmental half-lives in surface waters varied from 11.6 to 72.4 days, depending on latitude and season. The variation of half-life with depth in natural waters is given in Table 7.1.1.1.2/ 39.	
5.3.	**Conclusion**	The study shows that flufenoxuron is photodegraded rapidly in surface water with a half-life of about 12 days in Summer. The main metabolite is 2,6-diflourobenzamide.	
5.3.1.	Reliability	1	X
5.3.2.	Deficiencies	No	X

Section A7.1.1.1.2 **BPD Annex Point IIA, VII.7.6.2.2**	**Phototransformation in water including identity of transformation products** 7.1.1.1.2 Quantum yield

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/02/2005
Materials and Methods	Applicant's version is acceptable providing the inclusion of the following amendments: - 3.1.1. Lot/batch number: add to text "S1101 [*(^{14}C-radiolabeled substance)*] - 3.1.7. Further relevant properties: The entry should be read as: "*The solubility of Flufenoxuron in water is* [1.86 µg/l] *at pH 4,* [1.36 µg/l] *at pH 7 and* [3.69 µg/l] *at pH 9,* [(see Doc IIIA, section 3.5)]. [During the study, the test substance was tested at its limit of solubility (2 ppb), a lower concentration would not have been possible due to the low specific activity of the substance.]. *Flufenoxuron is hydrolytically stable under neutral and acidic conditions.* [The photolytic behaviour of flufenoxuron was investigated in buffered solution of pH 5]. - 3.2 Reference substance: Replace *3,6-difluorobenzamide* with ***2**,6-difluorobenzamide*. - 3.3 test solution: change the following sentence to " […] *The purity was checked by TLC before the start of the main experiment*. [10 µL of this stock solution were transferred to a 10 mL flask and made up to volume with acetonitrile] *and LSC determined the* [diluted stock solution] concentration to be 0.9027 µg/µL. - 3.4.2 Properties of the light source: in Table 7.1.1.1.2/8, In the field "*Emission wavelength spectrum*" change link to Figure 7.1.1.1.2/13 to link to Figure 7.1.1.1.2/4. In the field "*Light Intensity*", the correct value, as stated in the study report, is [19.7 W/m²]. - 3.4.8 Sampling: add at the end of the paragraph: [Due to the stability of the substance to hydrolysis at pH 5, dark control samples were taken on day 4.8 and 15.] - 3.4.9 Change the second sentence: *"The mean recovery values after evaporation were determined to be in the range of* [72.4% to 110% of the initial applied radioactivity]*"*. - 3.5.1 Method of analysis for transformation products: add [*see section 3.2*]
Results and discussion	Applicant's version is acceptable providing the inclusion of the following amendments: 4.2 Actinometer data: Change link to *Table 7.1.1.1.2/10* to *Table 7.1.1.1.2/9.* 4.4.3 $k^{c}_{p:}$ it should be specified that this data is obtained excluding from calculation samples with <80% recovery. 4.5 Specification of the transformation products: change the entry to: [Beside the parent item up to three radioactive fractions were observed. The main metabolite was identified as 2,6-difluorobenzamide (see *Table 7.1.1.1.2/40*). None of the other photodegradates exceeded 10% of the radioactivity applied].

Conclusion	Applicant's version is acceptable providing the inclusion of the following amendments: 5.2.1 $k^{c}_{p:}$ it should be specified that this data is obtained excluding from calculation samples with <80% recovery. 5.3.2 deficiencies: Add the following statements: - Only the 2,6-difluorobenzoiyl moiety was radiolabelled. - The amount of volatiles was not determined. - Samples with < 80% recovery were excluded from calculation] - A statement on the validity of the study was not provided in view of the validity criteria proposed in draft OECD Guideline 314, in line with the recommendations of the technical guidance document on dossier preparation (Part III-4, section A7.1.1.1.2, point 5.3).
Reliability	3 See deficiencies above
Acceptability	Acceptable Other studies are available. Despite the deficiencies, the results of this study may be kept into document III to reinforce the validated information.
Remarks	

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.1.1.1.2/34: Description of test solution and controls

Criteria	**Details**
Purity of water	Distilled, sterile water

Preparation of buffer	1.64 g of sodium acetate was dissolved in 900 mL of water; the pH was adjusted to 5.0 with 0.1 M acetic acid, and diluted to 2L with water. The buffer was sterilized by autoclaving 30 min at 121 ºC and subsequent manipulations done in a sterile box.
Test concentrations (µg a.s./L)	1.975 µg/L
Temperature (°C)	20 ± 3ºC
Preparation of actinometer solution	1.004 g of uranyl nitrate [$UO_2(NO_3)_2 \cdot 6H_2O$; MW 502.1] and 1.260 g oxalic acid [$C_2H_2O_4 \cdot 2H_2O$; MW 126.0] were each dissolved in 100 mL of water and mixed in a ratio of 1:1 (v/v) before use. Initial concentrations were 0.02 M uranyl ions and 0.1 M oxalic acid.
Controls	A dark control sample was prepared as for the irradiated samples.
Identity and concentration of co-solvent	Acetonitrile – 1%

Table 7.1.1.1.2/35: Description of test system

Criteria	**Details**
Laboratory equipment	The solutions were irradiated in thermostated quartz covered glass vessels of 4.0 cm^2 area in a SUNTEST CPS, original Hanau apparatus. The light intensity was determined with a LI-1800 spectrophotometer.
Test apparatus	A uranyl oxalate actinometer was used
Properties of artificial light source:	
Nature of light source	Xenon Lamp
Emission wavelength spectrum	See Figure 7.1.1.1.2/26
Light intensity	40-76 mW/cm^3
Filters	Cut-off for wavelengths <290 nm

Table 7.1.1.1.2/36: Actinometer data

Uranyl ion and oxalic acid concentrations	Initial concentrations were 0.02 M uranyl ions and 0.1 M oxalic acid. After 20 minutes of irradiation, the number of molecules of oxalic acid reacted was determined by titration to be 6.560×10^{19}.
ϕ^a	0.56
P_{inc}	The total number of incident photons was 1.696×10^{20} photons in 1200 seconds

Table 7.1.1.1.2/ 37: Radio-TLC analysis after photolysis of difluorobenzamide-labeled Flufenoxuron in buffer solution pH 5 [%TAR]

DAT	Flufenoxuron	2,6-difluorobenzamide CL 211558 (Reg. No. 102719)	Sum	Flufenoxuron (dark control)
0	96.3	n.d.	96.3	96.3
0.166	94.2	n.d.	94.2	n.a.
0.54	93.6	6.8	100.4	n.a.
1.0	85.7	8.3	94.0	n.a.
3.1	56.5	26.5	83.0	n.a.
4.8	49.6	40.7	90.3	92.4
9.0	21.9	70.0	91.9	n.a.
15.0 *	67.3*	27.5*	94.8*	94.9

* result considered and outlier and not used in calculations; n.d. = not detected, n.a. = not analyzed

Table 7.1.1.1.2/ 38: Theoretical photolytic half-life (days) of Flufenoxuron in surface water

Latitude	Spring	Summer	Fall	Winter
30°N	12.9	11.6	18.2	24.5
40°N	13.9	11.7	23.4	37.6
50°N*	15.6	12.1	34.4	72.4

Table 7.1.1.1.2/ 39: Theoretical photolytic half-life (days) of Flufenoxuron in river water

Depth	Spring	Summer	Fall	Winter
0 cm	13.9	11.7	23.4	37.6
10 cm	14.6	12.3	24.7	39.6
20 cm	15.4	13.0	26.0	41.6
30 cm	16.2	13.6	27.3	43.6

Table 7.1.1.1.2/40: Specification and amount of transformation products

Code-Number	CAS and/or IUPAC Chemical Name*(s)*	Amount [%] of parent compound
Reg. No. 102719 CAS No. 18063-03-1	2,6-difluorobenzamide	Max. 70% at 9 days

Figure 7.1.1.1.2/17: Energy distribution of xenon lamp

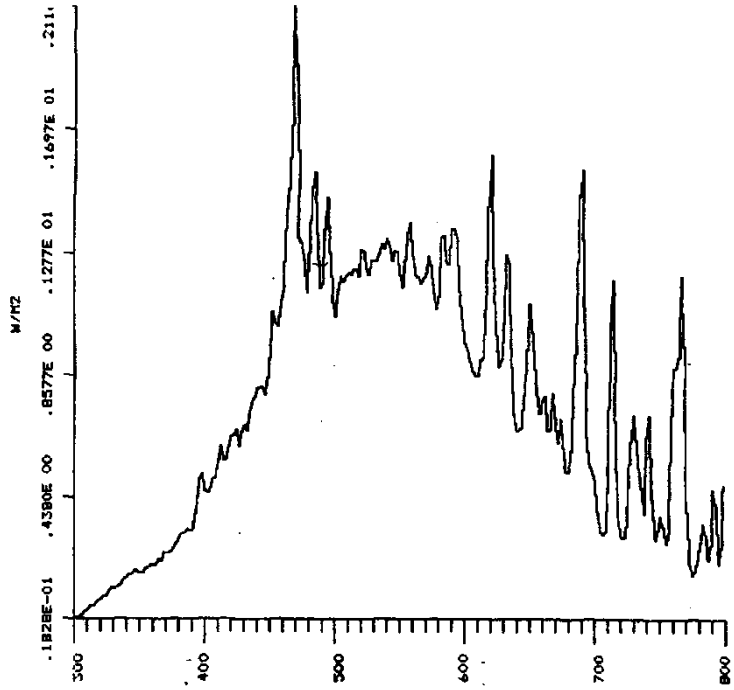


Figure 7.1.1.1.2/18: Absorption spectrum of Flufenoxuron

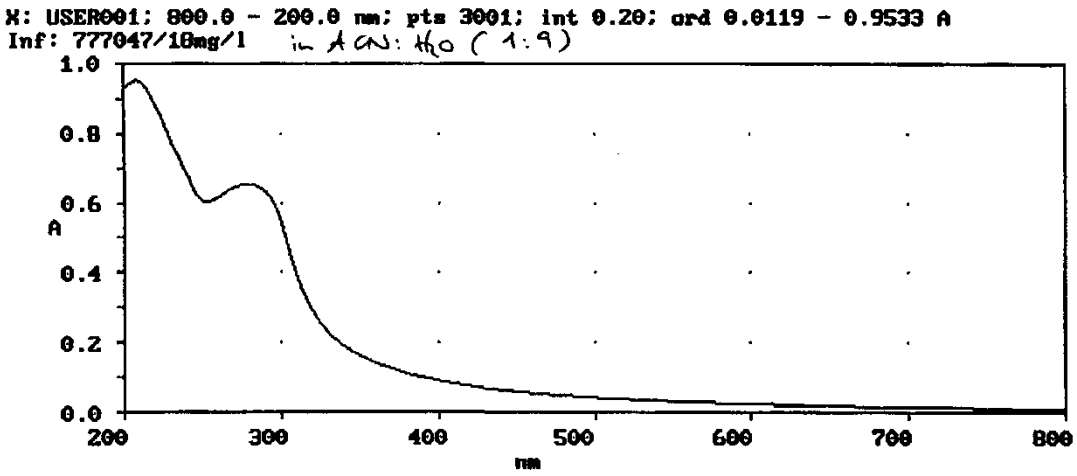


Figure 7.1.1.1.2/19: Absorption spectrum of actinometer

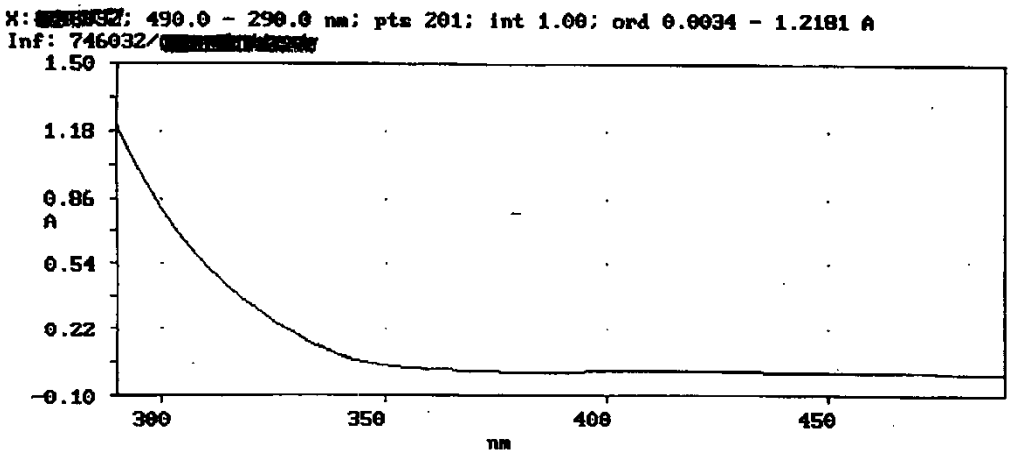


Figure 7.1.1.1.2/20: Photolysis of Flufenoxuron and fitted curve – all data

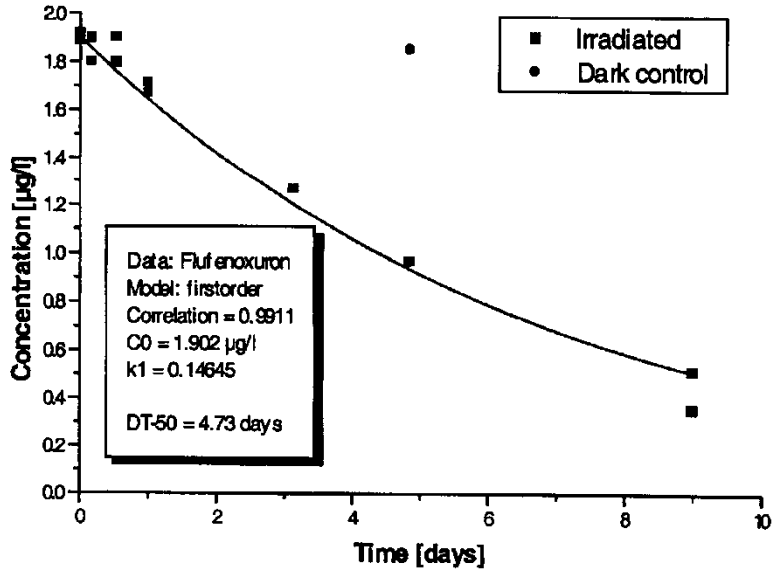
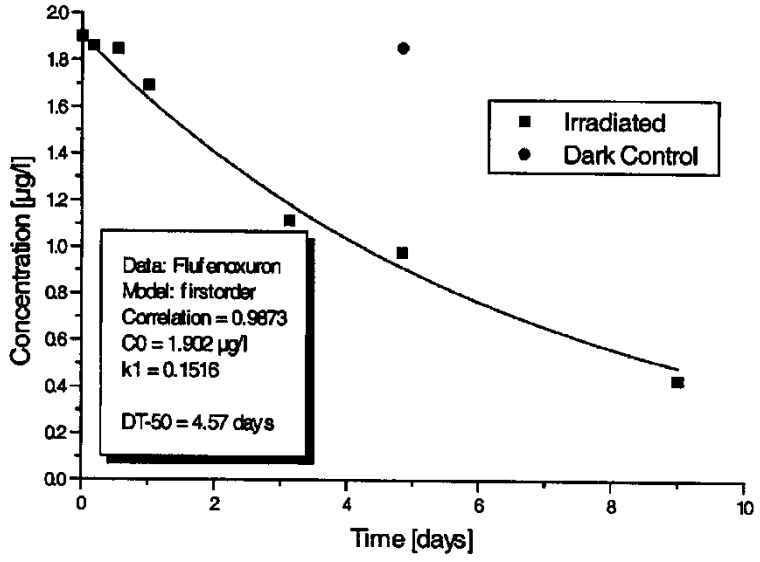


Figure 7.1.1.1.2/21: Photolysis of Flufenoxuron and fitted curve – only replicates >80%



Section A7.1.1.1.2 Phototransformation in water including identity of transformation products

BPD Annex Point IIA, VII.7.6.2.2

7.1.1.1.2 Aqueous photolysis (Flufenoxuron)

Official use only

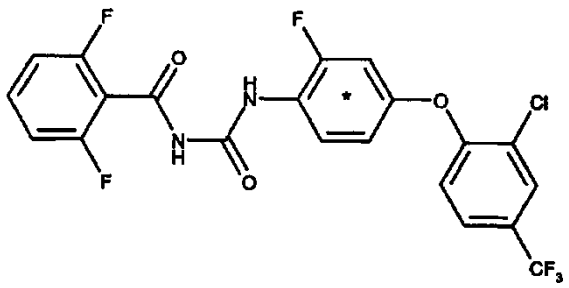
1. REFERENCE

1.1.	**Reference**	**4) Hassink J (2003)** Aqueous Photolysis of BAS 307 I. XXXX. unpublished XXXX
1.2.	**Data protection**	Yes
1.2.1.	Data owner	BASF
1.2.2.	Companies with letter of access	XXXX
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I.

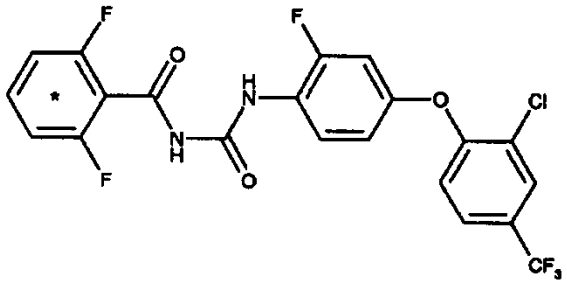
2. GUIDELINES AND QUALITY ASSURANCE

2.1.	**Guideline study**	Yes, Commission Directive 94/37/EEC amending Council Directive 91/414/EEC
2.2.	**GLP**	Yes, (Laboratory certified by Landesamt fuer Umweltschutz und Gewerbeaufsicht, Mainz, Germany)
2.3.	**Deviations**	No

3. MATERIALS AND METHODS

3.1.	**Test material**	^{14}C-labelled Flufenoxuron
3.1.1.	Lot/Batch number	XXXX
3.1.2.	Specification	Deviating from specification given in section 2 as follows
3.1.3.	Purity	[fluoroaniline-ring-U-^{14}C]-flufenoxuron - >99% radiopure [difluorobenzamide-ring-U-^{14}C]-flufenoxuron - >99% radiopure
3.1.4.	Radiolabeling	 [fluoroaniline-ring-U-^{14}C]-flufenoxuron

Section A7.1.1.1.2	**Phototransformation in water including identity of transformation products**
BPD Annex Point IIA, VII.7.6.2.2	7.1.1.1.2 Aqueous photholysis (Flufenoxuron)



[difluorobenzamide-ring-U-^{14}C]-flufenoxuron

3.1.5.	Specific Activity	[fluoroaniline-ring-U-^{14}C]-flufenoxuron - 3.89 MBq/mg [difluorobenzamide-ring-U-^{14}C]-flufenoxuron - 7.61 MBq/mg	
3.1.6.	UV/VIS absorption spectra and absorbance value	Absorbance of the test substance and actinometer are given in Table 7.1.1.1.2/41.	
3.1.7.	Further relevant properties	The solubility of Flufenoxuron in water is 186 µg/l at pH 4, 136 µg/l at pH 7 and 369 µg/l at pH 9. Flufenoxuron is hydrolytically stable under neutral and acidic conditions.	X
3.2.	**Reference substances**	A pyridine actinometer was used, and reference standards used to identify photolysis products are given in Table 7.1.1.1.2/42.	
3.3.	**Test solution**	About 2 mg of each label was dissolved in 1 mL of acetone each to give solutions of about 2 mg/mL. 370 µL (0.803 µg) of [difluorobenzamide-ring-U-^{14}C]-flufenoxuron and 290 µL (0.812 µg) of [fluoroaniline-ring-U-^{14}C]-flufenoxuron were brought to 1000mL with pH 7 buffer solution prepared from Titrisol phosphate buffer by 10-fold dilution and sterile filtration. Initial concentrations were 1.6 and 1.7 nM. Aliquots (50 mL) were used as dark control and for photolysis.	
3.4.	**Testing procedure**		
3.4.1.	Test system	Nine glass vessels (volume approximately 50 mL) with quartz glass covers were situated in three rectangular thermostated blocks. Six vessels were filled with test solution. Each vessel had an air inlet and outlet. Incoming air was sterilized by filtration and passed through 0.5 M NaOH to moisten and remove CO_2. The outlet passed through three successive traps; ethylene glycol, H_2SO_4, and NaOH. Three vessels were filled with actinometer solution and no volatiles were trapped. The experiments were performed in SUNTEST devices. The dark control samples were stored in a climatic chamber at 22 ± 1ºC.	
3.4.2.	Properties of light source	A xenon lamp with a 290 nm UV filter was used with an intensity of ca. 3 mW/cm^2. The intensity of the light source at relevant wavelengths is given in Table 7.1.1.1.2/41	
3.4.3.	Determination of irradiance	A pyridine/PNAP actinometer was used with a PNAP concentration of 2 x 10^{-5} M and pyridine concentration of 7.8x 10^{-2} M. The resulting	

Section A7.1.1.1.2 **Phototransformation in water including identity of transformation products**

BPD Annex Point IIA, VII.7.6.2.2 7.1.1.1.2 Aqueous photholysis (Flufenoxuron)

		quantum yield for the actinometer was 1.3 x 10^{-3}.
3.4.4.	Temperature	22 ± 1ºC
3.4.5.	pH	The study was conducted at pH 7.
3.4.6.	Duration of the test	15 days continuous irradiation
3.4.7.	Number of replicates	A single replicate of each label was analyzed at each interval.
3.4.8.	Sampling	Samples were analyzed after 0, 1, 3, 7, 10, and 15 days of continuous photolysis
3.4.9.	Analytical methods	At each sampling 50 mL samples were extracted three times with 30 mL of ethyl acetate. The extracts were combined, aliquots analyzed by LSC, evaporated to dryness and redissolved in 200µL acetonitrile for HPLC analysis. See Table 7.1.1.1.2/43 for HPLC conditions.
3.5.	**Transformation products**	Transformation products tested: Yes
3.5.1.	Method of analysis for transformation products	Transformation products were monitored by HPLC with reference standards.
		4. RESULTS
4.1.	**Screening test**	Not applicable
4.2.	**Actinometer data**	The disappearance of the actinometer is presented graphically in Figure 7.1.1.1.2/ 22 and Figure 7.1.1.1.2/23. The calculated rate constants are given in Table 7.1.1.1.2/48.
4.3.	**Controls**	No significant degradation was observed in dark controls. See

Section A7.1.1.1.2 **Phototransformation in water including identity of transformation products**

BPD Annex Point IIA, VII.7.6.2.2 7.1.1.1.2 Aqueous photholysis (Flufenoxuron)

		Table 7.1.1.1.2/46 and Table 7.1.1.1.2/47.	
4.4.	**Photolysis data**		
4.4.1.	Concentration values	Concentrations of flufenoxuron and metabolites during the photolysis are given in	
		Table 7.1.1.1.2/46 and Table 7.1.1.1.2/47.	
		The results and the fitted curves are presented in Figure 7.1.1.1.2/ 24 and Figure 7.1.1.1.2/25.	
4.4.2.	Mass balance	Mass balance ranged from 70 to 123%. See	X
		Table 7.1.1.1.2/44 and	
		Table 7.1.1.1.2/45.	
4.4.3.	k^c_p	The determined rate constants and DT_{50} and DT_{90} values for the test substance, the difluorobenzamide metabolite, and the actinometers are given in Table 7.1.1.1.2/48.	
4.4.4.	Kinetic order	Pseudo first order	
4.4.5.	Reaction quantum yield (ϕ)	The determination of the quantum yield was based on the following equation: $$\Phi_{ts} = \frac{\Phi_{ac} * \Sigma(\varepsilon_{(\lambda)ac} I_{(\lambda)ac}) * DT50_{ac}}{}$$	

Section A7.1.1.1.2 **Phototransformation in water including identity of transformation products**

BPD Annex Point IIA, VII.7.6.2.2

7.1.1.1.2 Aqueous photholysis (Flufenoxuron)

$$\Sigma(\varepsilon_{(\lambda)ts}\, I_{(\lambda)ts}) * DT50_{ts}$$

Φ_{ts}: Quantum yield of the test substance

Φ_{ac}: Quantum yield of the actinometer

$\varepsilon_{(\lambda)ts}$: absorption coefficient of the test substance

$\varepsilon_{(\lambda)ac}$: absorption coefficient of the actinometer

$I_{(\lambda)ts}$: light intensity of the used irradiation source during irradiation of the test substance

$I_{(\lambda)ac}$: light intensity of the used irradiation source during irradiation of the actinometer

$DT50_{ts}$: half-life of the test substance

$DT50_{ac}$: half-life of the actinometer

The intensity of the irradiation source and absorption coefficients of the test substance and the actinometer as a function of wavelength are shown in Table 7.1.1.1.2/49.

The quantum yield was determined to be 1.3×10^{-3} for the fluoroaniline label and 2.2×10^{-3} for the difluorobenzamide label giving a mean of 1.75×10^{-3}.

4.4.6. Half-life ($t_{1/2E}$)

With quantum yield, absorption spectrum, and with a program which uses the algorithms developed by FRANK and KLÖPFFER for the direct photochemical transformation of chemicals in water (Frank, R, and Klöpffer, W. (1985), Ermittlung von Strahlungsdaten und Entwicklung eines Programms zur Abschätzung der abiotischen Transformation von Chemikalien in natürlichen Gewässern, Forschungsbericht Nr. 106 020 46), the theoretical photolytic half-life of Flufenoxuron in the top layer of aqueous systems was calculated for the main application periods. The values are given in Table 7.1.1.1.2/50. X

4.5. Specification of the transformation products

The only transformation product identified was 2,6-difluorobenzamide. The photolytic half-life of this degradation product was determined to be 14 days. See Table 7.1.1.1.2/49 and Table 7.1.1.1.2/51, and Figure 7.1.1.1.2/25

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1. Materials and methods

Sterilized glass vessels with quartz glass coverings containing 50 ml test solution ([fluoroaniline-ring-U-^{14}C]-flufenoxuron at 1.7 nM and [difluorobenzamide-ring-U-^{14}C]-flufenoxuron at 1.6 nM) were irradiated in a thermostated block. Each vessel had an air inlet and an air outlet. The incoming air was moistened, sterilized, and the CO_2 was removed. A trapping system for volatiles was connected to each vessel. The thermostated vessels were located under a xenon lamp with a light intensity of about 3 mW/cm^2 and a cut-off for wavelengths < 290 nm to simulate natural sunlight. The duration of the experiment was 15 days under continuous irradiation.

Appropriate volumes of each test solution were stored in a climatic chamber to be used as dark control. The temperature was 22 ± 1°C during the experiments.

Section A7.1.1.1.2	**Phototransformation in water including identity of transformation products**
BPD Annex Point IIA, VII.7.6.2.2	7.1.1.1.2 Aqueous photholysis (Flufenoxuron)

		Samples were taken 0, 1, 3, 7, 10, and 15 days after treatment. The 50 ml water samples were extracted three times with ethyl acetate, the extracts combined and measured for radioactivity by LSC. For HPLC analysis the extracts were evaporated to dryness and redissolved in acetonitrile. For the determination of the quantum yield of Flufenoxuron, a mixture of p-nitroacetophenone (2×10^{5} M) and pyridine (7.8×10^{-2} M) was used as chemical actinometer. The vessels with the actinometer solution were irradiated simultaneously with the test solutions.
5.2.	**Results and discussion**	Under continuous irradiation by a xenon lamp, the DT_{50} values for flufenoxuron and the corresponding actinometer were 1.9 days and 1.0 day for the difluorobenzamide label and 7.2 and 2.2 days for the fluoroaniline label. The only product accounting for more than 10% TAR was 2,6-difluorobenzamide, which had a DT_{50} of 14 days under the conditions of the test, and $^{14}CO_2$ from the fluoroaniline label.
5.2.1.	ϕ^{c}_{E}	The quantum yield for flufenoxuron was determined to be 1.75×10^{-3}.
5.2.2.	$t_{1/2E}$	The calculated half-life of flufenoxuron in the top layer of aqueous systems in Spring and Summer varied from 39.2 days in April to 21.7 days in June.
5.3.	**Conclusion**	Although no specific guideline is referenced, the study meets accepted criteria for an aqueous photolysis study such as OPPTS 835.2210. The study shows that flufenoxuron is degraded photolytically in aqueous systems with an expected environmental half-life of about a month, the only significant product is 2,6-difluorobenzamide which is also degraded rapidly with a half-life of about 14 days under continuous artificial irradiation (2-3 x parent under same conditions).
5.3.1.	Reliability	1
5.3.2.	Deficiencies	No

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/02/2005

Section A7.1.1.1.2 **BPD Annex Point IIA, VII.7.6.2.2**	**Phototransformation in water including identity of transformation products** 7.1.1.1.2 Aqueous photholysis (Flufenoxuron)

Materials and Methods	Applicant's version is acceptable providing the inclusion of the following amendments: - 3.1.7. Further relevant properties: The entry should be read as: "*The solubility of Flufenoxuron in water is* [1.86 µg/l] *at pH 4,* [1.36 µg/l] *at pH 7 and* [3.69 µg/l] *at pH 9,* [(see Doc IIIA, section 3.5)]. [During the study, the test substance was tested at about 1 µg/L.]. *Flufenoxuron is hydrolytically stable under neutral and acidic conditions.* - 3.2 Reference substance: Add in Table 7.1.1.1.2/15: CL 932338 = Reg.No. 4064702, CL 245508 = Reg.No. 206955, CL 211558 = Reg.No. 102719.
Results and discussion	Applicant's version is acceptable providing the inclusion of the following amendments: Table 7.1.1.1.2/21 Change DT_{50} of 2,6-difluorobenzamide to 14.6. - 4.4.6 Half-life: The statement "*the theoretical photolytic half-life of Flufenoxuron in the top layer of aqueous systems was calculated for the main application periods.*" is not applicable to biocidal product, that could be used during the whole year period. These estimations for sunny months only may not be used for risk assessment. TNG on data requirements (Chapter 2, section 7.1.1.1.2) recommends that the results submitted should correspond to the light intensities and spectral distribution from northern to southern European regions, during spring and autumn. Spring value is expected to be more favourable than autumn value. - No statement on the validity of the study was provided. - According to the TNG on data requirements, section 2, point 7.1.1.1.2 (p 44) "The results submitted should correspond to the light intensities and spectral distribution from northern to southern European regions, for example, in 40 and 65 degrees (proposed average 50 degrees) northern latitude during spring and autumn.
Conclusion	Applicant's version is acceptable.
Reliability	2
Acceptability	Acceptable
Remarks	RMS recommends this study as "key study" for the following reasons: - two sites of radiolabelling were considered instead of one site in the other studies; - DT_{50} for metabolite are available ; Actinometer data were included.
IUCLID	Light spectrum: change < 290nm to > 290 nm.
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*

Section A7.1.1.1.2 **BPD Annex Point IIA, VII.7.6.2.2**	**Phototransformation in water including identity of transformation products** 7.1.1.1.2 Aqueous photholysis (Flufenoxuron)

Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.1.1.1.2/41 Absorption for Flufenoxuron and actinometer

Wavelength	Absorption Flufenoxuron	Absorption actinometer
292.5	0.6399	0.1016
295	0.4922	0.0869
297.5	0.356	0.0754
300	0.251	0.0665
302.5	0.1734	0.0594
305	0.1214	0.0536
307.5	0.085	0.0484
310	0.0606	0.0436
312.5	0.0429	0.0389
315	0.0302	0.0343
317.5	0.0215	0.0297
320	0.0151	0.0254
322.5	0.0103	0.021
325	0.0075	0.0168
327.5	0.0056	0.013
330	0.0028	0.0093
332.5	0.0016	0.003
340-800	0	0

Table 7.1.1.1.2/42 Reference substances

Substance	Lot Number, Purity
Flufenoxuron	XXXX
CL 932338 N-{4-[2-chloro-4-(trifluoromethyl)phenoxy]-2-fluorophenyl}urea	**XXXX**
CL 245508 2,6-difluorobenzoic acid	**XXXX**
CL 211558 2,6-difluorobenzamide	**XXXX**

Table 7.1.1.1.2/43 HPLC Conditions

	HPLC LC 176 Autosampler Midas, Spark Gykotek HPLC pump 580 KontronHPLC/UV detector 535 HPLC Radioactivity monitor Berthold LB 509 Data system Chromeleon V.6.11
Flufenoxuron analysis:	
Precolumn:	ODS II, 4 x 3.0 mm
Column:	Luna (Phenomenex) C5, 5µ, 250 x 4.6 mm
Eluent:	A: water/formic acid (1000+1, v/v) B: acetonitrile/formic acid (1000+1,v/v)
Gradient:	0 min 5% B, 40 min 100% B, 45 min 100% B
Flow Rate:	1 mL/min
Actinometer analysis:	
Column:	Shperisorb ODS II, 5µ, 250 x 4.6 mm
Eluent:	A: water/acetonitrile/formic acid (950+50+1, v/v/v) B: water/acetonitrile/formic acid (50+950+1,v/v/v)
Flow Rate:	1 mL/min

Table 7.1.1.1.2/44 Distribution of radioactivity during aqueous photolysis of difluorobenzamide-labeled Flufenoxuron and in dark control at pH 7 [%TAR]

Days after treatment	**Photolysis**			**Dark control**
	Water	**Volatiles***	**Material balance**	**Water**
0	100.0	n.a.	100.0	n.a.
1	107.9	1.10	109.0	108.6
3	114.1	1.44	115.5	105.0
7	122.7	0.88	123.6	103.8
10	90.0	0.51	90.5	97.8
15	109.3	0.63	109.9	106.0

* radioactivity was found only in the NaOH-traps

Table 7.1.1.1.2/45: Distribution of radioactivity during aqueous photolysis of fluoroaniline-labeled Flufenoxuron and in dark control at pH 7 [%TAR]

Days after treatment	Photolysis			Dark control
	Water	Volatiles*	Material balance	Water
0	100.0	n.a.	100.0	n.a.
1	93.7	2.12	95.8	102.1
3	69.5	0.35	69.9	110.6
7	85.6	3.65	89.3	97.4
10	-**	1.47	-**	96.2
15	58.4	19.7	78.1	101.1

* radioactivity was found only in the NaOH-traps; ** outlier due to insufficient recovery, i.e. not considered for further evaluation

Table 7.1.1.1.2/46: HPLC peak distribution for photolysis of difluorobenzamide-labeled Flufenoxuron in buffer solution pH 7 [%TAR]

DAT	Flufenoxuron	2,6-difluoro-benzamide CL 211558 Reg.No. 102719	2,6-difluoro-benzoic acid CL 245508 Reg.No. 206925	Others	Sum	Flufenoxuron Dark Control
0	99.4	n.d.	n.d.	n.d.	99.4	n.a.
1	70.7	16.4	n.d.	14.2*	101.3	106.7
3	26.4	72.0	n.d.	n.d.	98.4	102.1
7	16.3	84.5	n.d.	n.d.	100.8	101.5
10	15.3	61.3	n.d.	n.d.	76.6	96.0
15	72.5**	29.0**	n.d.	n.d.	101.5**	104.8

* two peaks, each less than 10 % TAR;**outlier, not considered for half-live calculations; n.d. = not detected, n.a. = not analyzed

Table 7.1.1.1.2/47: HPLC peak distribution for photolysis of fluoroaniline- labeled Flufenoxuron in buffer solution pH 7 [%TAR]

DAT	Flufenoxuron	"Urea" CL 932338 Reg.No. 4064702	Others	Sum	Flufenoxuron Dark Control
0	92.4	n.d.	n.d.	92.4	n.a.
1	79.2	n.d.	n.d.	79.2	100.3
3	59.9	n.d.	n.d.	59.9	109.5
7	75.2	n.d.	n.d.	75.2	95.9
15	n.d.	n.d.	n.d.	n.d.	99.7

n.d. = not detected

Table 7.1.1.1.2/48: Degradation half-lives and DT_{90} for Flufenoxuron, 2,6-difluorobenzamide (CL 211558, Reg.No. 102719) and actinometers under continuous irradiation

	DT50 [d]		DT90 [d]		k	
	a.s.	actinometer	a.s.	actinometer	a.s.	actinometer
Flufenoxuron (BAS 307 I)						
difluorobenzamide-label	1.9	1.0	6.2	3.5	0.3708	0.663
fluoroaniline-label	7.2	2.2	24.0	7.1	0.0958	0.322
mean of both labels	4.6	--	15.1	--	--	--
2,6-difluorobenzamide (CL 211558, Reg.No. 102719)	14	--	48.5	--	--	--

Table 7.1.1.1.2/49: Calculation of quantum yield of Flufenoxuron

		Test Substance		Actinometer	
λ (nm)	I(λ) (μEinstein/m^2 s)	ε(λ) (L/mol cm)	I(λ) ε(λ) (μEinstein/mol s)	ε(λ) (L/mol cm)	I(λ) ε(λ) (μEinstein/mol s)
292.5	0.305	6319	1926	5184	1580
295	0.374	4860	1819	4434	1659
297.5	0.586	3515	2060	3847	2255
300	0.802	2479	1987	3393	2720
302.5	1.020	1712	1747	3031	3093
305	1.243	1199	1490	2735	3399
307.5	1.621	839	1361	2469	4003
310	2.005	598	1200	2224	4460
312.5	2.395	424	1015	1985	4754
315	2.791	298	832	1750	4885
317.5	3.230	212	686	1515	4894
320	3.675	149	548	1296	4762
322.5	4.126	102	420	1071	4421
325	4.585	74	340	857	3930
327.5	4.965	55	275	663	3293
330	6.208	28	172	474	2946
333.3	7.865	16	124	153	1204
340-800		0	0	0	0
	Σ I(λ) ε(λ)		18001		58256
	Fluoroaniline label				
	DT_{50} (h)		173		53
	Quantum yield		1.3×10^{-3}		1.3×10^{-3}
	difluorobenzamide label				
	DT_{50} (h)		46		24
	Quantum yield		2.2×10^{-3}		1.3×10^{-3}

Table 7.1.1.1.2/50: Theoretical photolytic half-life of Flufenoxuron in the top layer of aqueous systems

Month of application	Environmental half-life	
	DT50 [h]	DT50 [d]
April	535.5	39.2
May	411.3	26.6
June	356.7	21.7
July	378.0	23.5
August	371.0	25.5

Table 7.1.1.1.2/51: Specification and amount of transformation products

Code-Number	CAS and/or IUPAC Chemical Name*(s)*	Amount [%] of parent compound
Reg. No. 102719 CL 211558 CAS No. 18063-03-1	2,6-difluorobenzamide	Max. 84.5% at 7 days

Figure 7.1.1.1.2/ 22: Disappearance of the actinometer - fluoroaniline label

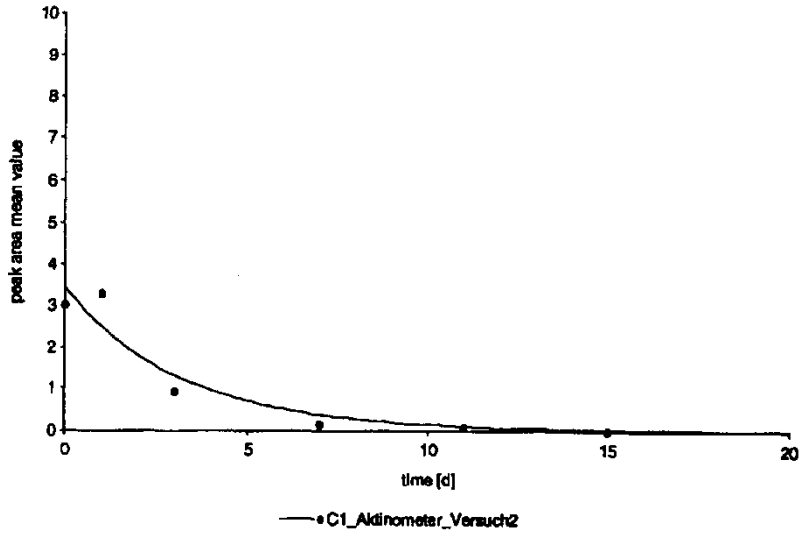


Figure 7.1.1.1.2/23 Disappearance of the actinometer - difluorobenzamide label

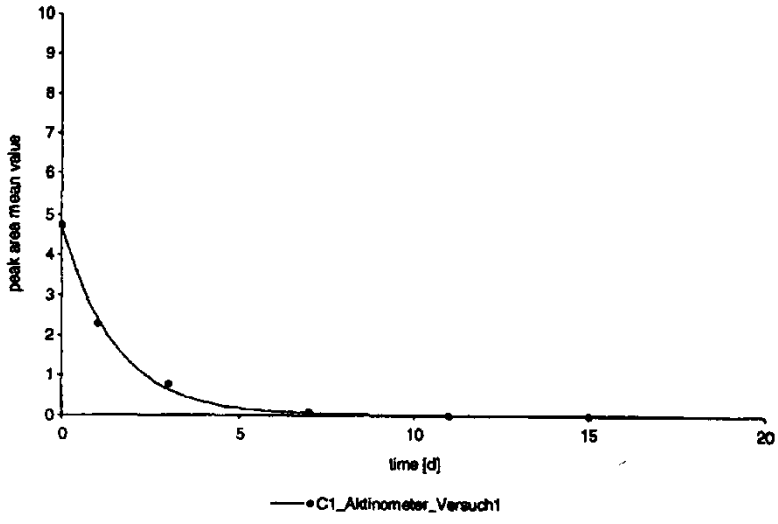


Figure 7.1.1.1.2/ 24 Observed residues and fitted curve - fluoroaniline label

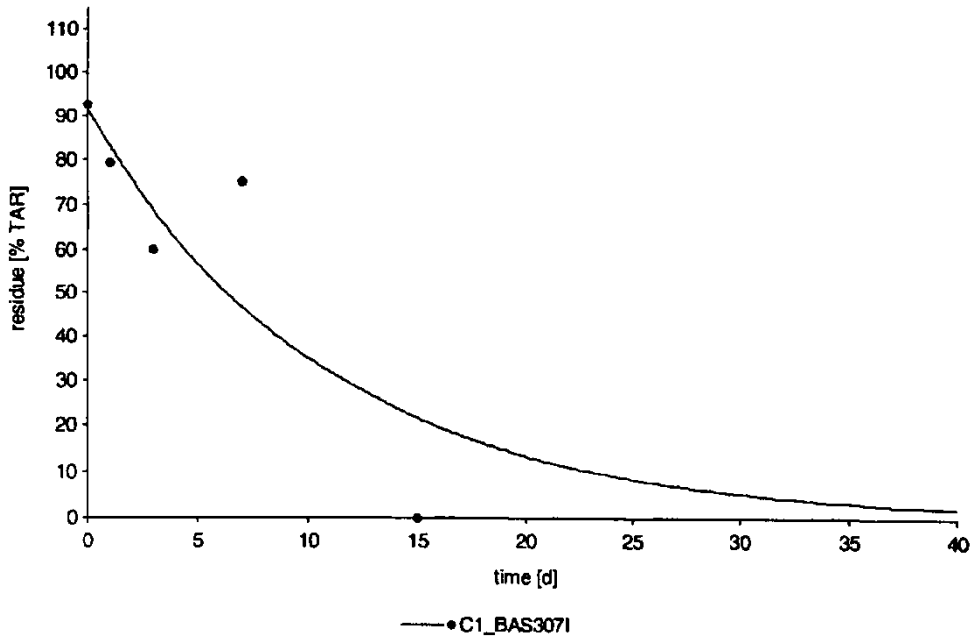
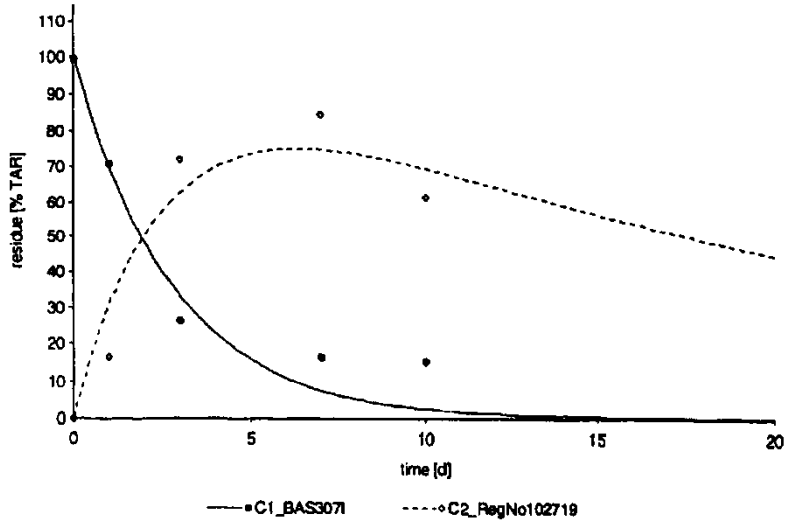


Figure 7.1.1.1.2/25 Observed residues and fitted curve - difluorobenzamide label



Phototransformation in water including identity of transformation products

Section A7.1.1.1.2 7.1.1.1.2 Photolysis in natural water

BPDAnnex Point IIA, VII.7.6.2.2

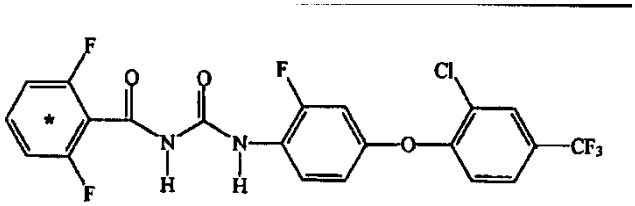
Official use only

		1. REFERENCE
1.1.	**Reference**	**5) Mamouni A and van der Gaauw A (2001)** [^{14}C]-Flufenoxuron (BAS 307 I): Photolysis in Natural Water. XXXX unpublished XXXX **6) Mamouni A and van der Gaauw A (2001)** Amendment No.1: [^{14}C]-Flufenoxuron (BAS 307 I): Photolysis in Natural Water. XXXX unpublished XXXX
1.2.	**Data protection**	Yes
1.2.1.	Data owner	BASF
1.2.2.	Companies with letter of access	XXXX
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I.
		2. GUIDELINES AND QUALITY ASSURANCE
2.1.	**Guideline study**	Yes, JAMFF Guideline, 9 Nohsan 5089: 16, 1997
2.2.	**GLP**	Yes, (Laboratory certified by Swiss Agency for the environment, forests, and landscape; Berne, Switzerland)
2.3.	**Deviations**	No
		3. MATERIALS AND METHODS
3.1.	**Test material**	[Amide-^{14}C]-Flufenoxuron
3.1.1.	Lot/Batch number	XXXX
3.1.2.	Specification	See below
3.1.3.	Purity	Radiopurity – 100% Chemical purity - >99%
3.1.4.	Specific Activity	32.36 µCi/mg

Phototransformation in water including identity of transformation products

Section A7.1.1.1.2 7.1.1.1.2 Photolysis in natural water

BPDAnnex Point IIA, VII.7.6.2.2

3.1.5.	Radiolabeling		
3.1.6.	Expiration Date	June 21, 2001	
3.1.7.	UV/VIS absorption spectra and absorbance value	See Figure 7.1.1.1.2/26	
Further relevant properties		The solubility of Flufenoxuron in water is 186 µg/l at pH 4, 136 µg/l at pH 7 and 369 µg/l at pH 9. Flufenoxuron is hydrolytically stable under neutral and acidic conditions.	
3.2.	**Reference substances**	Flufenoxuron and its degradates	X
3.2.1.	Lot/Batch number	Flufenoxuron XXXX XXXX	
3.2.2.	Purity	XXXX	X
3.3.	**Test solution**	See Table 7.1.1.1.2/ 52	
3.4.	**Testing procedure**		
3.4.1.	Test system	100 mL aliquots of the test solution in sterilized distilled or pond water, in cylindrical Pyrex vessels 9.0 cm in diameter giving an aqueous layer about 4 cm deep, were continuously irradiated using a SUNTEST CPS, Original Hanau apparatus equipped with a 1.8 kw xenon arc lamp with UV filter. The vessels were cooled by a recirculating water bath and covered with quartz glass plates. The vessels were equipped with air inlet and outlet for collection of volatiles and continuously ventilated with sterile, CO_2-free, moistened air. The effluent air was passed through ethylene glycol and NaOH traps to collect volatiles and CO_2. The solutions were stirred continuously with magnetic stirrers.	
3.4.2.	Properties of light source	See Table 7.1.1.1.2/ 54 and Figure 7.1.1.1.2/27	
3.4.3.	Determination of irradiance	The spectrum of the lamp was recorded using a Li-Cor LI-1800 portable spectroradiometer at the point samples were irradiated during the study.	
3.4.4.	Temperature	25 ± 1ºC	
3.4.5.	pH	The pH of the distilled water varied from 6.3 to 6.5 over the course of	

Phototransformation in water including identity of transformation products

Section A7.1.1.1.2 7.1.1.1.2 Photolysis in natural water

BPDAnnex Point IIA, VII.7.6.2.2

		the study. The pH of the pond water varied from 7.9 to 8.2 over the course of the study.	
3.4.6.	Duration of the test	Samples were irradiated continually for up to 15 days	
3.4.7.	Number of replicates	A single replicate of each water type was prepared and analyzed for each interval.	
3.4.8.	Sampling	A vessel of each water type and associated traps were removed and analyzed at 0, 1, 3, 5, 7, 10, and 15 days for irradiated samples and at 0 and 15 days for the controls.	
3.4.9.	Analytical methods	Radioactivity in the traps and test solutions was determined by liquid scintillation counting. The remainder of the test solutions were concentrated by rotary evaporation at 30ºC, dissolved in about 3 mL of MeOH, evaporated to about 1 mL, and aliquots were analyzed by HPLC with UV and ^{14}C detection (See Table 7.1.1.1.2/ 55) and TLC (See Table 7.1.1.1.2/ 56). The TLC-plates were visualized by UV for unlabeled reference compounds. The radioactive zones were detected and quantitated by a Berthold Automatic TLC-Linear Analyzer (LB 2842) equipped with an EPSON PC AX Processing System (LB 292) and imaged on a Fuji BAS 1000 phosphor imaging plate. The sterility of the test solutions was checked by plate counts at the start and end of the irradiation period.	X
3.5.	**Transformation products**	Transformation products tested: Yes	
3.5.1.	Method of analysis for transformation products	Transformation products were identified by comparison of HPLC retention times and TLC Rf-values with reference standards.	X
		4. RESULTS	
4.1.	**Screening test**	Not performed	
4.2.	**Actinometer data**	No actinometer used.	
4.3.	**Controls**	The amount of Flufenoxuron in the dark control solutions was 99.8 and 93.4% of the applied dose at day 0 and day 15, respectively for the distilled water and 101 and 92.7% for the pond water.	
4.4.	**Photolysis data**		

Phototransformation in water including identity of transformation products

Section A7.1.1.1.2 7.1.1.1.2 Photolysis in natural water

BPDAnnex Point IIA, VII.7.6.2.2

4.4.1.	Concentration values	The concentrations of Flufenoxuron and metabolites at each sampling interval are given in Table 7.1.1.1.2/ 57 and Table 7.1.1.1.2/ 58. Dissipation curves and regression results are shown in Figure 7.1.1.1.2/28 and Figure 7.1.1.1.2/29. The distilled water values of 1.925 for day 5 and 1.111 for day 10 and pond water values of 0.655 for day 10 were not used in the kinetic analysis due to poor mass balance for these samples.	
4.4.2.	Mass balance	The mass balance ranged from 99.4 to 143.2% for the distilled water. The values of 118.2% for day 5 and 143.2% for day 10 were not used in the kinetic analysis. The mass balance for the pond water varied from 86.9 to 104.6%. The value of 86.9% on day 10 was not used in the kinetic analysis.	
4.4.3.	k^c_p	Distilled water – 0.0976 $days^{-1}$ Pond water – 0.1024 $days^{-1}$	
4.4.4.	Kinetic order	Pseudo first order	
4.4.5.	k^c_p / k^a_p	No actinometer was used.	
4.4.6.	Reaction quantum yield (ϕ^c_E)	Not determined	
4.4.7.	k_{pE}	Not determined	
4.4.8.	Half-life ($t_{1/2E}$)	Not determined	
4.4.9.	Half-life ($t_{1/2}$) correlated to Latitude 35ºN spring sunlight	Distilled water – 17.7 days Pond water – 17.0 days	
4.4.10.	Half-life ($t_{1/2}$) correlated to Latitude 50ºN summer sunlight	Distilled water – 21.4 days Pond water – 20.5 days	
4.5.	**Specification of the transformation products**	A single photoproduct accounting for more than 10% of the applied dose was identified. 2,6-difluorobenzamide accounted for 89% and 74% of the applied dose at 15 days for distilled water and pond water, respectively. Four other metabolites were detected at 1 to 7 % of the dose. See Table 7.1.1.1.2/ 57 to Table 7.1.1.1.2/ 59	X

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1.	**Materials and**	This study was conducted according to JMAFF guidelines. Solutions of radiolabeled test substance at 0.0021 ppb in distilled and pond water	

Phototransformation in water including identity of transformation products

Section A7.1.1.1.2 7.1.1.1.2 Photolysis in natural water

BPDAnnex Point IIA, VII.7.6.2.2

	methods	were irradiated continuously for up to 15 days using a Xenon lamp at 25ºC. The parent and transformation products were quantitated and identified by LSC, HPLC, and TLC.	X
5.2.	**Results and discussion**	The calculated photolysis half-lives of flufenoxuron, in spring sunlight in Tokyo, Japan, were 17.7 and 17.0 days for distilled and pond water, respectively. The calculated photolysis half-lives under summer sunlight in southern Europe were 21.4 and 20.5 days. Only one photoproduct accounted for more than 10 % of the dose at any time during the study. After 15 days of irradiation, 2,6-difluorobenzamide accounted for 88.9% and 74.0% of the dose in distilled and pond water, respectively.	
5.2.1.	k^c_p	Distilled water – 0.0976 $days^{-1}$ Pond water – 0.1024 $days^{-1}$	
5.2.2.	k_{pE}	Not determined	
5.2.3.	ϕ^c_E	Not determined	
5.2.4.	$t_{1/2E}$	Not determined	
5.2.5.	Half-life ($t_{1/2}$) correlated to Latitude 35º N spring sunlight	Distilled water – 17.7 days Pond water – 17.0 days	
5.2.6.	Half-life ($t_{1/2}$) correlated to Latitude 50º N summer sunlight	Distilled water – 21.4 days Pond water – 20.5 days	
5.3.	**Conclusion**	Flufenoxuron is photolytically degraded in water with expected half-lives of about 17 days at 35ºN in spring sunlight and 20 days at 50ºN in summer sunlight.	
5.3.1.	Reliability	1	
5.3.2.	Deficiencies	No	

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/02/2005

Phototransformation in water including identity of transformation products

Section A7.1.1.1.2 7.1.1.1.2 Photolysis in natural water

BPDAnnex Point IIA, VII.7.6.2.2

Materials and Methods	Applicant's version is acceptable, provided the following amendments: - 3.1.7. Further relevant properties: The entry should be read as: "*The solubility of Flufenoxuron in water is* [1.86 µg/l] *at pH 4,* [1.36 µg/l] *at pH 7 and* [3.69 µg/l] *at pH 9,* [(see Doc IIIA, section 3.5)]. [During the study, the test substance was tested at its limit of solubility (2.093 ppb), a lower concentration would not have been possible due to the low specific activity of the substance.]. *Flufenoxuron is hydrolytically stable under neutral and acidic conditions.* - 3.2 Reference substance: remark: Flufenoxuron was only ^{14}C radiolabeled on the amide ring. Therefore, despite the inclusion of CL 932338 as reference substance, this "urea" part may not be present as radioactive degradate due to the labeling position of the substance. - 3.2.2 Purity: Change "*AC 811678*" to "*Flufenoxuron*" - 3.3 Test solution: in table 7.1.1.1.2/25, in the field *Test concentrations (mg a.s./L),* change the entry to "2.093 µg a.s./L or "0.0021 mg a.s./L". - 3.4.9 As one replicate was analyzed, the recovery rate and the repeatability of the analytical method cannot be evaluated as recommended in the OECD guideline. - 3.5.1 Into the study, it is said that *"no characterization work was performed on M2 to M6"*. Only *"the main photodegradate was characterized by chromatography with reference standard as 2,6 difluorobenzamide (M1)"* - 3.5 pH: remark: it should be noticed that flufenoxuron is stable at pH 7 and hydrolysed at pH 9. Flufenoxuron at pH 8 in natural water may undergo partial hydrolysis. Results in the dark controls indicate that it was not the case.
Results and discussion	Applicant's version is acceptable, provided the following amendments: - 4.5 Specification of the transformation products: change to "[…] [Five] *other metabolites were detected at 1 to 7 % of the dose.* [No characterization work was performed on these metabolites.] **Metabolite M3?**
Conclusion	Applicant's version is acceptable, provided the following amendments: *Material and methods: second sentence: the correct value is 2.093 µg/L (or ppb) instead of 0.0021 ppb* 5.3.2 deficiencies: Add the following statements: *[- Flufenoxuron was only ^{14}C radiolabeled on the amide ring,* *- Minor metabolites were not identified.]* - No statement on the validity of the study was provided.
Reliability	3
Acceptability	Acceptable
Remarks	Data derived from experiment in natural pond water confirms the results obtained with distilled water.
	COMMENTS FROM ...

Phototransformation in water including identity of transformation products

Section A7.1.1.1.2

7.1.1.1.2 Photolysis in natural water

BPDAnnex Point IIA, VII.7.6.2.2

Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.1.1.1.2/ 52: Description of test solution and controls

Criteria	**Details**
Purity of water	Deionized water was further purified using an ELGA water purification unit. Pond water was collected on September 30,2000 from a pond in Ormalingen (BL/CH) at a depth of 10-20 cm approx 1m from shore. The pond did not receive effluent discharges and is not located near areas of human activity. The water was passed through a 0.2 mm sieve before determining parameters Both waters were sterilized by autoclaving for 30 minutes at 121ºC. The parameters of the waters are given in Table 7.1.1.1.2/ 53
Test concentrations (mg a.s./L)	0.0021 µg/ml
Temperature (°C)	25 ± 1ºC
Preparation of a.s. solution	1.0 mL of 0.21 µg/ml of Flufenoxuron in acetonitrile was added to 100 ml of test water
Controls	Dark Controls – prepared as for irradiated samples and stored in the dark at 25 ± 1ºC
Identity and concentration of co-solvent	Acetonitrile - 1% v/v

Table 7.1.1.1.2/ 53: Parameters of test waters

	pH	**Oxygen (mg/l)**	**Redox (mv)**	**Electrical Conductivity (µS/cm at 22.7ºC**	**Suspended Solids (g/l)**
Distilled Water	6.66	8.3	153	<0.06	n.d.
Pond Water	8.02	8.0	215	103.5	0.5

Table 7.1.1.1.2/ 54: Description of test system

Criteria	**Details**
Test apparatus	SUNTEST CPS, Original Hanau
Properties of artificial light source:	
Nature of light source	Xenon-arc lamp
Emission wavelength spectrum	See Figure 7.1.1.1.2/26
Light intensity	19.4 w/m^2 at 300 to 400 nm
Filters	UV-edge 290 nm

Table 7.1.1.1.2/ 55: HPLC Conditions

Instrument:	
Pump:	Merck-Hitachi L-6200
Autosampler:	Merck-Hitachi AS-2000
UV detector:	Merck-Hitachi L-4000 (245 nm)
^{14}C detector:	Packard Flow scintillation analyzer, 500TR
Conditions:	
Pre-column:	4 cm x 4mm, 5µm LiChrospher 100 C-18
Column:	25 cm x 4.6 mm, 5 µm Zorbax SB-Phenyl
Mobile Phase	Solvent A: 0.5%acetic acid in water/methanol (95:5 v:v) Solvent B:Methanol
Floe Rate:	1.0 ml/min
Gradient:	0% B to 100% B in 15 minutes, hold for 5 minutes, return to 0%Bin 0.1 minute and hold for 10 minutes.
Injected Volume:	200-400 µl
Retention Times:	Flufenoxuron – 18.0 min. R1 – 9.0 min. R2 – 16.5 min.

Table 7.1.1.1.2/ 56: TLC Conditions

Plates:	Silica gel 60 F 254, 5 cm x 20 cm, 0.25mm layer thickness (Merck)
Solvent Systems:	SS 1:Toluene/ethyl acetate + 0.2% ammonia solution 25%NH_3 (1:1 v:v) SS 2:Toluene/ethyl acetate + 1% ammonia solution 25% NH_3 (1:1 v:v) SS 3: Methanol/water (1:1 v:v) SS 4:Toluene/ethyl acetate + 1% formic acid (1:1 v:v)
	To reduce adsorbed radioactivity at the origin, plates were developed in SS 3 to about 6 cm, dried and developed in SS1.
Rf Values:	SS 1 / SS 2 Flufenoxuron 0.79 / 0.72 R1 0.45 / 0.41 R2 0.26 / 0.33

Table 7.1.1.1.2/ 57: Flufenoxuron and metabolites in irradiated distilled water vs time

DAT	Flufenoxuron	2,6-difluorobenzamide CL 211558 Reg.No. 102719	Others*	Sum
0	99.8	n.d.	n.d.	99.8
1	97.5	2.2	5.5	105.1
3	88.1	20.0	n.d.	108.2
5	92.0	26.3	n.d.	118.2
7	61.3	31.4	6.7	99.4
10	53.1	85.0	5.0	143.2
15	11.8	88.9	6.9	107.6

* sum of several peaks, each individual peak < 6.9%

Table 7.1.1.1.2/ 58: Flufenoxuron and metabolites in irradiated pond water vs time

DAT	Flufenoxuron	2,6-difluorobenzamide CL211558 Reg.No. 102719	Others*	Sum
0	101.1	n.d.	n.d.	101.1
1	91.8	4.1	3.1	98.9
3	78.2	13.6	n.d.	91.8
5	60.3	27.5	3.7	91.5
7	50.9	43.2	n.d.	94.1
10	31.3	55.6	n.d.	86.9
15	20.0	74.0	10.7	104.6

* sum of several peaks, each individual peak < 6%

Table 7.1.1.1.2/ 59: Specification and amount of transformation products

Lab/Report Code, CAS, and/or IUPAC Chemical Name(s)	Amount [%] of parent compound measured
XXXX	Distilled water - 89% at end of study Pond water - 74.0% at end of study

Figure 7.1.1.1.2/26: UV-Vis Absorption Spectrum of Flufenoxuron

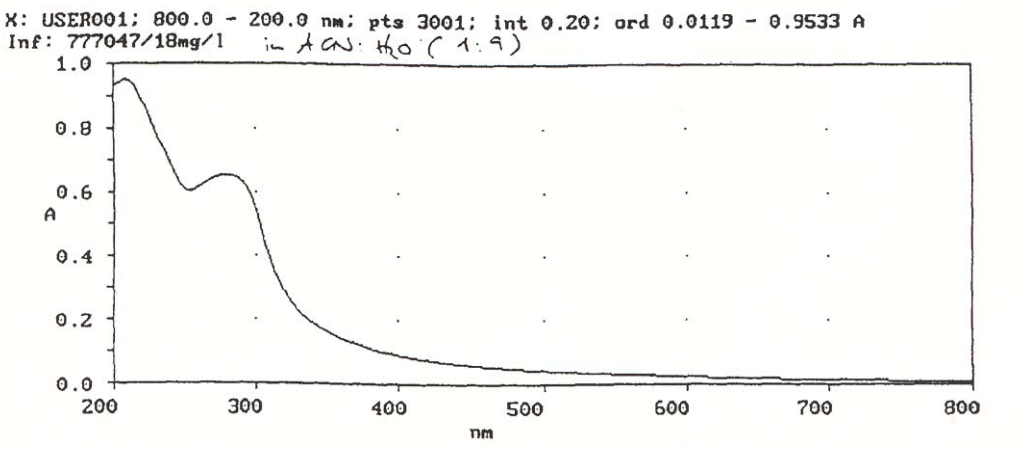


Figure 7.1.1.1.2/27**:** **Spectrum of Xenon Lamp**

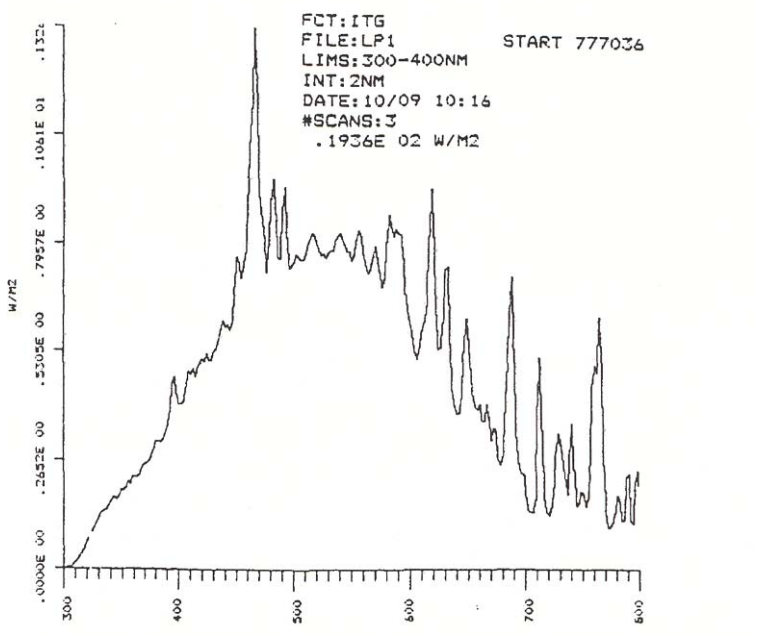
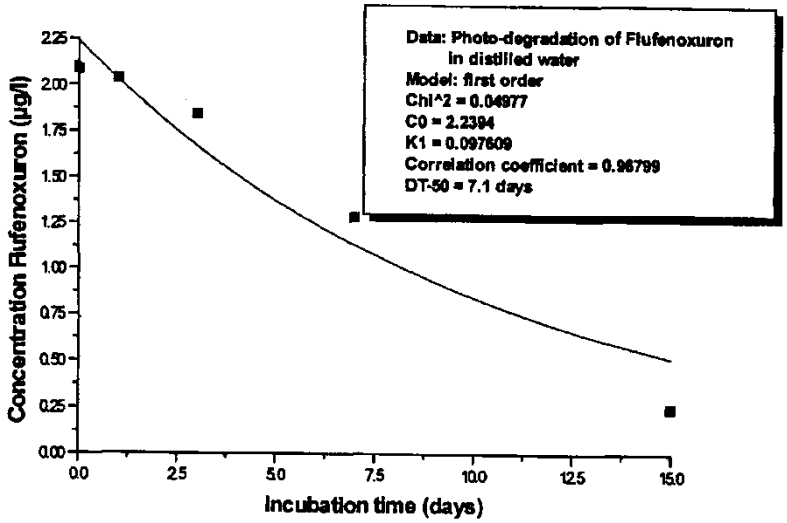


Figure 7.1.1.1.2/28**:** Dissipation of Flufenoxuron from irradiated distilled water



Model: $C = C_0 e^{-kt}$

C_0 = 2.239 µg/l

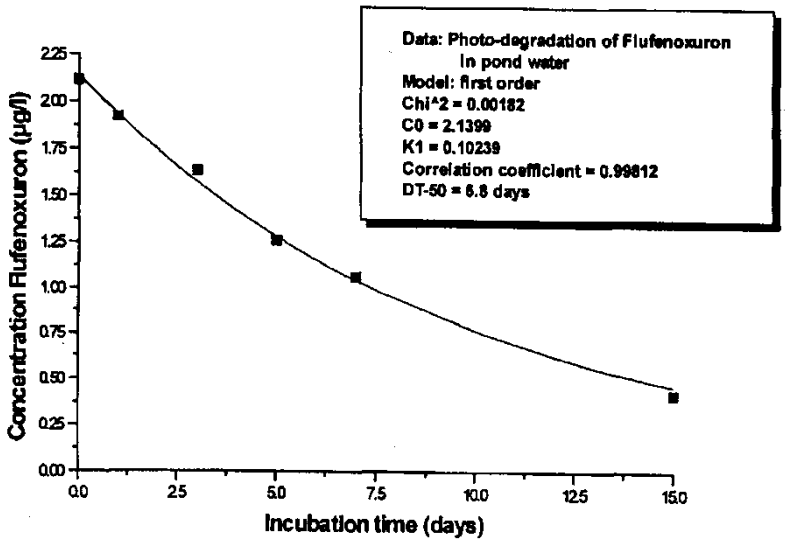
k = 0.0976 $days^{-1}$

Correlation = 0.9678

DT_{50} = (ln 2)/k = **7.1 days**

DT_{90} = (ln 10)/k = **23.6 days**

Figure 7.1.1.1.2/29: Dissipation of Flufenoxuron from irradiated pond water



Model: $C = C_0 e^{-kt}$

C_0 = 2.140 µg/l

k = 0.1024 $days^{-1}$

Correlation = 0.9981

DT_{50} = (ln 2)/k = 6.8 days

DT_{90} = (ln 10)/k = 22.5 days

Section A7.1.1.2.1	**Ready Biodegradability**
BPD Annex Point IIA, VII.7.6.1.1	7.1.1.2.1 Ready Biodegradability (Flufenoxuron)

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**1) Turner SJ, Watkinson RJ (1986)** WL115110: An assessment of ready biodegradability. XXXX, XXXX (unpublished)	
1.2.	**Data protection**	No	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	No data protection claimed	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Yes, OECD 301 B & D	
2.2.	**GLP**	No, at the time the study was conducted GLP was not compulsory.	
2.3.	**Deviations**	No	
		3. MATERIALS AND METHODS	
3.1.	**Test material**		
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	Deviating from specification given in section 2 as follows	
3.1.3.	Purity	99 ± 1%	
3.1.4.	Further relevant properties	The solubility of Flufenoxuron in water is 186 µg/l at pH4, 136 µg/l at pH 7 and 369 µg/l at pH9. Flufenoxuron is hydrolytically stable under neutral and acidic conditions.	X
3.1.5.	Composition of Product	Not applicable	
3.1.6.	TS inhibitory to microorganisms	No	X
3.1.7.	Specific chemical analysis	None	
3.2.	**Reference substance**	Yes, Sodium Benzoate was used to demonstrate the activity of the microbial inoculum.	
3.2.1.	Initial	Closed bottle test - 3 mg/L	

Section A7.1.1.2.1	**Ready Biodegradability**
BPD Annex Point IIA, VII.7.6.1.1	7.1.1.2.1 Ready Biodegradability (Flufenoxuron)

	concentration of reference substance	Modified Sturm test – 20 mg/L
3.3.	**Testing procedure**	
3.3.1.	Inoculum / test species	Microorganisms were obtained from Sittingbourne Sewage works (closed bottle test) and Canterbury Sewage works (modified Sturm test) and prepared according to the prescribed methods for these tests (no further details given in the report).
3.3.2.	Test system	No details are given on laboratory equipment used.
3.3.3.	Test conditions	For the closed bottle test a concentration of 3 mg/l was used. The bottles were incubated at 20±1°C and the extent of the biodegradation was determined by measuring the oxygen concentration in the bottles at 5, 15, and 28 days. For the modified Sturm test a concentration of 20 mg/l was used. The test medium was dispensed into the Sturm vessels, inoculated and aerated with 60 ml/min of CO_2-free air and incubated at 20±1°C. The extent of biodegradation at 2, 5, 8, 12, 16, and 28 days was determined by titrating the total CO_2 released from the incubation. The medium was acidified on day 27 to release the total CO_2 by day 28.
3.3.4.	Method of preparation of test solution	As Flufenoxuron was not completely solubilized in water at the concentrations used, it was supplied to the inoculum as an emulsion in a non-biodegradable detergent (Dobane PT sulphonate).
3.3.5.	Initial TS concentration	For the closed bottle test – 3 mg/L, ThOD = 4.53mg/L For the modified Sturm test – 20 mg/L, $ThCO_2$ = 37.8 mg/L
3.3.6.	Duration of test	28 days
3.3.7.	Analytical parameter	DOC removal, CO_2 evolution
3.3.8.	Sampling	Closed bottle test – 5, 15, and 28 days Modified Sturm test – 2, 5, 8, 12, 16, and 28 days
3.3.9.	Intermediates/ degradation products	Not identified
3.3.10.	Nitrate/nitrite measurement	Not applicable
3.3.11.	Controls	Sodium benzoate was used to demonstrate the activity of the inoculum alone and in combination with flufenoxuron. Controls

Section A7.1.1.2.1	**Ready Biodegradability**
BPD Annex Point IIA, VII.7.6.1.1	7.1.1.2.1 Ready Biodegradability (Flufenoxuron)

		with no inoculum (control) and medium plus inoculum only (blank) were included.
3.3.12.	Statistics	No statistical analysis was used.
		4. RESULTS
4.1.	**Degradation of test substance**	
4.1.1.	Graph	For the closed bottle test, the percentage of ThOD versus time is shown for the reference and test substances in Figure 7.1.1.2.1/30 and for the modified Sturm test, the percentage of $ThCO_2$ versus time is shown in Figure 7.1.1.2.1/32.
4.1.2.	Degradation	No more than 4% biodegradation was observed in either test.
4.1.3.	Other observations	None
4.1.4.	Degradation of TS in abiotic control	No significant degradation occurred in abiotic controls
4.1.5.	Degradation of reference substance	See Figure 7.1.1.2.1/31 and Figure 7.1.1.2.1/32.
4.1.6.	Intermediates/ degradation products	Not monitored
		5. APPLICANT'S SUMMARY AND CONCLUSION
5.1.	**Materials and methods**	The biodegradability of flufenoxuron was determined by testing according to OECD 301B (modified Sturm test) and 301D (closed bottle test).
5.2.	**Results and discussion**	No more than 4% degradation of the test substance was observed in either test. Sodium benzoate was degraded as expected with no difference in degradation in the presence of Flufenoxuron.
5.3.	**Conclusion**	Flufenoxuron is not readily biodegradable.
5.3.1.	Reliability	1
5.3.2.	Deficiencies	No

Section A7.1.1.2.1	**Ready Biodegradability**
BPD Annex Point IIA, VII.7.6.1.1	7.1.1.2.1 Ready Biodegradability (Flufenoxuron)

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	*01/02/2005*
Materials and Methods	Applicant's version is acceptable, provided the following amendments: - 3.1.4. Further relevant properties: The entry should be read as: "*The solubility of Flufenoxuron in water is* [1.86 µg/l] *at pH 4,* [1.36 µg/l] *at pH 7 and* [3.69 µg/l] *at pH 9,* [(see Doc. IIIA, section 3.5)]. *Flufenoxuron is hydrolytically stable under neutral and acidic conditions.* - 3.1.6 TS inhibitory to microorganisms: A "microbial inhibition test" using *Pseudomonas fluorescens* at 10 mg flufenoxuron/L. was performed together with "Closed bottle test" and "modified Sturm test". No significant inhibition was observed. See also Doc. IIIA section 7.4.1.4.
Results and discussion	Applicant's version is acceptable
Conclusion	Applicant's version is acceptable
Reliability	1
Acceptability	acceptable
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table A7.1.1.2.1/1: Pass levels and validity criteria for tests on ready biodegradability

	Fulfilled	**Not fulfilled**
Pass levels		
70% removal of DOC resp. 60% removal of ThOD or $ThCO_2$		X
Pass values reached within 10-d window (within 28-d test period) - not applicable to MITI-I-Test - 14-d window acceptable for Closed-Bottle-Test		X
Criteria for validity		
Difference of extremes of replicate values of TS removal at plateau (at the end of test or end of 10-d window) < 20%	X	
Percentage of removal of reference substance reaches pass level by day 14	X	

Figure 7.1.1.2.1/30 Biodegradation of flufenoxuron as determined by oxygen consumption

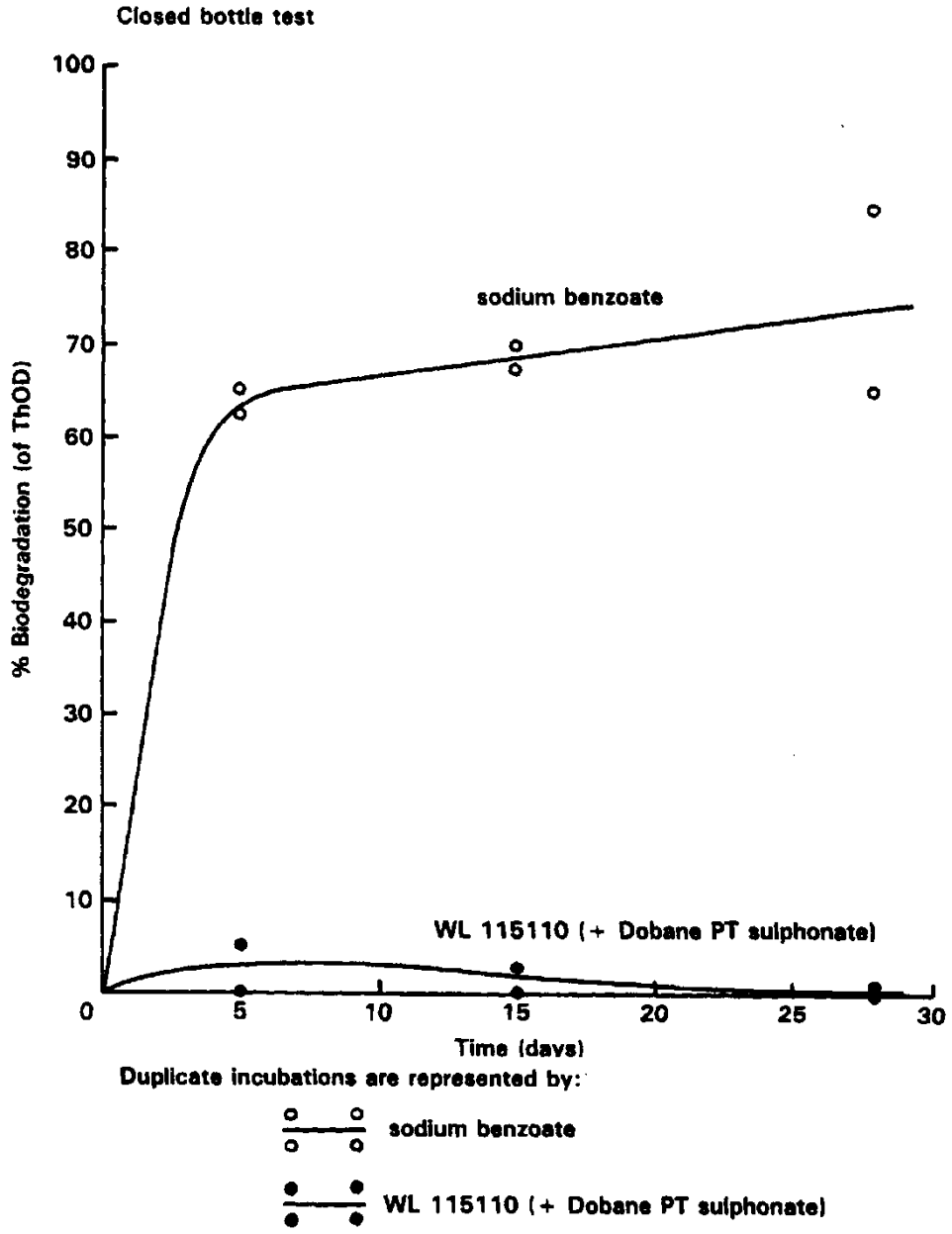


Figure 7.1.1.2.1/31 Effect of flufenoxuron on sodium benzoate degradation

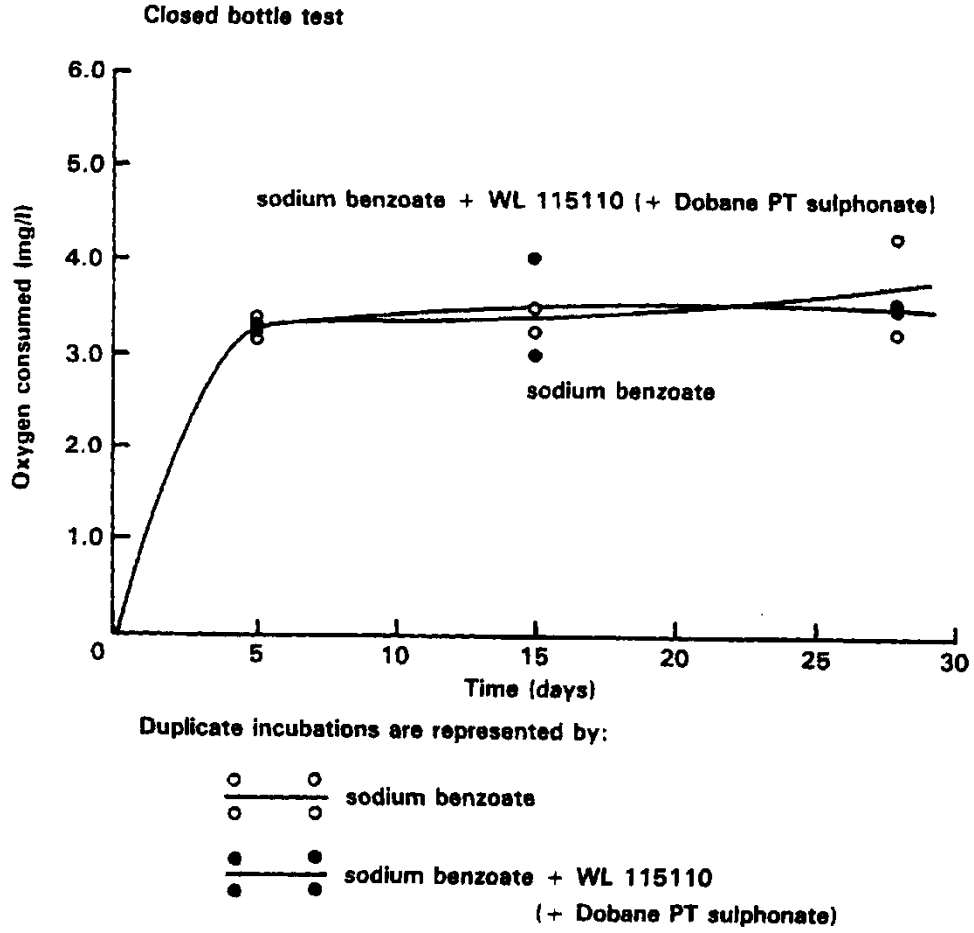
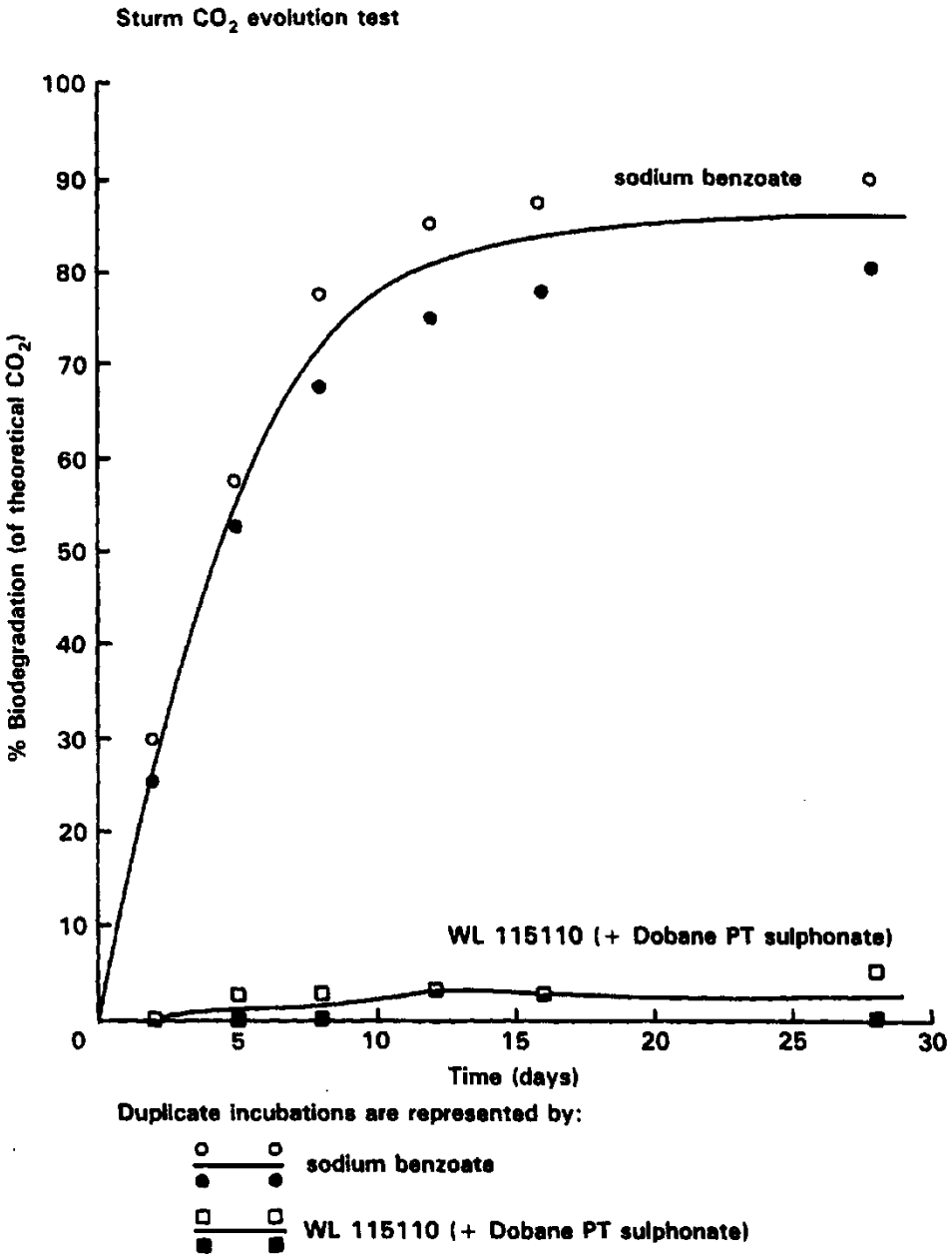


Figure 7.1.1.2.1/32 Biodegradation of flufenoxuron determined by carbon dioxide evolution



Section A7.1.1.2.2 Biodegradability (ready/inherent)

BPD Annex Point IIA, VII.7.6.1.2 Inherent biodegradability

	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [X]	**Technically not feasible [ ] Scientifically unjustified [X]**	
Limited exposure [ ]	**Other justification [ ]**	
Detailed justification:	In a closed bottle test (see IIIA 7.1.2.1), Flufenoxuron was shown as not readily biodegradable. In addition, studies presented under IIIA 7.1 and IIIA 7.2 provided adequate data on its environmental behaviour and its subsequent risk assessment for the supported uses as a wood preservative (PT 8). Therefore, no further testing on inherent biodegradability is required.	
Undertaking of intended data submission [ ]	Not applicable	

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/02/2005
Evaluation of applicant's justification	Applicant's version is acceptable. *TNG on data requirements (Chapter 2, section 7.1.1.1.2) recommends that "[this test] may be performed if the compound is not readily degradable unless a simulation test is performed. Simulation tests are preferred instead of new tests on inherent biodegradability."*
Conclusion	Applicant's version is acceptable.
Remarks	

Section A7.1.1.2.2	**Biodegradability (ready/inherent)**
BPD Annex Point IIA, VII.7.6.1.2	Inherent biodegradability

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A7.1.1.2.3 **Biodegradation in seawater**

BPD Annex Point IIIA, XII.2.1

	JUSTIFICATION FOR NON-SUBMISSION OF DATA	**Official use only**
Other existing data [ ]	**Technically not feasible [ ] Scientifically unjustified [X]**	
Limited exposure [ ]	**Other justification [X]**	
Detailed justification:	Not applicable as treated wood and/or treatment will not be in contact with seawater	
Undertaking of intended data submission [ ]	Not applicable	

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/02/2005
Evaluation of applicant's justification	Applicant's version is acceptable. TNG on data requirements (Chapter 3, section 7.1.1.2.3) recommends that "If a substance is to be used or released in marine environments in considerable amounts (e.g. it is known to be repeatedly used or continuously released in marine environments), then a seawater biodegradation test according to OECD guideline 306 will be required."
Conclusion	Applicant's version is acceptable.
Remarks	

Section A7.1.1.2.3 **Biodegradation in seawater**

BPD Annex Point IIIA, XII.2.1

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A7.1.2.1.1 **Rate and Route of Degradation in aquatic Systems**

BPD Annex Point IIIA, XI.-2.1 7.1.2.1.1 Biological sewage treatment – Aerobic biodegradation

	JUSTIFICATION FOR NON-SUBMISSION OF DATA	**Official use only**
Other existing data [X]	**Technically not feasible [ ]** **Scientifically unjustified [X]**	
Limited exposure [ ]	**Other justification [ ]**	
Detailed justification:	In closed bottle and modifed Sturm tests with sewage microorganisms (see IIIA 7.1.2.1), Flufenoxuron was shown as not readily biodegradable. In addition, studies presented under IIIA 7.1 and IIIA 7.2 provided adequate data on its environmental behaviour and its subsequent risk assessment for the supported uses as a wood preservative (PT 8). This use pattern is not expected to result in significant releases to sewage systems. Therefore, no further testing on aerobic degradation is required.	
Undertaking of intended data submission [ ]		

Section A7.1.2.1.1 **Rate and Route of Degradation in aquatic Systems**

BPD Annex Point IIIA, XI.-2.1 7.1.2.1.1 Biological sewage treatment – Aerobic biodegradation

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/02/2005
Evaluation of applicant's justification	Applicant's version is acceptable. According to TNG on data requirements (Chapter 3, section 7.1.2.1.1) "An aerobic simulation test is required if the biocide enters a sewage treatment plant before release to the environment."
Conclusion	Applicant's version is acceptable.
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section 7.1.2.1.2 **Rate and Route of Degradation in aquatic Systems**

BPD Annex Point IIIA, XII 2.1 7.1.2.1.2 Anaerobic biodegradation

	JUSTIFICATION FOR NON-SUBMISSION OF DATA	**Official use only**
Other existing data [X]	**Technically not feasible [ ] Scientifically unjustified [X]**	
Limited exposure [ ]	**Other justification [ ]**	
Detailed justification:	Based on data presented under AIII 7.1 (no impact on activated sludge respiration up to >1000 mg/l) and under AIII 7.2 (no soil degradation observed under anaerobic conditions), it is likely that Flufenoxuron would have same pattern under anaerobic aquatic system. In addition, it is very unlikely that anaerobic aquatic system would be exposed to Flufenoxuron when used according to the recommendations as wood preservative (See Chapter 5). Therefore, no anaerobic biodegradation study was performed.	
Undertaking of intended data submission [ ]	Not applicable	

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/02/2005
Evaluation of applicant's justification	Applicant's version is acceptable. According to TNG on data requirements (Chapter 3, section 7.1.2.1.2) "An anaerobic degradation study is required if exposure to anaerobic conditions is likely."
Conclusion	Applicant's version is acceptable.
Remarks	

Section 7.1.2.1.2	**Rate and Route of Degradation in aquatic Systems**
BPD Annex Point IIIA, XII 2.1	7.1.2.1.2 Anaerobic biodegradation

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A7.1.2.2.1	**Rate and route of degradation in aquatic systems**
BPD Annex Point IIIA, XII.2.1	7.1.2.2.1 Biodegradation in freshwater – Aerobic aquatic degradation study

	JUSTIFICATION FOR NON-SUBMISSION OF DATA	**Official use only**
Other existing data [X]	**Technically not feasible [ ] Scientifically unjustified [X]**	
Limited exposure [ ]	**Other justification [ ]**	
Detailed justification:	The behaviour of Flufenoxuron in water compartment is adequately described by existing photolysis, hydrolysis and water/sediment studies. Therefore no further aerobic aquatic degradation study is required.	
Undertaking of intended data submission [ ]	Not applicable	

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/02/2005
Evaluation of applicant's justification	Applicant's version is acceptable.
Conclusion	Applicant's version is acceptable.
Remarks	

Section A7.1.2.2.1	**Rate and route of degradation in aquatic systems**
BPD Annex Point IIIA, XII.2.1	7.1.2.2.1 Biodegradation in freshwater – Aerobic aquatic degradation study

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A7.1.2.2.2	**Rate and route of degradation in aquatic systems**
BPD Annex Point IIIA, XII.2.1	7.1.2.2.2 Biodegradation in freshwater – Water/sediment degradation study

0. Justification of the choice of the key study	**RMS Comment (01/02/05):** Two studies are submitted for this endpoint and are summarized in Document IIIA. 1) Ebert D (2003) see page 2. 2) Fent G. (2003) see page 21. The notifier did not provide any justification for the choice of a key study but has identified in the IUCLID document Reference 1 (Ebert D (2003), see page 1) with a "Risk assessment" flag. RMS agrees with this identification and recommend this study as "key study" for the following reasons: - This study was conducted according to OECD Guideline 308, while the second study was conducted in outdoor conditions (variation of temperature, natural sunlight irradiation…) and suffer some deficiencies (preparation of mass balance without quantification of volatile compounds).

Section A7.1.2.2.2	**Rate and route of degradation in aquatic systems**
BPD Annex Point IIIA, XII.2.1	7.1.2.2.2 Biodegradation in freshwater – Water/sediment degradation study

Official use only

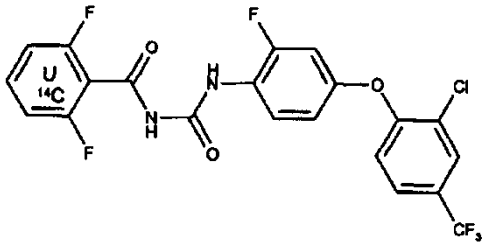
1. REFERENCE

1.1.	**Reference**	**1) Ebert D (2003)** Degradation of BAS 307 I (Flufenoxuron) in water/sediment systems under aerobic conditions. XXXX. unpublished XXXX
1.2.	**Data protection**	Yes
1.2.1.	Data owner	BASF
1.2.2.	Companies with letter of access	XXXX
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I

2. GUIDELINES AND QUALITY ASSURANCE

2.1.	**Guideline study**	Yes, BBA Guideline, Part IV, 5-1, US-EPA Subdivision N, 162-4 SETAC Europe, OECD 308
2.2.	**GLP**	Yes (laboratory certified by Landesanstalt fuer Pflanzenbau und Pflanzenschutz Rheinland-Pfalz, Mainz).
2.3.	**Deviations**	No

3. MATERIALS AND METHODS

3.1.	**Test material**	[difluorobenzamide-U-^{14}C]-Flufenoxuron [fluoroaniline-U-^{14}C]-Flufenoxuron
3.1.1.	Lot/Batch number	[difluorobenzamide-U-^{14}C]-Flufenoxuron - 759-1011 [fluoroaniline-U-^{14}C]-Flufenoxuron - CFQ12392
3.1.2.	Specification	See 3.1.3 to 3.1.5
3.1.3.	Radiolabeling	 [difluorobenzamide-U-^{14}C]-Flufenoxuron

Section A7.1.2.2.2	**Rate and route of degradation in aquatic systems**
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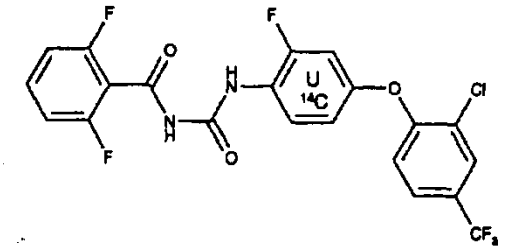

[fluoroaniline-U-^{14}C]-Flufenoxuron

3.1.4.	Purity	[difluorobenzamide-U-^{14}C]-Flufenoxuron - >99% radiopure [fluoroaniline-U-^{14}C]-Flufenoxuron - >99% radiopure	
3.1.5.	Specific Activity	[difluorobenzamide-U-^{14}C]-Flufenoxuron - 7.6 MBq/mg [fluoroaniline-U-^{14}C]-Flufenoxuron - 3.89 MBq/mg	
3.1.6.	Further relevant properties	The water solubility of Flufenoxuron is 0.0043 ppm. Flufenoxuron is hydrolytically stable under neutral and acidic conditions.	X
3.1.7.	Composition of Product	Not applicable	
3.1.8.	TS inhibitory to microorganisms	No	
3.2.	**Reference substance**	Yes, Reference substances used for co-chromatography are shown in Table 7.1.2.2.2/ 60.	
3.3.	**Testing procedure**		
3.3.1.	Test system	The distribution and degradation of Flufenoxuron was studied in two natural systems of water and sediment. The water/sediment systems were taken from a pond (Kellmetschweiher) and a pond-like side arm of the river Rhine (Berghäuser Altrhein), respectively, both in Rhineland-Palatinate, Germany. Characteristics of the water/sediment systems are given in Table 7.1.2.2.2/ 64. The study was performed using an open gas flow system with a trapping device for volatiles. The test vessels were filled with a 2 – 2.5 cm sediment layer (180-190 g of wet sediment) and a 6 cm water layer (ca 290 mL) which were allowed to equilibrate for 18 days before treatment. Two radiolabeled forms of Flufenoxuron, benzamide-[^{14}C] and fluoroaniline-[^{14}C], were used and applied separately to the test systems. Flufenoxuron in 100 µL of acetone (<0.1% in the system) was applied to the water at a rate of 4 µg a.s. per test vessel. Two flasks per system were heat sterilized (121°C, 30 min) prior to application of the test substance. To ease the isolation and identification of degradation products, some water/sediment systems were additionally treated at an application rate of 40 µg a.s. per test vessel, as water solubility was then by far exceeded, these were not used for distribution or kinetics	X

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		analysis. Incubation was done in the dark at a temperature of 20 ± 1°C for up to 100 days after treatment. A single sample was taken from each water/sediment system and each label at 0h, 6h, and 1, 2, 7, 14, 30, 57, and 100 days after treatment.	
3.3.2.	Analytical procedures	For analysis, the water was carefully decanted and the sediment was transferred to centrifuge tubes for extraction with acetonitrile. The radioactivity in the water was partitioned with ethyl acetate. The acetonitrile and ethyl acetate extracts of sediment and water and the extracted water were measured for radioactivity by LSC. The organic phases were concentrated by rotary evaporation and analyzed by HPLC and TLC. Identity of metabolites was confirmed by HPLC/MS-MS. Conditions are given in Table 7.1.2.2.2/ 61 to Table 7.1.2.2.2/ 63.The amount of non-extractable residues in the sediment was determined by combustion. Sediment samples containing more than 7% TAR bound residues were further extracted with 0.5N NaOH for fractionation into fulvic acids, humic acids, and humins.	
3.3.3.	Intermediates/ degradation products	Flufenoxuron degradates were identified by co-chromatography (HPLC and TLC) with reference substances. HPLC/MS-MS was also used to confirm some samples.	
3.3.4.	Controls	Two flasks per system were heat sterilized (121°C, 30 min) prior to application of the test substance.	
3.3.5.	Statistics	Results were analyzed by Model Maker 3.0.4 to determine rates for two models, one for the simple first order disappearance of Flufenoxuron from the total system, and a multi compartment model, including compartments for water, sediment, and Flufenoxuron degradate CL932338 (Reg. No. 4064702).	
		4. RESULTS	
4.1.	**Degradation of test substance**		
4.1.1.	Distribution of Radiocarbon and Mass Balance	The distribution of radiocarbon and mass balance for each interval is shown in Table 7.1.2.2.2/6 for the Kellmetschweiher system and Table 7.1.2.2.2/7 for the Berghäuser Altrhein system. The overall mass balance ranged from 84.6% to 98.2% with an average of 95.5%.	X
4.1.2.	Graph	The degradation of Flufenoxuron in the total system is shown in Figure 7.1.2.2.2/ 33 for the Kellmetschweiher system and Figure 7.1.2.2.2/ 35 for the Berghäuser Altrhein system. The distribution of Flufenoxuron between the water and sediment, its degradation, and the formation and degradation of CL 932338 are shown in Figure 7.1.2.2.2/ 34 and Figure 7.1.2.2.2/ 36.	
4.1.3.	DT_{50}/DT_{90}	The DT_{50} for Flufenoxuron in the whole systems was 61 days in the Kellmetschweiher system and 45 days in the Berghäuser Altrhein system. Flufenoxuron moved rapidly from the water to the sediment	x

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with a DT_{50} in the water of 0.3 to 0.4 days. CL 932338 was the only metabolite at sufficient levels for analysis and its DT_{50} in the sediment was determined to be 21 days in the Kellmetschweiher system and 10 days in the Berghäuser Altrhein system. A summary of DT_{50} and DT_{90} values and the associated r^2 values is given in Table 7.1.2.2.2/ 69.

The following equation was used to recalculate the DT_{50} to a reference temperature of 12°C:

DT_{50} (12°C) = DT_{50} (20°C) x e (0.08 x 20-12))

The DT_{50} obtained for Flufenoxuron in sediment (whole system) was 116 days for the Kelmetschweiher and 85 days for Berghäuser Altrhein. For the metabolite CL 932338 the recalculated DT_{50} is 40 days (Kelmetschweiher) and 19 days (Berghäuser Altrhein).

No recalculation was performed for the DT_{50} in water, because the disappearance from the water phase is mainly an adsorption and not a degradation process.

4.1.4.	Degradation of TS in abiotic control	No degradation occurred in the sterilized systems, with >90% of the original Flufenoxuron extracted from the sediment after 101 days of incubation.
4.1.5.	Intermediates/ degradation products	CL 211558, 2,6-difluorobenzamide, was found in the water of the Kellmetschweiher system at up to 4% of the dose at the end of the study and in the Berghäuser Altrhein system at a maximum of 3% at 57 days after treatment. CL 932338 ("urea" metabolite) was found in the Kellmetschweiher system at a maximum of 4.2% in the water and 19.3% in the sediment on day 57, and in the Berghäuser Altrhein system the maximums were 2% in the water at 14 days and 13% in the sediment at 30 days.
4.1.6.	Bound Residues	Bound residues increased throughout the study for both labels and both systems, reaching maximums of 32.5 and 37.1% in the system and 39.7 and 57.3% in the Berghäuser Altrhein system for the difluorobenzamide and fluoroaniline labels respectively. The results of the separation into fulvic acid, humic acid, and humins is given in Table 7.1.2.2.2/ 70.
4.1.7.	Mineralization to CO_2	Mineralization to CO_2 was significant for the benzamide label, accounting for 30.2 and 29.2% of the original radiocarbon at 100 days in the Kellmetschweiher and Berghäuser Altrhein systems, respectively. Mineralization was less for the fluoroaniline label accounting for only 0.9 and 6.5 % of the original radiocarbon at 100 days in the Kellmetschweiher and Berghäuser Altrhein systems, respectively

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1.	**Materials and methods**	The distribution and degradation of Flufenoxuron was studied in two natural water/sediment systems according to OECD, SETAC, and USEPA guidelines. Two forms of ^{14}C labeled Flufenoxuron were applied separately to pre-equilibrated water/sediment systems. Systems were analyzed after incubation in the dark at 20 ± 1ºC for up to 100 days. The water was partitioned with ethyl acetate and the sediment

Section A7.1.2.2.2	**Rate and route of degradation in aquatic systems**
BPD Annex Point IIIA, XII.2.1	7.1.2.2.2 Biodegradation in freshwater – Water/sediment degradation study

		extracted with acetonitrile, followed by combustion. Extracts were analyzed by LSC, HPLC, and TLC, with confirmation of the identity of metabolites in selected samples by HPLC/MS-MS. Sediment samples containing more than 7% TAR bound residues were further extracted with 0.5N NaOH for fractionation into fulvic acids, humic acids, and humins.
5.2.	**Results and discussion**	Flufenoxuron moved rapidly from the water into the sediment. Flufenoxuron was degraded with a DT_{50} in the whole systems of 85 and 116 days at a reference temperature of 12°C (45 and 61 days at 20°C). CL 932338 was the predominant metabolite with 19% of the dose in the sediment at 57 days after application. CL 211558 was also found at a maximum of 4% in the water. As much as 40% of the original dose of radiocarbon was unextracted from the sediment with acetonitrile. The proposed degradation pathway for Flufenoxuron in aquatic systems is shown in Figure 7.1.2.2.2/ 37. The importance of microbes in the degradation of Flufenoxuron in aquatic systems was shown by no degradation in sterile systems.
5.3.	**Conclusion**	Flufenoxuron moves rapidly to sediments in aquatic systems where it is microbially metabolized, resulting primarily in bound residues and mineralization to CO_2. The only metabolite reaching > 5% of the applied dose at any time during the study was CL 932338 (“urea, Reg. No. 4064702). The DT_{50} for Flufenoxuron in the whole system was 85 to 116 days at a reference temperature of 12°C (45 to 61 days at 20°C). , and the DT_{50} for CL 932338 in the sediment was 19 to 40 days at a reference temperature of 12°C (10 to 21 days at 20°C).
5.3.1.	Reliability	1
5.3.2.	Deficiencies	No

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	09/05/2010

Section A7.1.2.2.2	**Rate and route of degradation in aquatic systems**
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Materials and Methods	Applicant's version is acceptable except for the following sections: 3.1.6. Further relevant properties: The solubility value in the study report is "about 4 µg/L". The value of 0.0043 ppm is not truly different, but the source is not known. 3.3.1. Test system – Table 7.1.2.2.2. remark: The organic C content of the two sediment is low (0.86% and 1.47%). OECD Guideline 308 recommends the use of a sediment with a high organic C content (2.5 – 7.5%) and a difference of 2% organic C content between the " high" and "low" organic C content sediments.
Results and discussion	Applicant's version is acceptable provided the amendment of the following sections: 4.1.1 Distribution of radiocarbon and mass balance: add the following sentence "*HPLC analysis of the water and sediment extracts for the two water/sediment systems are shown in Table 7.1.2.2.2/8 and 7.1.2.2.2./9."* 4.1.3 DT50/DT90 The DT_{50} obtained for Flufenoxuron in ~~*sediment (*~~whole system~~)~~ was 116 days for the Kelmetschweiher and 85 days for Berghäuser Altrhein.
Conclusion	Applicant's version is acceptable.
Reliability	2 Recovery: Mass balance is acceptable during the whole incubation period (table 7.1.2.2.2/6 to 8). The recuperation rate was checked at T=0 with two analysis. The limit of detection is not given into the document as it is recommended by the OECD guidelines n°308. A statement on the validity of the study was not provided in view of the validity criteria proposed in OECD Guideline 308 , under point 5.3 (recovery, Repeatability and sensitivity of analytical method, Confidence intervals for hydrolysis kinetic data). Nevertheless, the material balance deficit was no more than 20%.
Acceptability	Acceptable
Remarks	

	COMMENTS FROM
Date	
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	Applicant's version is acceptable.
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.1.2.2.2/ 60 Reference substances for co-chromatography

	Batch No.	**Specific Activity purity**
Flufenoxuron	XXXX	Not labeled, 99.3%
Reg No. 206925 (CL 245508)	**XXXX**	Not labeled, 99%
Reg No. 102719 (CL211558)	**XXXX**	17.87 MBq/mg, >97%
Reg No. 4064702 (CL932338)	**XXXX**	3.48 MBq/mg, >98%

Table 7.1.2.2.2/ 61 HPLC Conditions

HPLC System	Gilson Abimed autoinjector 231 XL 2 Kontron HLC pumps 420 Kontron UV detector 430 Bethold Scintillator pump 5035 (6.0 ml/min.) Berthold radioactivity detector LB 507 A (with Z2000-4/2 liquid cell)	
Pre-column	Phenomenex Ultracarb 10 ODS (30), 50 x 10 mm	
Column	Phenomenex Ultracarb 7 ODS (30), 250 x 10 mm	
Solvent A	water:acetonitrile:acetic acid, 900:100:1	
Solvent B	acetonitrile:acetic acid. 1000:1	
Gradient	Time (min) 0 15 29 31 37.5	%B 0 100 100 0 0
Flow rate	1 mL/min	
UV detection	254 nm	
^{14}C detection	Packard Flow Scintillation Analyzer	
Retention time	Flufenoxuron - 24.5 min CL932338 - 21.0 min CL 211558 - 14.8 min	

Table 7.1.2.2.2/ 62 High performance TLC (HPTLC) conditions

Stationary phase	HPTLC Silica gel F254 (20 x20 cm, Merck No. 1.05715)
Mobile phase	acetonitrile:acetic acid 100:1
Samples were applied with an automated sample applicator (Linomat, CAMAG). Plates were developed in glass chambers, neutralized in an NH_3 atmosphere, and imaged with a Fujix BAS 1000 imager using TINA 2.08 analysis software.	
R_f	Flufenoxuron – 0.90 CL932338 – 0.67 CL211558 – 0.76

Table 7.1.2.2.2/ 63 HPLC/MS-MS conditions

HPLC System	HP 1100 consisting of G1322A degasser, G1312A binary pump, G1313A autosampler, G1316A column oven, G1314A UV-detector, RHEODYNE six port valve, and Gilson-ABIMED 206 fraction collector.
Column	Phenomenex Ultracarb 10 ODS (30), 250 x 4.6 mm, AT06
Solvent A	water:acetonitrile:acetic acid, 900:100:1
Solvent B	acetonitrile:acetic acid. 1000:1
Gradient	Time (min) %B 0 0 15 100 29 100 31 0 38 0
Flow rate	1 mL/min
UV detection	254 nm
^{14}C detection	Berthold LB507A
Split	ca. 90/10
MS Equipment	PE-SCIEX API3 SN198 Q1/Q3, with Rad 2.6 and MacSpec 3.3 software
Ionization	ESI
CAD/CAD-Gas	+ / Ar

Table 7.1.2.2.2/ 64 Characterisation of the water/sediment systems

Designation **Origin**		**System A** **Kellmetschweiher** **Rhineland-Palatinate, FRG**	**System B** **Berghäuser Altrhein** **Rhineland-Palatinate, FRG**
Sediment	sand [%]	76.4	29.0
	silt [%]	14.3	61.8
	clay [%]	9.3	9.1
	textural class (German scheme)	loamy sand	loamy silt
	pH ($CaCl_2$)	6.9	7.3
	organic C [%]	0.86	1.47
	total N [%]	0.09	0.35
	total P [mg/kg]	97.9	566
	CEC [mVal/100g]	18.2	34.9
	ATP [µg/kg]	46	1291
	plate counts [cfu/g]		
	bacteria	1.9×10^8	5.1×10^8
	actinomycetes	9.7×10^4	3.0×10^6
	fungi	1.9×10^4	1.3×10^6
Water	pH	8.4	8.3
	hardness [mmol/l]	1.99	1.71
	TOC [mg/l]	12.9	3.0
	total N [mg/l]	<1	<1
	total P [mg/l]	<0.05	0.05

Table 7.1.2.2.2/ 65 Material balance and distribution of radioactivity after application of [^{14}C]-Flufenoxuron to water/sediment system Kellmetschweiher

DAT	%TAR								
	water			sediment			volatiles		material balance
	ethyl acetate	remaining H_2O	total	acetonitrile	non-extractable	total	CO_2	others	
benzamide-label									
0	39.5	0.2	39.7	55.1	2.3	57.3	n.d.	n.d.	97.0
0.25	16.2	0.3	16.5	79.0	2.5	81.4	0.0	0.0	97.9
1	8.0	0.7	8.8	86.3	2.6	89.0	0.0	0.0	97.8
2	6.4	1.4	7.8	85.3	2.4	87.7	0.0	0.0	95.5
7	2.1	2.5	4.6	86.2	5.9	92.2	1.0	0.0	97.8
14	1.3	2.2	3.4	85.7	6.9	92.5	1.6	0.0	97.6
30	1.9	4.4	6.2	70.3	12.6	82.9	6.7	0.1	96.0
57	1.0	6.8	7.8	46.7	21.0	67.7	14.0	0.1	89.6
100	0.5	7.2	7.8	18.8	32.5	51.3	30.2	0.0	89.2
101 (s)	n.d.	n.d.	n.d.	93.6	1.8	95.5	n.d.	n.d.	96.6
fluoroaniline-label									
0	38.4	0.2	38.6	55.8	2.0	57.8	n.d.	n.d.	96.4
0.25	18.1	0.2	18.3	76.3	2.6	78.9	0.0	0.0	97.2
1	10.1	0.2	10.3	83.4	2.5	85.9	0.0	0.0	96.2
2	7.2	0.2	7.4	87.3	2.1	89.5	0.1	0.0	97.0
7	3.5	0.2	3.6	90.5	2.8	93.4	0.2	0.0	97.2
14	2.6	0.2	2.9	89.5	4.6	94.0	0.2	0.9	97.9
30	3.5	0.6	4.1	84.0	9.4	93.4	0.2	0.1	97.8
57	4.9	1.0	5.9	65.1	24.8	89.9	0.6	0.0	96.5
100	3.0	1.4	4.5	53.5	37.1	90.6	0.9	0.0	95.9
101 (s)	n.d.	n.d.	n.d.	92.8	1.7	94.5	n.d.	n.d.	95.2

s = sterilized ; n.d.= not determined

Table 7.1.2.2.2/ 66 Material balance and distribution of radioactivity after application of [^{14}C]-Flufenoxuron to water/sediment system Berghäuser Altrhein

DAT	%TAR								
	water			sediment			volatiles		material balance
	ethyl acetate	remaining H_2O	total	acetonitrile	non-extractable	total	CO_2	others	
benzamide-label									
0	34.1	0.1	34.2	61.2	2.0	63.2	n.d.	n.d.	97.4
0.25	17.2	0.2	17.4	69.9	9.2	79.2	0.0	0.0	96.6
1	7.5	0.6	8.1	84.9	5.1	90.0	0.0	0.0	98.2
2	5.3	1.2	6.5	85.3	5.6	90.9	0.0	0.0	97.4
7	2.3	3.2	5.6	82.3	6.2	88.6	0.6	0.0	94.8
14	1.6	5.7	7.3	59.2	16.4	75.6	1.6	0.1	84.6
30	1.1	4.5	5.6	59.3	19.6	78.9	7.0	0.2	91.7
57	0.9	5.4	6.2	34.9	30.3	65.2	18.5	0.2	90.1
100	0.3	3.2	3.5	15.4	39.7	55.1	29.2	0.0	87.9
101 (s)	n.d.	n.d.	n.d.	91.2	3.2	94.4	n.d.	n.d.	96.8
fluoroaniline-label									
0	41.2	0.2	41.4	52.0	2.2	54.2	n.d.	n.d.	95.6
0.25	20.1	0.2	20.3	71.2	4.7	75.9	0.0	0.0	96.3
1	9.7	0.2	9.9	81.1	3.2	84.3	0.0	0.0	94.3
2	6.5	0.2	6.7	86.4	3.5	89.9	0.0	0.0	96.7
7	2.9	0.3	3.2	89.1	5.4	94.5	0.1	0.0	97.8
14	3.6	0.5	4.2	81.8	9.8	91.6	0.2	0.1	96.0
30	2.5	0.7	3.2	76.1	16.8	92.9	0.3	0.4	96.7
57	1.5	2.1	3.6	44.9	43.8	88.7	3.4	0.0	95.7
100	0.8	2.2	3.0	30.5	57.3	87.8	6.5	0.0	97.3
101 (s)	n.d.	n.d.	n.d.	91.4	3.7	95.0	n.d.	n.d.	96.1

s = sterilized; n.d.= not determined

Table 7.1.2.2.2/ 67 HPLC analysis of the water and sediment extracts of system Kellmetschweiher after application of [^{14}C]-Flufenoxuron

DAT	%TAR				
	2,6-difluoro-benzamide CL 211558 benzamide-label	**"urea" CL 932338** fluoroaniline-label	**unknowns****	**Flufenoxuron** benzamide-label	**Flufenoxuron** fluoroaniline-label
water (ethyl acetate + remaining water)					
0				39.5	38.4
0.25				16.2	18.1
1		0.2		8.0	9.9
2		0.9		6.4	6.3
7	1.6	1.8	1.2	1.8	1.7
14		1.6			1.1
30	2.1	2.4	2.3		1.1
57	3.0	4.2	3.8		0.7
100	4.1	2.5	3.1		0.5
101 (s)*					
sediment					
0				55.1	55.8
0.25				79.0	76.3
1				86.3	83.4
2				85.3	87.3
7		2.7		86.2	87.8
14		3.2		85.7	86.3
30		8.6		70.3	75.4
57		19.3		46.7	45.9
100		16.9		18.8	36.6
101 (s)				93.6	92.8

* no HPLC analysis performed because of too low radioactivity; ** sum of up to 4 peaks (all detected with benzamide-label); s = sterilized; no value means not detected

Table 7.1.2.2.2/ 68 HPLC analysis of the water and sediment extracts of system Berghäuser Altrhein after application of [^{14}C]-Flufenoxuron

DAT	%TAR				
	difluoro-benzamide **CL 211558** benzamide-label	**"urea"** **CL 932338** fluoroaniline-label	**unknowns****	**Flufenoxuron** benzamide-label	**Flufenoxuron** fluoroaniline-label
water (ethyl acetate + remain. water)					
0				34.1	41.2
0.25				17.2	20.1
1		0.1		7.5	9.6
2	0.1	0.4		5.2	6.1
7	2.8	1.4	1.0	1.8	1.5
14	1.8	1.8	3.9		1.9
30	2.1	1.4	2.6		1.0
57	2.8		2.7		
100	0.9		2.2		
101 (s)*					
sediment					
0				61.2	52.0
0.25				69.9	71.2
1				84.9	81.1
2				85.3	86.4
7		3.2		82.3	85.9
14		12.1		59.2	69.7
30		13.0		59.3	63.1
57		10.9		34.9	34.0
100		2.3		15.4	28.2
101 (s)				91.2	91.4

* no HPLC analysis performed because of too low radioactivity; ** sum of up to 7 peaks (except one finding only detected with benzamide-label); s = sterilized; no value means not detected

Table 7.1.2.2.2/ 69 Degradation rates of Flufenoxuron and metabolite CL 932338 in water/sediment systems

System		**DT_{50} first order [days]**	**DT_{90} first order [days]**	**r^2**
System Kellmetschweiher (20°C)				
BAS 307 I	whole system	61	203	0.99
BAS 307 I	water	0.3	0.9	0.98
BAS 307 I	sediment	65	216	0.98
"urea", CL 932338	sediment	21	71	0.98
System Berghäuser Altrhein (20°C)				
BAS 307 I	whole system	45	150	0.99
BAS 307 I	water	0.4	1.2	0.99
BAS 307 I	sediment	46	152	0.99
"urea", CL 932338	sediment	10	32	0.99
System Kellmetschweiher (12°C)				
BAS 307 I	whole system	116	385	0.99
BAS 307 I	water	0.3*	0.9*	0.98
BAS 307 I	sediment	123	410	0.98
"urea", CL 932338	sediment	40	135	0.98
System Berghäuser Altrhein (12°C)				
BAS 307 I	whole system	85	285	0.99
BAS 307 I	water	0.4*	1.2*	0.99
BAS 307 I	sediment	87	288	0.99
"urea", CL 932338	sediment	19	61	0.99

* No degradation, therefore no temperature correction

Table 7.1.2.2.2/ 70 Characterization of sediment bound residues

System/Label	DAT	%TAR		
		fulvic acids	Humic acids	Humins
Kellmetschweiher	30	6.4	1.2	4.9
benzamide-label	57	10.4	1.9	8.6
	100	14.6	3.8	14.4
Kellmetschweiher	30	1.7	2.1	5.9
fluoroaniline-label	57	5.4	4.3	15.4
	100	6.1	5.6	23.0
Berghäuser Altrhein	0.25	2.7	0.9	6.9
benzamide-label	14	6.0	2.5	8.2
	30	7.7	3.5	5.9
	57	11.3	5.0	13.4
	100	12.2	5.7	18.0
Berghäuser Altrhein	14	0.9	2.7	6.7
fluoroaniline-label	30	1.1	4.2	11.5
	57	4.2	10.7	28.3
	100	6.1	13.5	38.2

Figure 7.1.2.2.2/ 33 Experimental data and calculated degradation curve for Flufenoxuron in System A (Kellmetschweiher), whole system

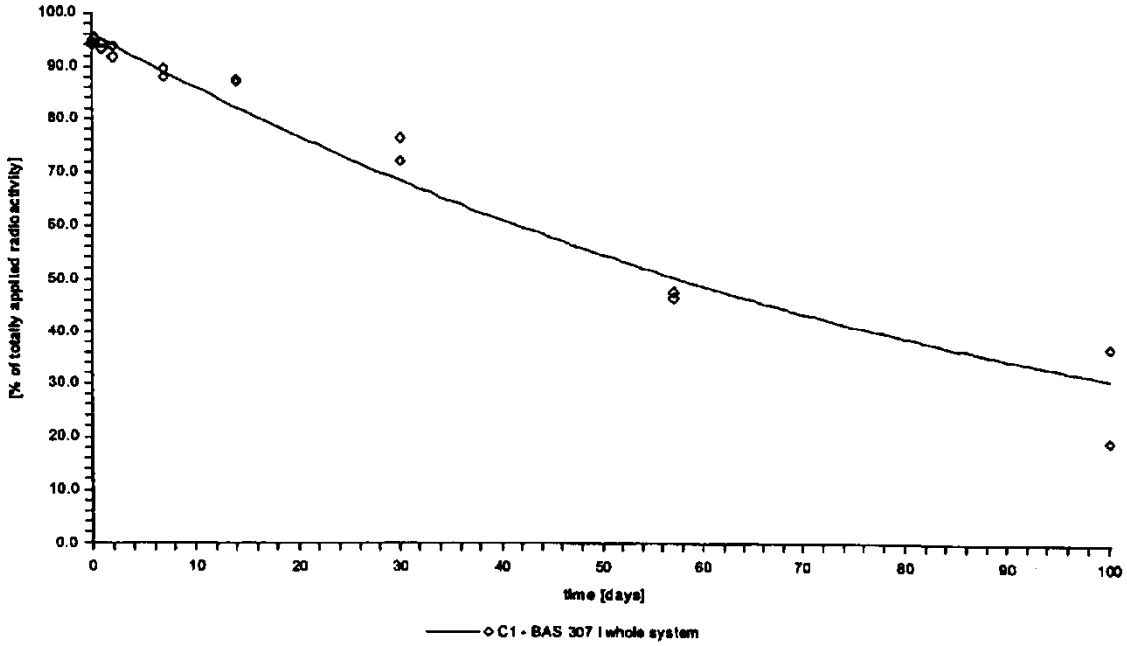


Figure 7.1.2.2.2/ 34 Experimental data and calculated degradation curve for Flufenoxuron and CL932338 in System A (Kellmetschweiher), water and sediment

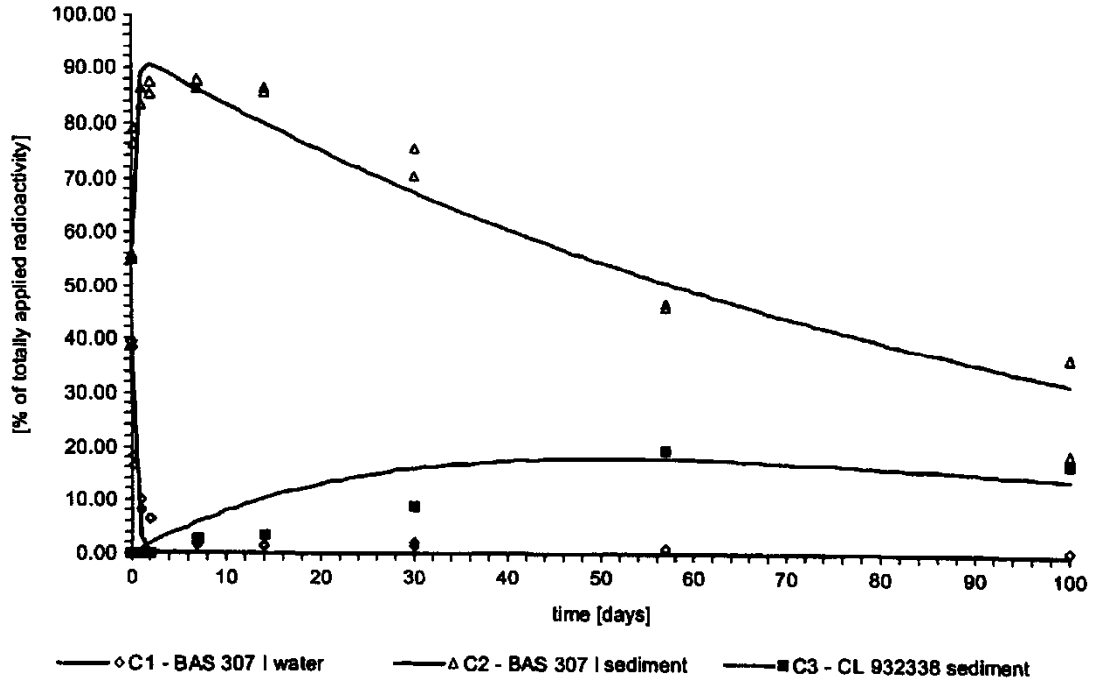


Figure 7.1.2.2.2/ 35 Experimental data and calculated degradation curve for Flufenoxuron in System B (Berghäuser), whole system

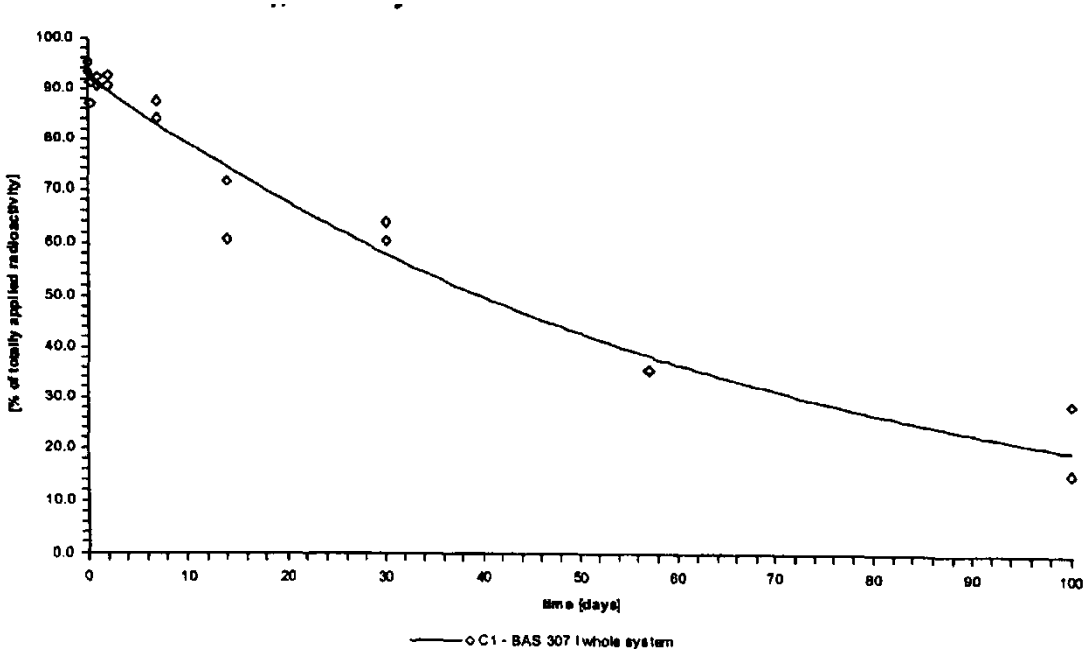


Figure 7.1.2.2.2/ 36 Experimental data and calculated degradation curve for Flufenoxuron and CL932338 in System B (Berghäuser), water and sediment

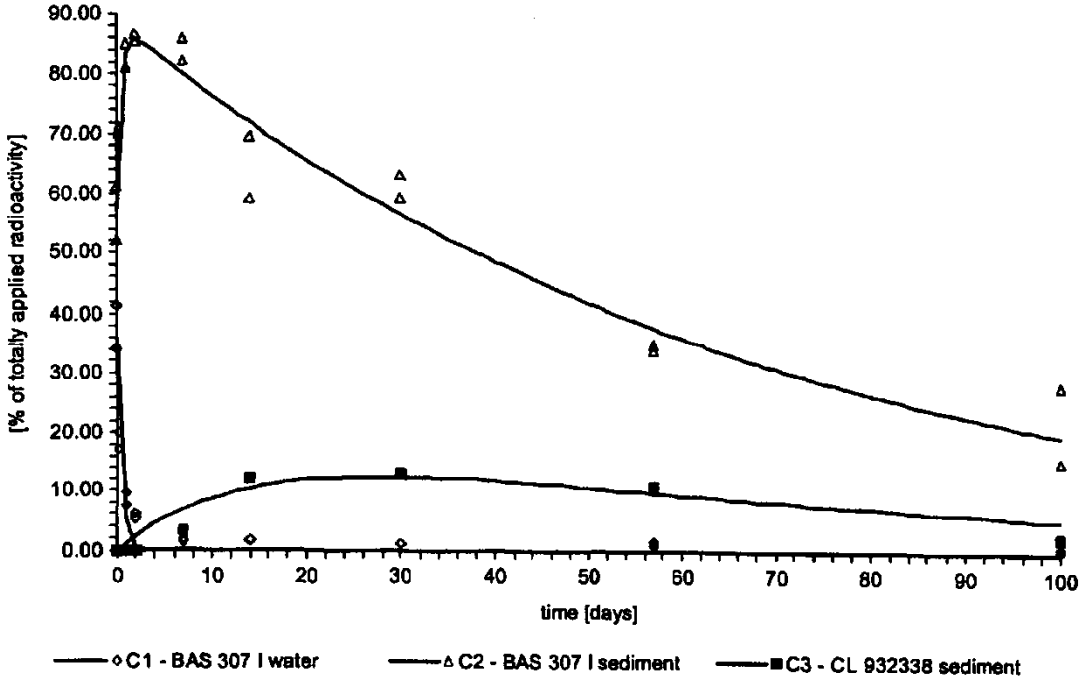
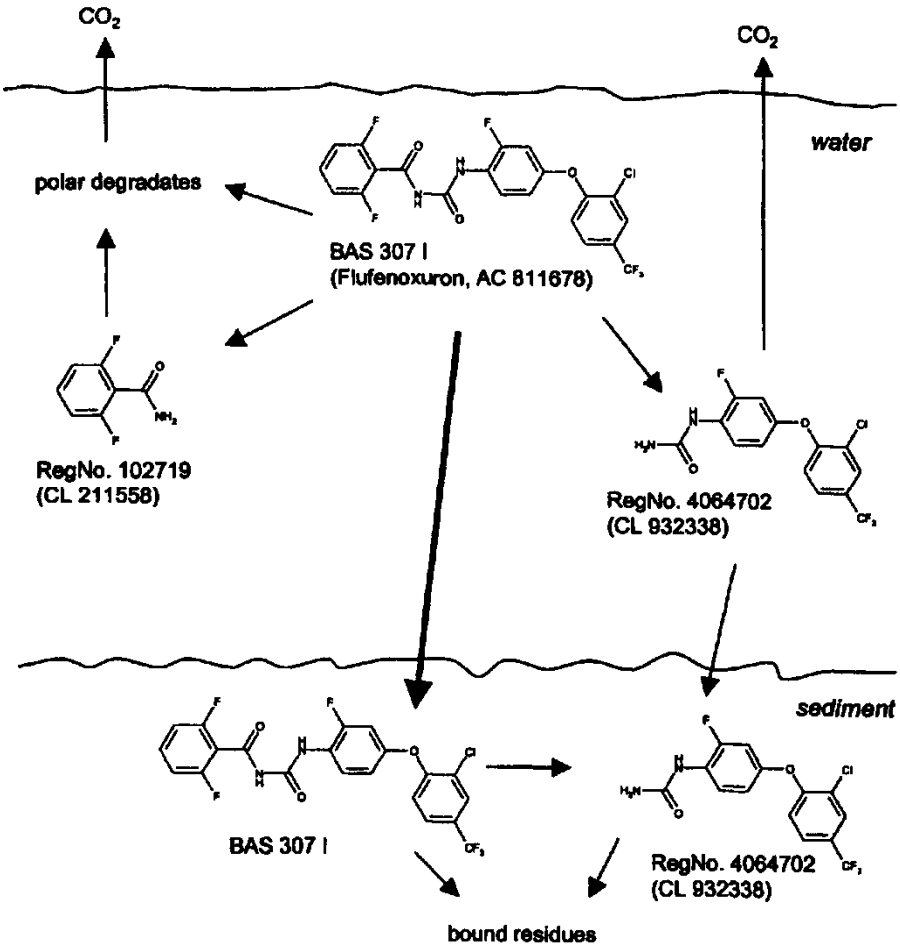


Figure 7.1.2.2.2/ 37 Proposed route of degradation of Flufenoxuron in water/sediment systems



Section A7.1.2.2.2	**Rate and route of degradation in aquatic systems**
BPD Annex Point IIA, XII.2.1	7.1.2.2.2 Biodegradation in freshwater – Water/sediment degradation study

Official use only

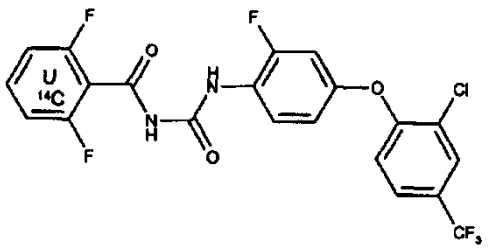
1. REFERENCE

1.1.	**Reference**	**2) Fent G. (2003)** Degradation and distribution of BAS 307 I in a water-sediment system under outdoor conditions. XXXX. unpublished XXXX
1.2.	**Data protection**	Yes
1.2.1.	Data owner	BASF
1.2.2.	Companies with letter of access	XXXX
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I

2. GUIDELINES AND QUALITY ASSURANCE

2.1.	**Guideline study**	Yes, OECD Guideline, "Aerobic and anaerobic transformation in aquatic sediment systems", Draft Aug 2001.
2.2.	**GLP**	Yes (laboratory certififed by Landesanstalt fuer Pflanzenbau und Pflanzenschutz Rheinland-Pfalz, Mainz)
2.3.	**Deviations**	Yes, realistic outdoor temperature fluctuations instead of constant temperature; natural sunlight irradiation instead of incubation in the dark; preparation of mass balance without quantification of volatile compounds

3. MATERIALS AND METHODS

Test material	[difluorobenzamide-U-^{14}C]-Flufenoxuron [fluoroaniline-U-^{14}C]-Flufenoxuron
Lot/Batch number	[XXXX
Specification	See below
Radiolabeling	 [difluorobenzamide-U-^{14}C]-Flufenoxuron

Section A7.1.2.2.2	**Rate and route of degradation in aquatic systems**
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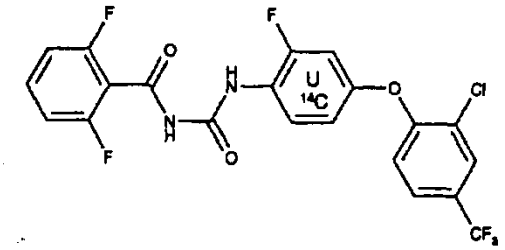

[fluoroaniline-U-^{14}C]-Flufenoxuron

Purity		[difluorobenzamide-U-^{14}C]-Flufenoxuron - >99% radiopure [fluoroaniline-U-^{14}C]-Flufenoxuron - >99% radiopure	
Specific Activity		[difluorobenzamide-U-^{14}C]-Flufenoxuron - 7.6 MBq/mg [fluoroaniline-U-^{14}C]-Flufenoxuron - 3.89 MBq/mg	
3.1.1.	Further relevant properties	The solubility of Flufenoxuron in water is 183 µg/l at pH 4, 136 µg/l at pH 7 and 369 µg/l at pH 9. Flufenoxuron is hydrolytically stable under neutral and acidic conditions.	X
	Composition of Product	Not applicable	
	TS inhibitory to microorganisms	No	
Reference substance		Yes. Reference substances used for co-chromatography are shown in Table 7.1.2.2.2/ 71.	
3.2.	**Testing procedure**		
3.2.1.	Test system	The water/sediment system taken for this study was of the same origin as one of the systems used for the aerobic aquatic metabolism (Kellmetschweiher). The water/sediment characteristics are summarized in Table 7.1.2.2.2/ 74. Glass test vessels were filled with about 2.0 cm sediment (about 400 g) and a water layer of about 20 cm height (about 2000 ml). The system was allowed to equilibrate for 11 days before treatment. To avoid algae blooms as long as possible, the vessels were covered with aluminum foil, which was finally removed at the day of application. The water/sediment systems were placed in big isolated plastic tanks, filled to a distinct level with water in order to simulate a bigger water body with respective temperature compensation. The tanks were located outdoors in the lysimeter station of the test facility (XXXX) in order to have outdoor temperature and light conditions (treatment date July 29th, 2002). In order to protect the vessels from rainfall they were placed under special Plexiglas covers, which allowed UV and visible light transmission. If no rainfall was forecast the Plexiglas cover was removed. Benzamide- and fluoroaniline-labeled Flufenoxuron were used for	X

Section A7.1.2.2.2	**Rate and route of degradation in aquatic systems**
BPD Annex Point IIA, XII.2.1	7.1.2.2.2 Biodegradation in freshwater – Water/sediment degradation study

		treatment in separate experiments. Flufenoxuron was applied at a rate of about 13 µg/l or 26 µg per test vessel. Samples were taken at 0, 2, 4, 7, 14, 30, 59, 100, and 120 days after application. One test vessel was worked up per sampling day except for day 0 where two replicates were taken and analyzed.	
3.2.2.	Analytical procedures	After decantation the water was subjected to liquid-liquid extraction with ethyl acetate. The organic phases were analyzed by LSC and HPLC. The remaining aqueous phases were measured by LSC and if radioactivity was still greater than 5% TAR, a 500 ml aliquot was evaporated to dryness, redissolved and also analyzed by HPLC. The sediments were extracted four times with acetonitrile (each extraction step 30 min). The corresponding extracts were combined, measured by LSC, and then concentrated and analyzed by HPLC. The identity of degradation products was verified by co-chromatography with reference substances using HPLC and TLC. See Table 7.1.2.2.2/ 72 and Table 7.1.2.2.2/ 73 for conditions. Volatiles could not be trapped, however, it is assumed that the increasing balance deficiencies occurring during this study can be attributed to the formation of CO_2 as found in the water/sediment study performed in the dark. The amount of non-extractable residues in the sediment was determined by combustion.	
3.2.3.	Intermediates/ degradation products	The identity of degradation products was verified by co-chromatography with reference substances using HPLC and TLC.	
3.2.4.	Controls	Two control vessels were treated with unlabeled Flufenoxuron and used for determination of physico chemical properties.	
3.2.5.	Statistics	Results were analyzed by Model Maker 3.0.4 to determine rates for two models, one for the simple first order disappearance of Flufenoxuron from the total system, and a multi compartment model, including compartments for water, sediment, and Flufenoxuron degradate CL 932338 (Reg. No. 4064702).	
		4. RESULTS	
4.1.	**Degradation of test substance**		
4.1.1.	Distribution of Radiocarbon and Mass Balance	The distribution of radiocarbon and mass balance for each interval is shown in Table 7.1.2.2.2/5. Because $^{14}CO_2$ was not accounted for, the mass balance decreased during the course of the study from >90% to 60 to 70%.	X
4.1.2.	Graph	The degradation of Flufenoxuron in the total system is shown in Figure 7.1.2.2.2/ 38. The distribution of Flufenoxuron between the water and sediment, its degradation, and the formation and degradation of CL 932338 are shown in Figure 7.1.2.2.2/ 39	X
4.1.3.	DT_{50}/DT_{90}	The DT_{50} for Flufenoxuron in the whole systems was 43 days. Flufenoxuron moved rapidly from the water to the sediment with a DT_{50}	

Section A7.1.2.2.2	**Rate and route of degradation in aquatic systems**
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		in the water of 4.7 days. CL 932338 was the only metabolite at sufficient levels for analysis and its DT_{50} was determined to be 36 days in the sediment and 174.6 days in the water. A summary of DT_{50} and DT_{90} values and the associated r^2 values is given in Table 7.1.2.2.2/ 77.	
4.1.4.	Intermediates/ degradation products	CL 211558, 2,6-difluorobenzamide, was found in the water at a maximum of 9% of the dose at 30 days, declining to 4%at the end of the study and in the sediment at a maximum of 12% at 59 days after treatment, declining to 8% at the end of the study.	X
4.1.5.	Bound Residues	Bound residues increased throughout the study for both labels, reaching maximums of 40 and 36% for the difluorobenzamide and fluoroaniline labels respectively.	
4.1.6.	Mineralization to CO_2	Mineralization to CO_2 was not monitored, but is presumed to account for the decreasing mass balance or 26 to 39% of the radiocarbon.	
		5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1.	**Materials and methods**	The distribution and degradation of Flufenoxuron was studied in a natural water/sediment system according to SETAC guidelines, except that it was conducted outdoors under natural light and subject to natural temperature fluctuations and no volatiles were collected. Two forms of ^{14}C labeled Flufenoxuron were applied separately to pre-equilibrated water/sediment systems. Systems were analyzed after incubation outdoors in summer in southwestern Germany for up to 120 days. The water was partitioned with ethyl acetate and the sediment extracted with acetonitrile, followed by combustion.	
5.2.	**Results and discussion**	Flufenoxuron moved rapidly from the water into the sediment. Flufenoxuron was degraded with a DT_{50} in the whole system of 43 days. CL 932338 reached 12% of the dose in the sediment at 59 days after application. As much as 40% of the original dose of radiocarbon was unextracted from the sediment with acetonitrile. The proposed degradation pathway for Flufenoxuron in aquatic systems is shown in Figure 7.1.2.2.2/ 40. The importance of microbes in the degradation of Flufenoxuron in aquatic systems was shown by no degradation in sterile systems.	
5.3.	**Conclusion**	Flufenoxuron moves rapidly to sediments in aquatic systems where it is metabolized, resulting primarily in bound residues and mineralization to CO_2. The only metabolite reaching > 5% of the applied dose at any time during the study was CL 932338 (“urea”, Reg. No. 4044702). The DT_{50} for Flufenoxuron in the whole system was 43 days, or 4.7 days in the water and 46.1 days in the sediment. The DT_{50} for CL 932338 was 175 days in the water and 36 days in the sediment.	
5.3.1.	Reliability	1	
5.3.2.	Deficiencies	No	

Section A7.1.2.2.2	**Rate and route of degradation in aquatic systems**
BPD Annex Point IIA, XII.2.1	7.1.2.2.2 Biodegradation in freshwater – Water/sediment degradation study

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/02/2005
Materials and Methods	Applicant's version is acceptable, provided the following amendments: - 3.1.1. Further relevant properties: The entry should be read as: "*The solubility of Flufenoxuron in water is* [1.86 µg/l] *at pH 4,* [1.36 µg/l] *at pH 7 and* [3.69 µg/l] *at pH 9,* [(see Doc IIIA, section 3.5)]. - 3.2.1 Test system: add a t the end of the second sentence: "*The water/sediment characteristics are summarized in* table 7.1.2.2.2/5*."*
Results and discussion	Applicant's version is acceptable, provided the following amendments: - 4.1.1 Distribution of Radiocarbon and Mass Balance: change link to "*Table 7.1.2.2.2/5*" to link to "*Table 7.1.2.2.2/16*." - 4.1.2 Graph: delete repeated word "Figure". - 4.1.4 Intermediates/degradation products: The first sentence should be read: "[CL932338] *was found in the water at a maximum of 9% of the dose at 30 days, declining […]."*
Conclusion	Applicant's version is acceptable.
Reliability	3 A statement on the validity of the study was not provided in view of the validity criteria proposed in OECD Guideline 308 , under point 5.3 (recovery, Repeatability and sensitivity of analytical method, Confidence intervals for hydrolysis kinetic data).
Acceptability	Not acceptable Deviations from OECD Guideline 308 (outdoor conditions) were included in the experimental protocol in order to increase the representativity of this study (higher Tier study). The limit of detection or limit of quantification is not given into the document. The material balance deficit was up to 38.8 %.
Remarks	The results obtain in outdoor conditions do not differs greatly from the result of the indoor study (dark conditions). - DT_{50} are slightly shorter in outdoor condition (DT_{50} whole system = 42.9d, Kellmetschweiher system) than in dark conditions (DT_{50} whole system = 61d, Kellmetschweiher system). Conversely, DT_{50} of metabolite CL 932338 in sediment are increased. - The metabolic pathway proposed are very similar, excepted for the limited possible formation of CL245508 and CL359882 in irradiated conditions.

Section A7.1.2.2.2 **Rate and route of degradation in aquatic systems**

BPD Annex Point IIA, XII.2.1 7.1.2.2.2 Biodegradation in freshwater – Water/sediment degradation study

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.1.2.2.2/ 71 Reference substances for co-chromatography

	Batch No.	**Purity**
Flufenoxuron	XXXX	99.3%
Reg. No. 241208 (CL359882)	**XXXX**	99%
Reg No. 206925 (CL 245508)	**XXXX**	99%
Reg No. 102719 (CL211558)	**XXXX**	100%
Reg No. 4064702 (CL932338)	**XXXX**	95%

Table 7.1.2.2.2/ 72 HPLC Conditions

HPLC System	Jasco LG-980-02S mixer Jasco PU-980 Intelligent HPLC pump Jasco AS1555 Intelligent sampler	
Pre-column	Phenomenex Ultracarb 10 ODS (30), 50 x 10 mm	
Column	Phenomenex Ultracarb 7 ODS (30), 250 x 4.6 mm	
Solvent A	water:acetonitrile:acetic acid, 900:100:1	
Solvent B	acetonitrile:acetic acid. 1000:1	
Gradient	Time (min)	%B
	0	0
	15	100
	29	100
	31	0
	37.5	0
Flow rate	1 mL/min	
UV detection	Jasco UV-1575 Intelligent UV/VIS detector,254 nm	
^{14}C detection	Canberra Packard A-525 AX Radio-HPLC-detector	

Table 7.1.2.2.2/ 73 TLC conditions

Stationary phase	Merck Silica gel plates, F_{254}, 0.25 mm
Mobile phase	Ethyl acetate:toluene, 1:1
R_f	Flufenoxuron – 0.53 CL932338 – 0.0.13

Table 7.1.2.2.2/ 74 Characterization of the water/sediment system Kellmetschweiher used for the water/sediment study with Flufenoxuron under outdoor conditions

water/sediment designation origin		Kellmetschweiher Schifferstadt, Rhineland Palatinate, Germany
water	pH at site of sampling	8.3
	TOC [mg/l]	15.8
	total hardness [mmol/l]	2.01
	plate counts [cfu/ml]	
	bacteria	8.8×10^3
	fungi	10
	actinomycetes	0
sediment	textural class (German scheme)	sand
	clay [%]	2.7
	silt [%]	1.7
	sand [%]	95.6
	plate counts [cfu/g]	
	bacteria	2.8×10^6
	fungi	2.9×10^3
	actinomycetes	1.3×10^4
	organic C [%]	0.14
	nitrogen total [%]	0.003
	phosphorus [mg/kg]	42

Table 7.1.2.2.2/ 75 Material balance and distribution of radioactivity after application of [^{14}C]-Flufenoxuron to water/sediment system Kellmetschweiher and incubation under outdoor conditions

DAT	%TAR							
	water			sediment			material balance	material balance deficit
	ethyl acetate	remaining H_2O	total	acetonitrile	non-extractable	total		
benzamide-label								
0*	75.2	0.5	75.7	18.2	0.1	18.2	93.9	6.2
2	57.1	2.7	59.8	31.9	0.7	32.6	92.4	7.6
4	35.4	3.2	38.6	51.6	1.5	53.1	91.7	8.3
7	23.5	4.3	27.8	58.5	3.1	61.6	89.4	10.6
14	16.4	7.7	24.1	53.4	7.6	61.0	85.1	14.9
30	6.3	8.9	15.2	38.6	25.9	64.5	79.7	20.3
59	1.6	6.5	8.1	25.6	38.2	63.8	71.9	28.1
100	1.4	7.4	8.8	25.2	27.2	52.4	61.2	38.8
120	1.6	7.0	8.6	23.3	39.6	62.9	71.5	28.5
fluoroaniline-label								
0*	68.8	0.7	69.5	21.3	0.2	21.5	91.0	9.1
2	55.7	2.3	58.0	34.9	0.8	25.7	93.7	6.3
4	40.4	2.6	43.0	47.3	1.4	48.7	91.7	8.3
7	26.8	3.5	30.3	59.4	2.3	61.7	92.0	8.0
14	20.7	4.0	24.7	61.3	4.6	65.9	90.6	9.4
30	15.2	6.7	21.9	49.6	15.0	64.6	86.5	13.5
59	7.3	9.1	16.4	34.9	29.8	64.7	81.1	18.9
100	5.4	7.9	13.3	30.8	29.4	60.2	73.5	26.5
120	5.0	8.1	13.1	30.7	36.3	67.0	80.1	19.9

* mean of two test vessels

Table 7.1.2.2.2/ 76 HPLC analysis of the water and sediment extracts of system Kellmetschweiher after application of [^{14}C]-Flufenoxuron

DAT	%TAR				
	"urea" CL932338 Reg.No. 4064702 fluoroaniline-label	**polar unknowns**** benzamide-label	**polar unknowns***** fluoroaniline-label	**Flufenoxuron** benzamide-label	**Flufenoxuron** fluoroaniline-label
water (ethyl acetate + remaining water)					
0*			1.3****	75.2	67.5
2	1.1			57.1	54.6
4	1.7			35.4	38.7
7	2.6			23.5	24.2
14	5.4	3.4		20.6	15.3
30	9.3	7.9	6.0	7.3	6.6
59	5.7	5.9	9.1	2.2	1.6
100	4.5	7.4	8.0	1.4	0.9
120	3.9	7.0	8.0	1.6	1.1
sediment					
0*				18.2	21.3
2				31.9	34.9
4	0.6			51.6	46.7
7	1.6			58.5	57.8
14	3.7			53.4	57.6
30	8.5			38.6	41.1
59	12.0			25.6	22.9
100	9.3			25.2	21.5
120	8.5			23.3	22.2

* mean of two test vessels; ** multiple polar peaks, each single peak ≤ 4.1% TAR; *** multiple polar peaks, each single peak < 2.5%TAR

Table 7.1.2.2.2/ 77 Degradation rates of Flufenoxuron and metabolite CL 932338 in water/sediment system Kellmetschweiher under outdoor conditions

system		**DT_{50} first order [days]**	**DT_{90} first order [days]**	**r^2**
Flufenoxuron	whole system	42.9	142.5	0.95
Flufenoxuron	water	4.7	15.5	0.97
Flufenoxuron	sediment	46.1	153.0	0.97
"urea", CL 932338	water	174.6	580.1	0.97
"urea", CL 932338	sediment	36.3	120.4	0.97

Figure 7.1.2.2.2/ 38 Experimental data and calculated degradation curve for Flufenoxuron in an outdoor aquatic system, overall model

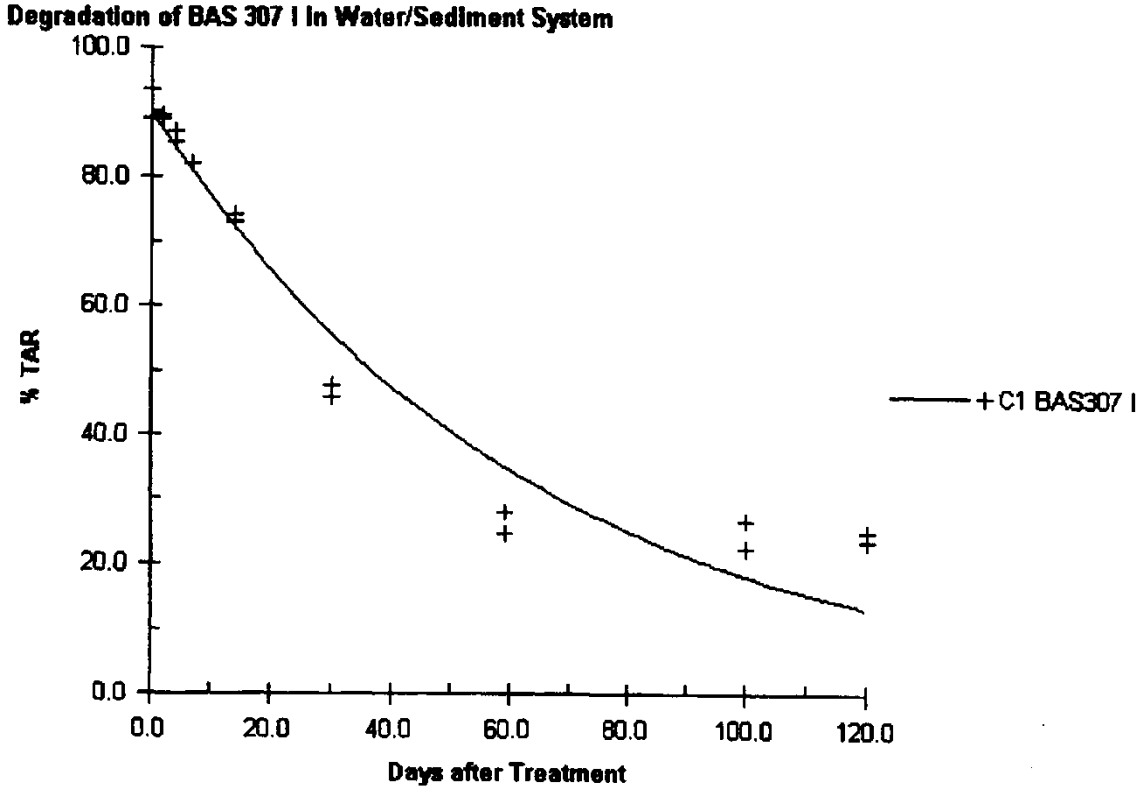


Figure 7.1.2.2.2/ 39 Experimental data and calculated degradation curve for Flufenoxuron and CL932338 in an outdoor aquatic system, water and sediment

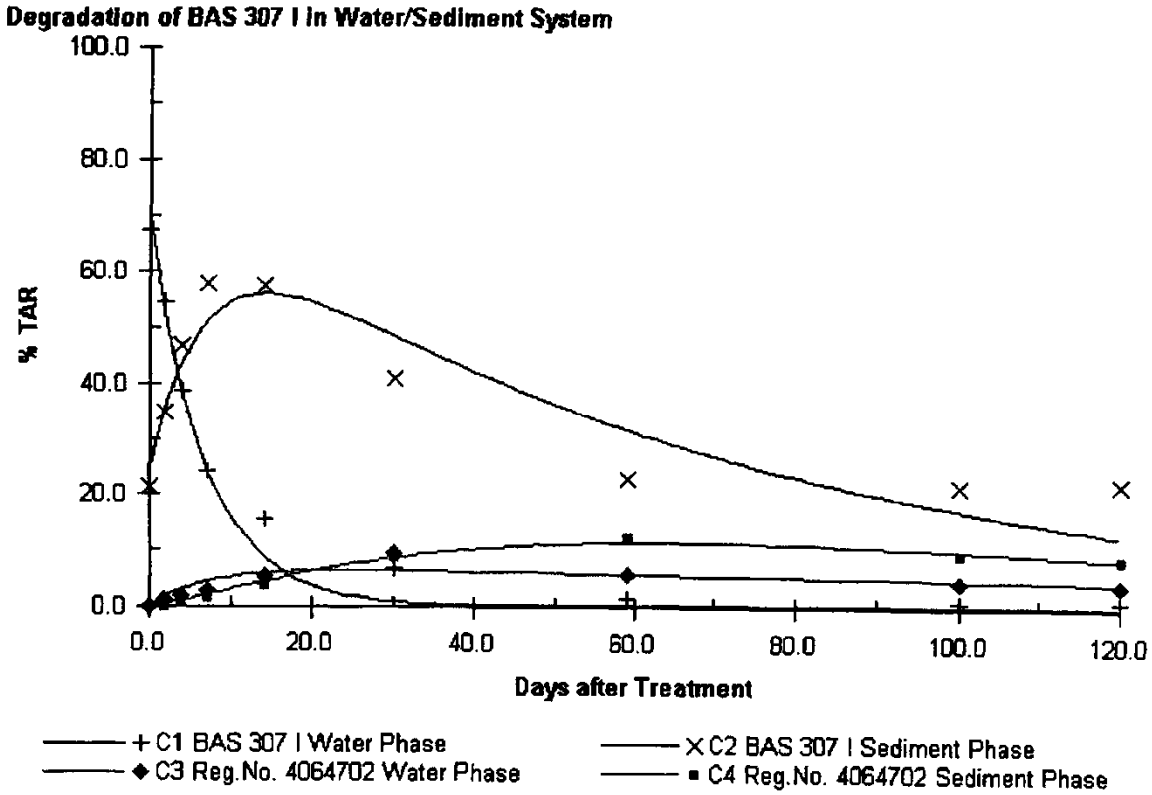


Figure 7.1.2.2.2/ 40 Proposed route of degradation of Flufenoxuron in the aquatic environment

Section A7.1.3 **Adsorption / Desorption screening test**

BPD Annex Point IIA, VII.7.7

	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [X]	**Technically not feasible [ ] Scientifically unjustified [X]**	
Limited exposure [ ]	**Other justification [ ]**	
Detailed justification:	Flufenoxuron and its "urea" metabolite are strongly binding to soil as shown in Table 7.1.3/ 1, Table 7.1.3/ 2 and Table 7.1.3/ 3 below. Details of the study are given under IIIA 7.2.3. Therefore no further studies are required.	
Undertaking of intended data submission [ ]	Not applicable	

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted

	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/02/2005
Evaluation of applicant's justification	Applicant's version is acceptable.
Conclusion	Applicant's version is acceptable.
Remarks	

Section A7.1.3 **Adsorption / Desorption screening test**

BPD Annex Point IIA, VII.7.7

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion. Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.1.3/ 1 Adsorption data for [^{14}C]-Flufenoxuron on different soils

Soil	pH ($CaCl_2$)	K_d (ml/g)	K_{OC} (ml/g)
***Hill & Standen* 1993**			
Godstone	6.1	1738	289747
Elm Farm	6.5	3206	178093
Woodstock	6.1	4250	137104
***Rosenwald* 2002**			
Chelmorton	6.1	2756 ± 1282	95030 ± 44220
Kenslow Farm	5.7	3441 ± 1782	88240 ± 45700

Table 7.1.3/ 2 Adsorption data for ^{14}C-"urea" metabolite (CL 932338) on different soils

Soil	pH ($CaCl_2$)	K_F (ml/g)	1/n	K_{FOC} (ml/g)	K_d* (ml/g)	K_{OC}* (ml/g)
Borgeby	5.6	118.5	0.978	8467	145.2	10371
Birnbaum	6.1	37.52	0.922	4690	68.50	8563
2.2 F222002	6.3	101.7	0.918	3928	199.0	7681
Sora Bevern	6.5	63.09	0.895	3711	145.1	8536
Stetten	7.5	52.37	0.968	5237	67.56	6756

Table 7.1.3/ 3 Desorption data for ^{14}C-"urea" metabolite (CL 932338) on different soils

Soil	K_{FdesI} (ml/g)	1/n	$K_{FOCdesI}$ (ml/g)
Borgeby	134.8	0.951	9625
Birnbaum	42.71	0.882	5339
2.2 F222002	60.69	0.819	2343
Sora Bevern H9	129.3	0.935	7604
Stetten	33.19	0.853	3319

Section A7.1.4	**Further studies on Adsorption / Desorption screening test (including metabolites)**
BPD Annex Point IIIA, XII.2.2	7.1.4 Field study on accumulation in the sediment

	JUSTIFICATION FOR NON-SUBMISSION OF DATA	**Official use only**
Other existing data [ ] **Limited exposure [ ]**	**Technically not feasible [ ] Scientifically unjustified [X]** **Other justification [ ]**	
Detailed justification:	Field study on accumulation in the sediment is not required as less than 70% of non-extractable form in the water/sediment study as indicated in *Guidance on data requirement of active substances and biocidal products, final draft version 4.3.2 October 2000)*	
Undertaking of intended data submission [ ]	Not applicable	

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted

	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/02/2005
Evaluation of applicant's justification	Applicant's version is acceptable.
Conclusion	Applicant's justification is acceptable.
Remarks	

Section A7.1.4	**Further studies on Adsorption / Desorption screening test (including metabolites)**
BPD Annex Point IIIA, XII.2.2	7.1.4 Field study on accumulation in the sediment

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A7.2.1	**Aerobic Degradation in Soil**
BPD Annex Point IIIA, VII.4, XII.1.1.	7.2.1 pH effect on soil degradation

0. Justification of the choice of the key study

RMS Comment (01/02/05):

TNG on data requirements for section 7.2.1 is an initial study on aerobic degradation in soil.

One study is submitted under the present section 7.2.1, investigating the pH effect on soil degradation.

Five further studies are submitted under section 7.2.2.1 "Aerobic degradation in soil, further studies" and one in Section 7.2.2.2 " Field soil dissipation and accumulation".

The following study although providing information on the effects of pH **will not be considered as key study** (no GLP, no specific guideline referenced, substance tested as preparation, …).

The notifier did not provide any justification for the choice of a key study but in the IUCLID document, this reference is not identified with a "Risk assessment" flag.

Section A7.2.1	**Aerobic Degradation in Soil**
BPD Annex Point IIIA, VII.4, XII.1.1.	7.2.1 pH effect on soil degradation

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**1) Richardson K (1987)** The effect of pH on the degradation of 14C-WL 155110. XXXX unpublished XXXX	
1.2.	**Data protection**	No	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	No data protection claimed	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	No specific guideline referenced. Methods used comparable to OECD 307 Aerobic and Anaerobic Transformation in Soil (August 2000). Although no specific guidelines are referenced, the study meets the essentials of an aerobic soil degradation study.	
2.2.	**GLP**	No, GLP was not compulsory at the time of the study	
2.3.	**Deviations**	Not applicable	

Section A7.2.1	**Aerobic Degradation in Soil**
BPD Annex Point IIIA, VII.4, XII.1.1.	7.2.1 pH effect on soil degradation

		3. MATERIALS AND METHODS	
3.1.	**Test material**	[aniline-^{14}C, -^{15}N]-Flufenoxuron	
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	See 3.1.1	
3.1.3.	Purity	99% radiopure	
3.1.4.	Specific activity	18.8 µCi/mg (0.7 mBq/mg)	
3.1.5.	Isotope Abundance	^{15}N – 44%	
3.1.6.	Radiolabeling	Fluoroaniline-U-^{14}C	
3.1.7.	Further relevant properties	The solubility of Flufenoxuron in water at pH 4 is 1.9 µg/l	X
3.2.	**Test solution**	The test substance was formulated as an emulsifiable concentrate. A 1 mg aliquot of standard was dissolved in the neat EC formulation (20µL, SF 06727) and 2 mL of water was added to give a final concentration of 488 µg/mL.	
3.3.	**Testing procedure**		
3.3.1.	Test system	A clay loam soil (Hoath, Kent, UK) was freshly sampled from the field and stored at 15°C at field moisture for less than 30 days. The properties of the soil are listed in Table 7.2.1/78. The soil was sieved through a 2 mm screen, adjusted to 42% MHC, and stored at 15ºC for two days before treatment with the test substance. Two experiments were performed, one at natural pH (7.8), the other at a pH of 10.5 by adding sodium carbonate to the soil. Since the experiment at pH 10.5 is considered to be too artificial, it is not described further in this section. Aliquots of 50 g (wet weight) of soil were spiked with 100µL of the formulation and incubated in loosely capped jars in the dark.	
3.3.2.	Temperature	22 ± 2 ºC	
3.3.3.	Duration of the test	90 days	
3.3.4.	Number of replicates	A single replicate was analyzed at each sampling interval	
3.3.5.	Sampling	Soils were sampled in duplicate at 0 and 29 days after treatment and singly at 60 and 90 days. Where duplicates were taken, one was extracted at the time of sampling and the other was stored at –18ºC.	
3.3.6.	Analytical methods	Soils were extracted for two hours with 100 mL of acetonitrile: water (7:3, v:v), filtered, and rinsed twice with 30 mL of acetontrile:water (7:3,v:v), twice with 30 mL of acetonitrile, and twice with 30 mL of	

Section A7.2.1	**Aerobic Degradation in Soil**
BPD Annex Point IIIA, VII.4, XII.1.1.	7.2.1 pH effect on soil degradation

		diethyl ether. The combined extracts were quantitated by LSC and the soil was dried and remaining radioactivity determined by combustion and LSC. An aliquot of the acetonitrile: water extract was partitioned between equal volumes of water and dichloromethane. The water was washed twice with dichloromethane and the organic phase was dried and reduced to a small volume. The concentrated organic phase and the water were analyzed by LSC. Subsamples of the organic phase were analyzed by TLC. Rf values of reference compounds see Table 7.2.1/79.	
3.4.	**Transformation products**	Transformation products tested: Yes	
3.4.1.	Method of analysis for transformation products	Flufenoxuron degradates were identified by TLC with reference standards in two normal phase systems.	X
		4. RESULTS	
4.1.	**Material balance**	Total recoveries ranged from 93 to 97 % of the applied radioactivity.	
4.1.1	Extractability	The amount of extractable radioactivity in the aerobic portion of the study decreased from >99% at day 0 to 76% at day 90, while unextracted radiocarbon increased from <1% to 20% (see Table 7.2.1/80).	
4.2.	**DT_{50}**	The DT_{50} was not reached in this study, but was estimated at 140 days by extrapolation.	
4.2.1.	Concentration values	The concentration of Flufenoxuron decreased from 98% of the applied dose (ca. 1 mg/kg) to 62% at 90 days after application (see Table 7.2.1/80).	
4.3.	**Specification of the transformation products**	"urea"-Flufenoxuron degradate (CL 932338, Reg.No. 4064702) in aerobic soil, reached 14 % of the dose at 90 days after treatment (see Table 7.2.1/80 and Table 7.2.1/81).	
		5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1.	**Materials and methods**	Although no specific guideline is referenced, this study was conducted according to the general principles of aerobic soil degradation studies. [Aniline-^{14}C, -^{15}N]-Flufenoxuron was applied to a clay loam at ca. 1mg/kg using an open system. Soil samples were analyzed at dosing and after 29, 60, and 90 days of incubation in the dark at 22ºC. Soil samples were analyzed by extraction with acetonitrile: water and partition with dichloromethane. The extracts were analyzed by liquid scintillation counting, and the dichloromethane phase by normal phase TLC.	
5.2.	**Results and discussion**		
5.2.1.	Material balance	Total recoveries ranged from 93 to 97 % of the applied radioactivity.	
5.2.2.	DT_{50}	The DT_{50} was not reached in this study, but was estimated at 140 days by	

Section A7.2.1	**Aerobic Degradation in Soil**
BPD Annex Point IIIA, VII.4, XII.1.1.	7.2.1 pH effect on soil degradation

		graphical extrapolation.	
5.2.3.	Transformation products	"urea"-Flufenoxuron degradate (CL 932338, Reg.No. 4064702) was the major metabolite of flufenoxuron under aerobic conditions, reaching 14% of the dose at 90 days after treatment.	
5.3.	**Conclusion**	Flufenoxuron is aerobically degraded in soil with a DT_{50} of about 140 days. "urea"-Flufenoxuron degradate (CL 932338, Reg.No. 4064702) accounted for 14% of the dose at 90 days after treatment. Unextractable residues accounted for 20% of the dose at 90 days. Mineralization to CO_2 was not monitored, but could not have been significant for the labeled portion of the test substance, due to good mass balance.	
5.3.1.	Reliability	1	X
5.3.2.	Deficiencies	No	X

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/02/2005
Materials and Methods	Applicant's version is acceptable, provided the following amendments: - 3.1.7: The test was performed in soils at pH > 7.8. Change the entry to: "*The solubility of Flufenoxuron in water is 1.86 µg/l at pH 4, 1.36 µg/l at pH 7 and 3.69 µg/l at pH 9, (see Doc IIIA, section 3.5). Flufenoxuron is hydrolytically stable under neutral and acidic conditions."* - 3.4.1: Method of analysis for transformation products: add at the end of the paragraph: "Non-labelled Flufenoxuron (B x 13 ST/86/022, compound control), WL115096 (a.k.a. CL 359882; 1693/038, OCR) and WL129183 (a.k.a. CL 932338; 2395/043, OCR) were used as TLC reference markers.

Section A7.2.1	**Aerobic Degradation in Soil**
BPD Annex Point IIIA, VII.4, XII.1.1.	7.2.1 pH effect on soil degradation

Results and discussion	Applicant's version is acceptable, provided the following amendments: 4.1: Material balance and 4.1.1 Extractability: note that the values in Table 7.2.1/3 for Flufenoxuron, "Urea" CL 9332338, and unextracted bound residus are expressed in percentage of the recovered radioactivity, and not as %TAR. 5.3.2 Deficiencies: Change "*No*" to "*Yes"* and add the following remarks: - *One natural "realistic" pH test (7.8) and one artificial unrealistc pH (pH 10.5, by adding sodiumcarbonate)* - *no GLP,* - *no specific guideline referenced,* - *substance tested as preparation,* - *no measurment of loss of volatiles.*
Conclusion	Applicant's version is acceptable
Reliability	3
Acceptability	Not acceptable The following study although providing acceptable information on the effects of pH **will not be considered as key study** (no GLP, no specific guideline referenced, substance tested as preparation, …). The stability of Flufenoxuron is low at high pH (hydrolysis), and the conditions of this test may be considered as too favourable for the study of degradation of Flufenoxuron.
Remarks	

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.2.1/78: Soil Characteristics

Soil designation	Hoath (Kent)
Textural class	clay loam
Origin	Hoath, Kent, UK
Particle size distribution [%] 0.06 – 2 mm 0.002 – 0.06 mm < 0.002 mm	 32 42 25
Organic matter [% dry weight] Organic carbon [%]	2.2 1.3
CEC [meq/100g]	16
pH	7.8
MWC [g H_2O/100g dry soil]	60

Table 7.2.1/79: TLC Conditions

Plate	Solvent System	Rf		
		Flufenoxuron	"urea" CL 932338, Reg.No. 4064702	"amine" CL359882 Reg.No. 241208
Merk Silica Gel F_{254} 0.25mm, 5715	Ethyl acetate:toluene 1:1	0.8	0.2	--
	Hexane:diethyl ether 1:1	0.4	0.04	--
	Hexane:diethyl ether 1:2	0.7	0.1	0.8
	Hexane:diethyl ether 1:3 + 0.1% aq ammonia	0.5	0.1	0.7

Table 7.2.1/80: Recovery of radioactivity and distribution of metabolites after application of [^{14}C]-Flufenoxuron to soil and incubation under aerobic conditions [%TAR (total applied radioactivity)]

DAT	**Flufenoxuron WL 115110**	**"urea" WL 129183 CL 932338**	**unextracted (bound residues)**	**material balance**
0	98	n.d.	<1	99
29	90	5	3	98
60	82	6	11	99
90	62	14	20	96

Table 7.2.1/81: Specification and amount of transformation products

Lab/Report Code, CAS, and/or IUPAC Chemical Name(s)	**Amount [%] of parent compound measured**
WL 129183 (CL 932338) CAS not available N-{4-[2-chloro-4-(trifluoromethyl) phenoxy]-2-fluoromethyl}urea	Max. 14% at 90 days

Section A7.2.2.1	**Rate and route of degradation**
BPD Annex Point IIIA, VII.4, XII.1.1, XII.1.4	IIIA 7.2.2.1 Aerobic degradation in soil

0. Justification of the choice of the key study

RMS Comment (01/02/05):

TNG on data requirements for section 7.2.2 is an initial study on aerobic degradation in soil.

One study was submitted under section 7.2.1, investigating the pH effect on soil degradation.

Five further studies are submitted under section 7.2.2.1 "Aerobic degradation in soil, further studies" and one in Section 7.2.2.2 " Field soil dissipation and accumulation".

The notifier did not provide any justification for the choice of a key study

- References 1 & 2 (Richardson, 1990; 1991) (see page 2 ; comments on page 6): was not identified by the notifier with a "Risk assessment" flag in the IUCLID document. RMS agrees that this study **would not be considered as key study** (only one ring labelled, one soil tested…). See also section 7.2.2.4. "Anaerobic degradation in soil."

- Reference 3 (Standen and Hill, 1993) (see page 12 ; comments on page 17) was not identified by the notifier with a "Risk assessment" flag in the IUCLID document. RMS agrees that this study **would not be considered as key study** (one soil tested…). See also section 7.2.2.4. "Anaerobic degradation in soil."

- Reference 4 (Goodyear and Gross, 2001) (see page 22 ; comments on page 27) is an "aerobic soil rate of degradation in three soils" study of reliability 2 and **is considered as key study for Flufenoxuron.**

- Reference 5 (Stephan and Ebert, 2003) (see page 38 ; comments on page 43) is an "aerobic soil rate of degradation in three soils" study of reliability 2 conducted with flufenoxuron and its metabolite Reg. No. 4064702 and **is considered as key study for Flufenoxuron and its metabolite Reg. No. 4064702.**

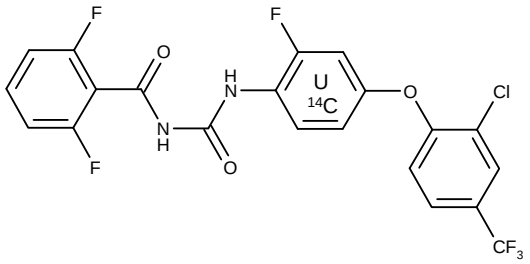
- Reference 6 (Beigel, 2004) (see page 52) is a calculation of DT_{50} at 10°C

Section A7.2.2.1	**Rate and route of degradation**
BPD Annex Point IIIA, VII.4, XII.1.1, XII.1.4	IIIA 7.2.2.1 Aerobic degradation in soil

Official use only

		1. REFERENCE
1.1.	**Reference**	**1) Richardson K (1990)** A comparison of the degradation of [aniline-^{14}C] Flufenoxuron in soil under aerobic and anaerobic conditions. XXXX unpublished XXXX **2) Richardson K (1991)** A comparison of the degradation of [aniline-^{14}C] Flufenoxuron in soil under aerobic and anaerobic conditions (corrigendum). XXXX unpublished XXXX
1.2.	**Data protection**	No
1.2.1.	Data owner	BASF
1.2.2.	Companies with letter of access	XXXX
1.2.3.	Criteria for data protection	No data protection claimed
		2. GUIDELINES AND QUALITY ASSURANCE
2.1.	**Guideline study**	No specific guideline referenced. Methods used comparable to OECD 307 Aerobic and Anaerobic Transformation in Soil (August 2000)
2.2.	**GLP**	Yes, (laboratory certified by Department of Health of the Government of the United Kingdom, United Kingdom)
2.3.	**Deviations**	Not applicable
		3. MATERIALS AND METHODS
3.1.	**Test material**	[aniline-^{14}C]-flufenoxuron
3.1.1.	Lot/Batch number	Sample No. 1094/2, synthesis ref. 3577-014
3.1.2.	Specification	See below
3.1.3.	Purity	99% radiopure
3.1.4.	Specific activity	31.5 µCi/mg (1.2 MBq/mg)

Section A7.2.2.1	**Rate and route of degradation**
BPD Annex Point IIIA, VII.4, XII.1.1, XII.1.4	IIIA 7.2.2.1 Aerobic degradation in soil

3.1.5.	Radiolabeling		
3.1.6.	Further relevant properties	The solubility of Flufenoxuron in water is 186 µg/l at pH 4, 136 µg/l at pH 7 and 369 µg/l at pH 9.	X
3.2.	**Test solution**	The test substance (49.6 mg) was milled to a fine (VMD = 0.8 µm) particle size in a ball mill with an aqueous dispersing agent and Zirconia beads. The resulting suspension was diluted to 100 mL and a 1.45 g aliquot was diluted with 28.6 g of deionized water on the day before application.	
3.3.	**Testing procedure**		
3.3.1.	Test system	Soil, sampled from 'motorway' field (O.S. Map reference – 896E/602N) at Sittingbourne Research Centre to a depth of 10 cm (see Table 7.2.2.1/82), was sieved (2 mm) and stored for 13 days at 4ºC. The soil was brought to room temperature and aliquots (50 g dry weight basis) were weighed into biometer flasks (Figure 7.2.2.1/41), adjusted to 21% moisture and left in the dark at 21ºC for 9 days before treatment with the test substance. Lucerne meal (0.25 g) was added to the anaerobic samples. One ml of treatment suspension (a treatment rate of 0.5mg/kg) was added to the soils. The anaerobic samples were immediately flooded with deionized water and purged with nitrogen. The aerobic samples were purged with moist, CO_2 free air. The soils were incubated in the dark at 21 ± 2 ºC. The flasks were flushed weekly, unless within 4 days of a sampling period, with either nitrogen or air, pushing any volatiles present into the KOH and polyurethane traps.	
3.3.2.	Temperature	21 ± 2 ºC	
3.3.3.	Duration of the test	152 days	
3.3.4.	Number of replicates	A single replicate each of aerobic and anaerobic soil was analyzed at each sampling period	
3.3.5.	Sampling	Soil samples were taken immediately after treatment and at 15, 30, 61, 90, and 152 days after treatment. KOH and polyurethane plugs were sampled at each soil sampling, and additional KOH samples were taken at 44, 75, 105, 120, 135, and 166 days (before the decision to terminate the study at 152 days).	
3.3.6.	Analytical methods	At each sampling period the KOH and the polyurethane plug were removed and the plug was extracted three times with methanol. Aliquots of the KOH and the MeOH extract were assayed using LSC.	

Section A7.2.2.1	**Rate and route of degradation**
BPD Annex Point IIIA, VII.4, XII.1.1, XII.1.4	IIIA 7.2.2.1 Aerobic degradation in soil

		Fresh KOH was added to the trap and the polyurethane plug was replaced if the soil was not sampled. After sampling, the soil was extracted with acetonitrile: water (7:3, v:v, 100 mL) for 2 hours, filtered, then rinsed with acetonitrile:water, acetonitrile, and diethyl ether. For the anaerobic experiment, the water layer was decanted and assayed by LSC. The combined extracts and washings were assayed by LSC. The soil was further extracted with 100 mL of 0.1M $CaCl_2$, followed by centrifuging and decanting and LSC of the aqueous phase. The samples were then extracted again with acetonitrile: water as before. The extracted soil was dried at room temperature and analyzed by combustion and LSC. An aliquot of the acetonitrile/water extracts was partitioned between equal volumes of water and dichloromethane.The aqueous phase was partitioned with up to 5 more volumes of dichloromethane then assayed by LSC. The combined organic phase was dried with anhydrous sodium sulphate, assayed by LSC, and concentrated under reduced pressure and analyzed by TLC with reference standards (See Table 7.2.2.1/83).The radioactivity on the plates was located and quantitated using an Isomess-3200 Linear Analyzer. Unlabeled reference standards were visualized with UV light. Combustion was done using a Packard 306 samples oxidizer and the $^{14}CO_2$ was trapped in 8 ml of Carbosorb, mixed with 13 ml of Permafluor, and analyzed by LSC. LSC was done with a Packard 2200 liquid scintillation counter. Optiphase 'Safe' scintillation fluid was used for assay of solutions.	
3.4.	**Transformation products**	Transformation products tested: Yes	
3.4.1.	Method of analysis for transformation products	Flufenoxuron degradates were identified by TLC with reference standards in two normal phase systems.	X
		4. RESULTS – AEROBIC EXPERIMENT (Results for the anaerobic part are summarized in Section A7.2.2.4)	
4.1.	**Material balance**	Total recoveries were all between 94.4 and 100.5 % of the total applied radioactivity (TAR) (aerobic part of the study).	
4.1.1	Extractability	The amount of extractable radioactivity in the aerobic part of the study decreased from 100.2% at day 0 to 56.7% at day 152, while unextracted radiocarbon increased from 0.3% to 34.0%. Mineralization to CO_2 accounted for 3.7% TAR at the end of the study. See Table 7.2.2.1/84.	
4.2.	**DT_{50}**	The DT_{50} in the aerobic study phase at experimental temperature condition was reached between the 90 and 152 day samplings and was estimated to be about 120 days. In order to estimate the half-life at 12°C, the temperature correction was	

Section A7.2.2.1	**Rate and route of degradation**
BPD Annex Point IIIA, VII.4, XII.1.1, XII.1.4	IIIA 7.2.2.1 Aerobic degradation in soil

		done with the following equation assuming a temperature difference to the reference condition of approx. 10°C: DT_{50} (12°C) = DT_{50} x e (0.08 x 10). The respective calculated DT_{50} is then 267 days.	
4.2.1.	Concentration values	The concentration of Fufenoxuron decreased from 100.2% TAR (0.5 mg/kg) to 35.8% at 152 days after application. See Table 7.2.2.1/84.	
4.3.	**Specification of the transformation products**	The "urea" Flufenoxuron degradate (CL932338, Reg.No. 4064702) reached 14.5% TAR at 152 days after treatment. The "amine" degradate (CL 359882, Reg.No. 241208) was detected, but only at 152 days and less than 1% TAR. (See Table 7.2.2.1/84 and Table 7.2.2.1/85).	
		5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1.	**Materials and methods**	Although no specific guideline is referenced, this study was conducted according to the general principles of aerobic and anaerobic soil degradation studies. [Aniline-^{14}C]Flufenoxuron was applied to a silty clay loam at 0.5mg/kg using a closed system with periodic flushing with either moist, CO_2 free air (aerobic) or nitrogen (anaerobic). Polyurethane foam and KOH were used to trap volatiles and CO_2 respectively. Anaerobic samples were amended with lucerne meal and flooded and flushed with nitrogen immediately after application. Soil samples were analyzed at dosing and after 15, 30, 61, 90, and 152 days of incubation in the dark at 25ºC. Soil samples were analyzed by extraction with acetonitrile: water and partition with dichloromethane. The extracts were analyzed by liquid scintillation counting, and the dichloromethane phase by normal phase TLC.	
5.2.	**Results and discussion**		
5.2.1.	Material balance	Total recoveries were all between 94.4 and 100.5 % TAR (aerobic part of the study). .	
5.2.2.	DT_{50}	The DT_{50} value of Flufenoxuron was reached between the 90 and 152 day samplings, and was estimated at about 120 days (21°C). Temperature correction to 12°C leads to an estimated DT_{50} of 267 days.	
5.2.3.	Transformation products	The "urea" Flufenoxuron degradate (WL129183, CL932338, Reg.No. 4064702) under aerobic conditions reached 14.5% TAR at 152 days after treatment. The "amine" degradate (WL115096, CL359882, Reg.No. 241208) was detected, but only at 152 days and less than 1% TAR.	X
5.3.	**Conclusion**	Flufenoxuron is aerobically degraded in soil with a DT_{50} of about 120 days at 21°C (267 days at 12°C). Its “urea” metabolite accounted for 15.6% TAR at 90 days after treatment and slighlty decreased to 14.5% TAR at 152 days. The conversion to unextractable residues is a major route, accounting for 34% TAR at 152 days, and mineralization to CO_2 accounted for only 4% TAR.	
5.3.1.	Reliability	1	

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5.3.2. Deficiencies No

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/02/2005
Materials and Methods	Applicant's version is acceptable providing the inclusion of the following amendments: - 3.1.7. Further relevant properties: The entry should be read as: "*The solubility of Flufenoxuron in water is* [1.86 µg/l] *at pH 4,* [1.36 µg/l] *at pH 7 and* [3.69 µg/l] *at pH 9,* [(see Doc IIIA, section 3.5)]. *Flufenoxuron is hydrolytically stable under neutral and acidic conditions.* - 3.4.1: Method of analysis for transformation products: add at the end of the paragraph: Unlabelled Flufenoxuron (XXXX) and putative degradation products, WL115096 (MG 1101) and WL129183 (MC1103) were used as reference standard for TLC.
Results and discussion	Applicant's version is acceptable.
Conclusion	Applicant's version is acceptable providing the inclusion of the following amendments: 5.2.3. Transformation products: change the first sentence to "*The "urea" Flufenoxuron degradate (WL129183, CL932338, Reg.No. 4064702) under aerobic conditions, reached* [a maximum of 15.6% TAR after 90 days and was] *14.5% TAR at 152 days after treatment*." - 5.3.2: deficiencies: - Only one soil was examined. - the test substance was labelled on one site only, - the test substance was applied as a suspension instead of a solution or formulated material - Certificates of analysis of the reference substances are not enclosed in the study report.
Reliability	2
Acceptability	Acceptable The study is acceptable but will not be retained as key study for aerobic degradation in soil as a study of higher quality is available.
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*

Section A7.2.2.1	**Rate and route of degradation**
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Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.2.2.1/82 Soil characteristics

Soil designation	Woodstock, Motorway field
Textural class	Silty clay loam
Origin	Woodstock, Kent, UK
Particle size distribution [%] sand silt clay	 18 49 33
Organic carbon [%]	2.1
CEC [meq/100g]	29.1
pH	6.3
MWC [g H_2O/100g dry soil]	67
Microbial Biomass (µg C/g dry soil)	Initial – 431 Final – 317

CEC cation exchange capacity; MWC maximum water holding capacity

Table 7.2.2.1/83 TLC Conditions

Plate	Solvent System	Rf		
		Flufenoxuron	"urea" WL129183 (CL 932338)	"amine" WL115096 (CL 359882)
Merk Silica Gel F_{254} 0.25mm, 5715	Diethyl ether:hexane 2:1, (v:v)	0.5	0.1	0.6
	Ethyl acetate:toluene, 1:1, (v;v)	0.8	0.3	0.8

Table 7.2.2.1/84 Distribution of radioactivity in Flufenoxuron treated soil under aerobic conditions [% total applied radioactivity]

DAT	$^{14}CO_2$	Flufenoxuron	"urea" WL129183 CL932338	"amine" WL115096 CL359882	others	water phase	unextracted	material balance
0	-	100.2	-	-	-	-	0.3	100.5
15	0.1	89.8	4.0	0.0	2.2	1.7	1.6	99.4
30	0.2	81.3	8.1	0.0	3.9	3.3	3.8	100.2
61	0.7	76.2	10.3	0.0	1.0	0.1	10.4	98.8
90	1.4	58.2	15.6	0.0	3.3	2.2	17.5	98.3
152	3.7	35.8	14.5	0.4	4.5	1.5	34.0	94.4

Table 7.2.2.1/85: Specification and amount of transformation products

Lab/Report Code, CAS, and/or IUPAC Chemical Name*(s)*	**Amount [%] of parent compound measured**
WL 129183 (CL932338) Not available N-{4-[2-chloro-4-(trifluoromethyl) phenoxy]-2-fluoromethyl}urea	Max. 15.6% at 90 days 14.5% at 152 days
WL 115096 (CL 359882) Not available 4-[2-chloro-4-(trifluoromethyl)phenoxy]-2-fluorobenezenamine	<1%

Figure 7.2.2.1/41: Biometer flask

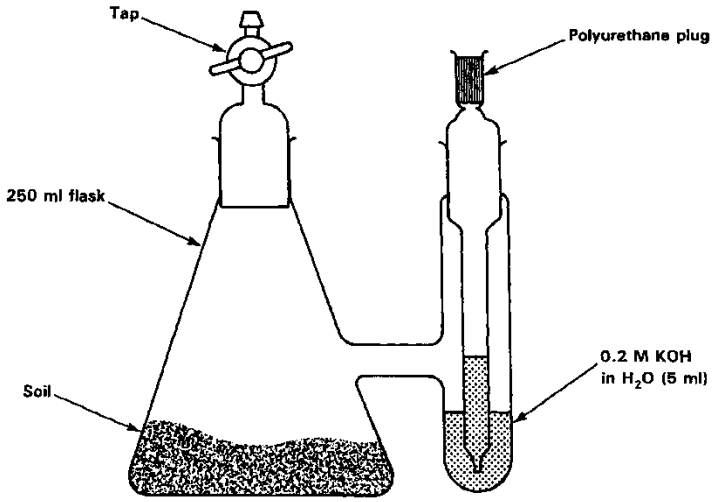
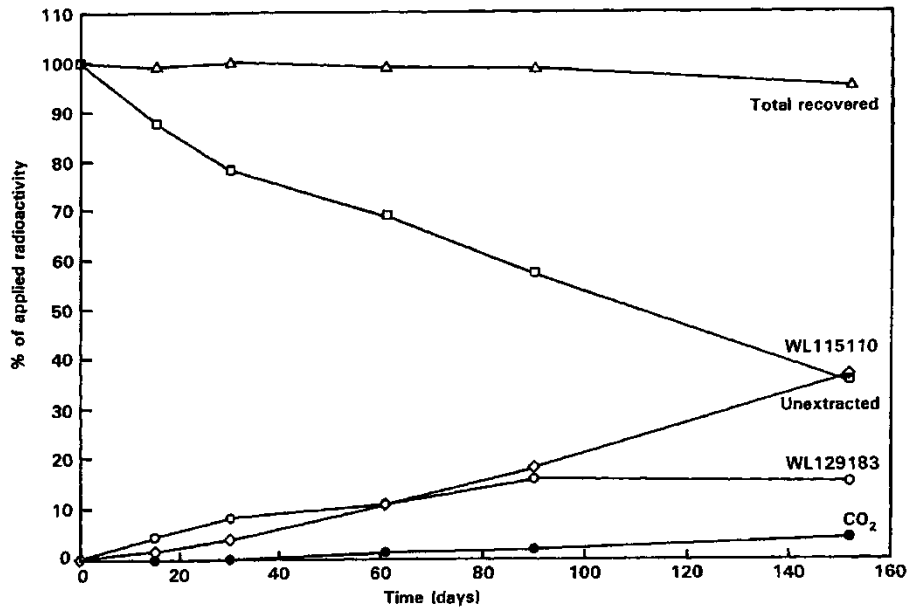


Figure 7.2.2.1/42: Degradation of 14C-Flufenoxuron in aerobic soil



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BPD Annex Points IIIA, VII.4, XII.1.1, XII.1.4	7.2.2.1 Aerobic degradation in soil

Official use only

		1. REFERENCE
1.1.	**Reference**	**3) Standen M & Hill A (1993)** CASCADE (flufenoxuron): A comparison of the degradation of [aniline-^{14}C]- and [toluyl-^{14}C]-CASCADE in soil under aerobic and anaerobic conditions. XXXX unpublished XXXX
1.2.	**Data protection**	No
1.2.1.	Data owner	BASF
1.2.2.	Companies with letter of access	XXXX
1.2.3.	Criteria for data protection	No data protection claimed
		2. GUIDELINES AND QUALITY ASSURANCE
2.1.	**Guideline study**	Yes, BBA Guideline, Part IV, 4-1 (Dec. 1986)
2.2.	**GLP**	Yes (laboratory certified by Department of Health of the Government of the United Kingdom, United Kingdom)
2.3.	**Deviations**	No
		3. MATERIALS AND METHODS
3.1.	**Test material**	[aniline-^{14}C]- and [toluyl-^{14}C]-flufenoxuron
3.1.1.	Lot/Batch number	XXXX
3.1.2.	Specification	See below
3.1.3.	Purity	[aniline-^{14}C]-flufenoxuron – >99% radiopure [toluyl-^{14}C]-flufenoxuron – >99% radiopure
3.1.4.	Specific Activity	[aniline-^{14}C]-flufenoxuron – 31.5 µCi/mg (1.2 MBq/mg) [toluyl-^{14}C]-flufenoxuron – 47.3 µCi/mg (1.8 MBq/mg)

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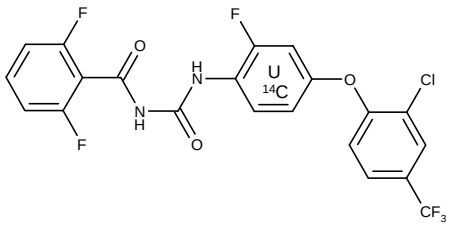
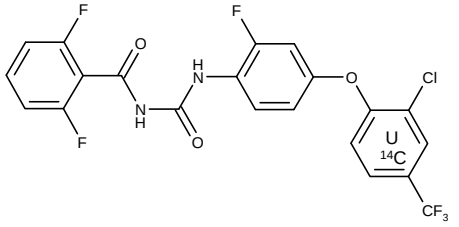
3.1.5.	Radiolabeling	 [^{14}C- aniline] Flufenoxuron  [^{14}C- toluyl] Flufenoxuron	
3.1.6.	Further relevant properties	The solubility of Flufenoxuron in water is 186 µg/l at pH 4, 136 µg/l at pH 7 and 369 µg/l at pH 9	X
3.2.	**Test solution**	The radiochemicals, in acetone solutions (202µl ≡ ~ 150 µg of toluyl label, 193 µl ≡ 150 µg of aniline label) were evaporated to dryness and redissolved in blank formulation (DF 07055, 30µl each). Deionized water (30 ml) was added to reach a concentration of the treatment solutions of 5.0 µg/ml for each label.	X X
3.3.	**Testing procedure**		
3.3.1.	Test system	Soil, sampled from 'motorway' field (O.S. Map reference – 896E/602N) at XXXX to a depth of 10 cm (see Table 7.2.2.1/86), was sieved (2 mm) and aliquots (50 g dry weight basis) were weighed into thirty-six 500 ml glass jars and four biometer flasks, and adjusted to approximately 37.5% MHC. For biomass determination, 100 g dry weight soil was weighed into four jars and adjusted to 40% WHC. The jars were capped with caps with two 1 mm holes in them, the biometer flaks were assembled, and all soils were weighed and left in the dark at 22ºC for 3 days to equilibrate. The treatment solutions (1.0 ml ≡ 5 µg test substance, application rate 0.1 mg/kg dry weight basis) were applied dropwise to the surface of the soils. The additional water brought the soil moisture content to 40% MHC. Immediately after treatment the soil jars were capped, reweighed, and incubated at 22 ± 2ºC in the dark. To determine the mineralization rate, soil was incubated in biometer flasks. Ten ml of 0.2 M KOH was added to the side arm of each biometer flask and the flasks were weighed and also incubated at 22°C in the dark. The flasks were connected to a manifold and twice weekly gently purge with air to aerate the soil and sweep CO_2 into the alkaline traps. The soil jars including the biomass samples were weighed to check for moisture loss at weekly intervals and the biometer flasks at each sampling. For the anaerobic experiment, lucerne meal (0.25 g) was thoroughly mixed into the soil after 30 days aerobic incubation and the samples were flooded to	

Section A7.2.2.1	**Rate and route of degradation**
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		a depth of about 1 – 1.5 cm with deionized water (70ml) and swirled to release air bubbles. The jars were purged with nitrogen and sealed.	
3.3.2.	Temperature	22 ± 2ºC	
3.3.3.	Duration of the test	150 days	
3.3.4.	Number of replicates	Duplicate samples were prepared for each label and soil combination at each interval, but only a single replicate was analyzed. The second replicate was stored at –18ºC immediately on sampling.	
3.3.5.	Sampling	Aerobic soils were sampled after 0, 30, 60, 90, and 150 days. The anaerobic soils were sampled after 60, 90, and 150 days after treatment. The alkaline traps in the biometer flasks were sampled every 14-16 days. The KOH was removed and replaced with fresh KOH. The soils were not sampled. Two samples biomass samples were analyzed at the beginning and at the end of the study.	
3.3.6.	Analytical methods	The aerobic soils were extracted with acetonitrile: water (7:3, v:v, 100 mL) for 2 hours, filtered, and then rinsed with acetonitrile:water, acetonitrile, and diethyl ether. The combined extracts and washings were assayed by LSC. The extracted soil was dried under vacuum at room temperature and combusted to determine unextracted radioactivity. From the anaerobic soils, the water was decanted, filtered and assayed by LSC. Acetonitrile was added to make the acetonitrile: water ratio approximately 7:3 and acetonitrile: water was added to bring the total volume to 100 ml. Extractions were then carried out as for the aerobic samples. Further characterization of the unextractable residues is described in Section A7.2.2.3. Aliquots of the acetonitrile/water extracts (100ml) were diluted with water (50 ml) and partitioned with dichloromethane (3 x 50 ml). The water was radioassayed by LSC and the combined organic phases were dried with anhydrous sodium sulfate and radioassayed by LSC, and concentrated under reduced pressure for analysis by TLC and HPLC with reference standards (See Table 7.2.2.1/87 and Table 7.2.2.1/88). The radioactivity on the TLC plates was located and quantitated using an Isomess-3200 Linear Analyzer and by autoradiography. Unlabeled reference standards were visualized with UV light. Combustion was done using a Packard 306 samples oxidizer and the $^{14}CO_2$ was trapped in 8 ml of Carbosorb, mixed with 13 ml of Permafluor, and analyzed by LSC. LSC was done with a Packard 2200 CA liquid scintillation counter. LKB Optiphase 'Safe' scintillation fluid was used for assay of solutions.	
3.4.	**Transformation products**	Transformation products tested: Yes	
3.4.1.	Method of analysis for transformation products	Flufenoxuron degradates were identified by TLC and HPLC cochromatography with reference standards.	X

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		4. RESULTS – AEROBIC EXPERIMENT (Anaerobic results are given in Section A7.2.2.4, characterization of bound residues is given in Section A7.2.2.3)	
4.1.	**Material balance**	Mass balance for the aerobic samples ranged from 101.6% and 101.1% (for the aniline and toluyl labels, respectively) at day 0 to 92.5% and 91.0% TAR on day 150. These totals do not include $^{14}CO_2$, which accounted for 5.1 to 6.7% of the applied radiocarbon at 150 days after treatment, bringing the minimum overall mass balance to approximately 97% (See Table 7.2.2.1/89)	
4.1.1.	Extractability	For the aerobic soils, 100.4% and 99.0% TAR (aniline and toluyl labels, respectively) was extractable with acetonitrile: water immediately after application, decreasing to 46.7% and 44.7% at 150 days after application. The unextractable radioactivity increased from 1.2 or 2.1% at day 0 to 45.7% or 46.3% at day 150. The percentage of radioactivity remaining in the water after dichloromethane partition was always < 1% TAR (See Table 7.2.2.1/89)	
4.2.	**DT_{50}**	The DT_{50} for Flufenoxuron in aerobic soil was approximately 90 days for both labels. In order to estimate the half-life at 12°C, the temperature correction was done with the following equation assuming a temperature difference to the reference condition of approx. 10°C: DT_{50} (12°C) = DT_{50} x e (0.08 x 10). The respective calculated DT_{50} is then 200 days.	X
4.2.1.	Concentration values	In the aerobic soil, Flufenoxuron decreased from 96.8% and 97.6% at day 0 to 36.4% and 32.9% at day 150. The amounts of Flufenoxuron and its metabolites in aerobic soil at each sampling interval are shown in Table 7.2.2.1/89.	
4.3.	**Specification of the transformation products**	No degradates exceeded 10% of the applied dose at any time during the study. The "urea" degradate reached a maximum of 7.1% and 7.3% at 60 days after treatment and declined to 4.5% by the end of the study. The "amine" degradate was detected but always in amounts <1% TAR (See Table 7.2.2.1/89)	
		5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1.	**Materials and methods**	This study was conducted according to BBA Guideline, Part IV, 4-1. [Aniline-^{14}C]- and [Toluyl-^{14}C]-Flufenoxuron were applied to a clay loam soil as a formulated material at 0.5mg/kg. Samples were incubated in the dark at 22ºC using an open system. Separate samples were incubated in a closed system (biometer flasks) with periodic flushing with air to maintain aerobic conditions and flush $^{14}CO_2$ into KOH traps. Anaerobic samples were incubated aerobically for 30 days then amended with lucerne meal and flooded and flushed with nitrogen immediately. Aerobic soil samples were analyzed at dosing and after 30, 60, 91, and 150 days. Anaerobic samples were analyzed at 60, 91, and 150 days after application. Soil samples were analyzed by extraction with	

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		acetonitrile: water and partition with dichloromethane. The extracts were analyzed by liquid scintillation counting, and the dichloromethane phase by HPLC and normal phase TLC.	
5.2.	**Results and discussion**		
5.2.1.	Material balance	Mass balance for the aerobic samples ranged from 101.6% and 101.1% (for the aniline and toluyl labels, respectively) at day 0 to 92.5% and 91.0% on day 150. These totals do not include $^{14}CO_2$, which accounted for 5.1 to 6.7% of the applied radiocarbon at 150 days after treatment, bringing the minimum overall mass balance to approximately 97% (See Table 7.2.2.1/89)	
5.2.2.			
5.3.	**DT_{50}**	The DT_{50} for flufenoxuron in aerobic soil was approximately 90 days for both labels under experimental conditions. Temperature correction to 12°C leads to an estimated DT_{50} of 200 days.	
5.3.1.	Transformation products	No Flufenoxuron degradate exceeded 10% of the applied dose at any time during the study.	
5.4.	**Conclusion**	The study meets the requirements of BAA Guideline, Part IV, 4-1. The study shows that Flufenoxuron is slowly degraded aerobically in soil with a DT_{50} of about 200 days at 12°C (90 days under experimental conditions), and that the only significant metabolite is the "urea" (CL 932338). Mineralization to CO_2 was 4 to 7% TAR at 150 days, and unextractables accounted for about 46% TAR at 150 days.	
5.4.1.	Reliability	1	X
5.4.2.	Deficiencies	No	

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/02/2005

Section A7.2.2.1	**Rate and route of degradation**
BPD Annex Points IIIA, VII.4, XII.1.1, XII.1.4	7.2.2.1 Aerobic degradation in soil

Materials and Methods	Applicant's version is acceptable providing the inclusion of the following amendments: - 3.1.7. Further relevant properties: The entry should be read as: "*The solubility of Flufenoxuron in water is* [1.86 µg/l] *at pH 4,* [1.36 µg/l] *at pH 7 and* [3.69 µg/l] *at pH 9,* [(see Doc IIIA, section 3.5)]. - 3.2 Test solution: add: "*the test substance was applied as dispersible concentrates*". "*Composition of DF 07055 was 100 g Flufenoxuron, 80 g tensiofix XN6, 100 g Gafac RM 510, 45 g Triton X100, N-methyl pyrrolidone, Cyclohexanone to 1 litre*" 3.4.1 Method of analysis for transformation products*: Change to: "Flufenoxuron degradates* [WL115096 and WL129183] *were identified by TLC and HPLC cochromatography with reference standards*.
Results and discussion	Applicant's version is acceptable providing the inclusion of the following amendments: - 4.2: DT_{50}: No details are provided on DT_{50} calculations. DT_{50} values were likely deduced from direct reading on the graph.
Conclusion	Applicant's version is acceptable providing the inclusion of the following amendments: - 5.4: Conclusion: add the following statement "*there was no significant differences between the aerobic degradation rate of both labels. Additionally, there were no difference in the amount and type of degradation products formed between the aniline and toluyl labels*. " 5.4.2 Deficiencies: add the following points - Degradation was tested on only one soil. - DT_{50}: No details are provided on DT_{50} calculations (r^2, …) - Certificates of analysis of the reference substances are not enclosed in the study report. - No validation of the analytical method was provided.
Reliability	2 In document IIIA, the results on CO_2 or bound residues formation was not quantitatively addressed.
Acceptability	Acceptable Despite the deficiencies cited above, the outcomes of this study are acceptable. This study will not be used as key study for the assessment of aerobic biodegradation in soil, but allow the comparison of the two labels "aniline" and "toluyl". This study also investigates the nature of bound residues (see section 7.2.2.3)
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*

Section A7.2.2.1	**Rate and route of degradation**
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Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.2.2.1/86: Soil Characteristics

Soil designation	Woodstock, Motorway field
Textural class	Clay loam
Origin	Woodstock, Kent, UK
Particle size distribution [%] sand silt clay	 30 42 28
Organic carbon [%]	2.7
CEC [meq/100g]	16.1
biomass [mg C/100 g]	55.6
pH	7.6
MWC [g H_2O/100g dry soil]	74.6

CEC cation exchange capacity; MWC maximum water holding capacity

Table 7.2.2.1/87: TLC Conditions

Plate	Solvent System	Rf-values		
		Flufenoxuron	"urea" WL129183 (CL932338)	"amine" WL115096 (CL359882)
Merk Silica Gel F_{254} 0.25mm, 5715	Diethyl ether:hexane 2:1, (v:v)	0.7	0.1	0.85
	Ethyl acetate:toluene, 1:1, (v;v)	0.81	0.24	0.81

Table 7.2.2.1/88: HPLC Operating Conditions

Apparatus				
System:	Beckman Gold HPLC system			
Detectors:	Beckman 171 radioactivity detector and Beckman 166 UV detector			
Conditions				
Column:	UltraCarb 7 ODS 30, 250 x 4.6 mm i.d.			
Eluent:	Time (min)	% Water	% Acetonitrile	Duration (min)
	0	20	80	
	1	10	90	8
	10	5	95	0.5
	20	20	80	2
Flow Rate:	1.0 mL/min			
Retention Times:	WL 129183 = 5.2 min. WL 115096 = 8.3 min. flufenoxuron = 10.6 min.			

Table 7.2.2.1/89: Identity of radioactivity after application of ^{14}C-Flufenoxuron to soil and incubation under aerobic conditions [% total applied radioactivity]

DAT	$^{14}CO_2$*	Flufenoxuron WL115110	"urea" WL129183 CL932338	"amine" WL115096 CL359882	others	water phase**	unextracted	material balance (without $^{14}CO_2$)
aniline-label								
0	-	96.8	-	-	3.6	0.1	1.2	101.6
30	0.3	86.1	5.1	0.0	2.2	0.2	9.2	102.8
60	1.1	64.9	7.1	0.0	3.1	0.5	22.9	98.5
91	2.4	52.6	6.3	0.4	4.3	0.7	30.7	94.8
150	5.1	36.4	4.5	0.0	5.3	0.5	45.7	92.5
toluyl-label								
0	-	97.6	-	-	1.4	0.0	2.1	101.1
30	0.3	83.4	5.4	0.5	2.0	0.1	8.2	99.6
60	1.3	67.7	7.3	0.8	3.1	0.4	20.3	99.6
91	3.0	51.0	7.1	0.8	4.8	0.6	30.8	95.1
150	6.7	32.9	4.5	0.0	6.7	0.6	46.3	91.0

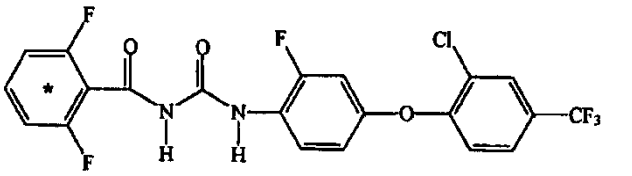
* determined from biometer flask incubations, not included in material balance
** water phase remaining after dichloromethane extraction

Table 7.2.2.1/90: Specification and amount of transformation products

Lab/Report Code, CAS, and/or IUPAC Chemical Name*(s)*	**Amount [%] of parent compound measured**
WL 129183 (CL 932338) Not available N-{4-[2-chloro-4-(trifluoromethyl) phenoxy]-2-fluoromethyl}urea	Max. 7.3% at 60 days 4.5% at 150 days
WL 115096 (CL 359882) Not available 4-[2-chloro-4-(trifluoromethyl)phenoxy]-2-fluorobenezenamine	<1%

Section A7.2.2.1 **Rate and route of degradation**

BPD Annex Points IIIA, VII.4, XII.1.1, XII.1.4 7.2.2.1 Aerobic degradation in soil

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**4) Goodyear A & Gross R (2001)** [^{14}C]-Flufenoxuron (BAS 307 I): Aerobic Soil Rate of Degradation in Three Soils. XXXX unpublished XXXX	
1.2.	**Data protection**	Yes	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Yes, SETAC (March 1995) Part 1, Section 1.1 Aerobic Degradation and OECD 307 Aerobic and Anaerobic Transformation in Soil (August 2000)	
2.2.	**GLP**	Yes (laboratory certified by Department of Health of the Government of the United Kingdom, United Kingdom)	
2.3.	**Deviations**	No	
		3. MATERIALS AND METHODS	
3.1.	**Test material**	[Amide ring-^{14}C]-flufenoxuron	
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	Deviating from specification given in section 2 as follows	
3.1.3.	Purity	>99% chemical purity, 95.0% radiopurity	
3.1.4.	Expiration Date	None given – Certification date June 6, 2000	
3.1.5.	Specific activity	32.36 µCi/mg	
3.1.6.	Radiolabeling		
3.1.7.	Further relevant	The solubility of Flufenoxuron in water is 186 µg/l at pH 4, 136 µg/l at pH 7 and 369 µg/l at pH 9	X

Section A7.2.2.1 **Rate and route of degradation**

BPD Annex Points IIIA, VII.4, XII.1.1, XII.1.4 7.2.2.1 Aerobic degradation in soil

	properties		
3.2.	**Reference materials**		
3.2.1.	Substance	Flufenoxuron	
3.2.1.1.	Lot/Batch number	AC7467-005	
3.2.1.2.	Purity	99.3%	
3.2.2.	Substance	2,6-difluorobenzamide (CL 211558, Reg No 102719)	
3.2.2.1.	Lot/Batch number	XXXX	
3.2.2.2.	Purity	100%	
3.3.	**Test solution**	A stock solution of [Amide ring-^{14}C]-Flufenoxuron was prepared by dissolving 4.67 mg in 3 ml acetone. A 0.398 ml aliquot was evaporated to dryness and redissolved in 8 ml of acetonitrile. The exact concentration in the application solution was determined by LSC to be 0.085 mg/ml, which was used to calculate the volume of solution to be applied (88 µl). The concentration was verified by LSC of aliquots immediately prior to, mid-way through, and following application. The mean result was used to calculate the quantity of [amide ring-^{14}C]-flufenoxuron applied to the soils.	
3.4.	**Testing procedure**		
3.4.1.	Test system	Four soils (See Table 7.2.2.1/91) were treated with [amide ring-^{14}C]-F lufenoxuron. The soils were sampled a week to 2 months before use in the study and were stored in the dark at 4ºC until used. The soils were sieved through a 2 mm screen before use and pre-incubated for 4 days under conditions approximating the test temperature and moisture conditions. Aliquots (50 g dry weight basis) were weighed into the incubation flasks and aliquots of the application solution were applied by syringe (88µl ≡ 7.5 µg, 0.15µg/g soil). The soils were gently mixed and the solvent allowed to evaporate. Control samples for biomass determination were treated with 88µl of acetonitrile. The flasks were connected to a vacuum manifold with incoming air washed with soda lime and water and effluent passed through ethandiol, 2% paraffin in xylene, and two 2 M NaOH traps. The test system was maintained at 45% MWHC at a temperature of 20 ± 2ºC in the dark.	X
3.4.2.	Temperature	20 ± 2°C	
3.4.3.	Duration of the test	120 days	
3.4.4.	Number of replicates	Duplicate treated samples were analyzed from each soil type at each interval. Duplicate control samples for each soil type were analyzed for biomass at the beginning and end of the study	
3.4.5.	Sampling	Soil samples were analyzed at 0, 2, 7, 14, 30, 59, 90, and 120 days after application. Volatiles traps were analyzed when the units to which they	

Section A7.2.2.1 **Rate and route of degradation**

BPD Annex Points IIIA, VII.4, XII.1.1, XII.1.4 7.2.2.1 Aerobic degradation in soil

		were attached were removed for analysis, or every 30 to 40 days.	
3.4.6.	Analytical methods	Soils were extracted by shaking 30 minutes with acetonitrile (4 x 100 ml). The extracts were separated by centrifugation, combined, filtered, and concentrated by rotary evaporation for chromatographic analysis. The extracts were co-chromatographed with reference standards using HPLC and TLC (See Table 7.2.2.1/92 and Table 7.2.2.1/93, respectively).	
3.5.	**Transformation products**	Transformation products tested: Yes	
3.5.1.	Method of analysis for transformation products	Flufenoxuron degradates were co-chromatographed with sample extracts by HPLC and TLC.	
		4. RESULTS	
4.1.	**Material balance**	The overall mass balance ranged from 103.2% to 96.4% with an average of 99.3%.	X
4.1.1.	Extractability	The extractable radiocarbon decreased from 100% on day 0 to 52, 22, and 38% for the Chapel Hill, Newhaven, and Baylam soils respectively at 120 days. The unextractable radiocarbon increased to 21 to 25% by the end of the study, with 23 to 52% mineralized to CO_2. See Table 7.2.2.1/94 and Figure 7.2.2.1/43, Figure 7.2.2.1/44, Figure 7.2.2.1/45.	
4.2.	**DT_{50}/DT_{90}**	At experimental conditions (20°C) the following results were obtained:	

	Chapel Hill Farm clay loam	Newhaven Cottage clay loam	Baylam sandy loam
DT_{50} (days)	124	36	64
DT_{90} (days)	432	191	449

At a reference temperature of 12°C the following dissipation times were calculated using the equation DT_{50} (12°C) = DT_{50} (20°C) x e (0.08 x (T-T12)):

	Chapel Hill Farm clay loam	Newhaven Cottage clay loam	Baylam sandy loam
DT_{50} (days)	235	68	121
DT_{90} (days)	819	362	852

4.2.1.	Kinetic model	A compartmental model (Model Maker 4.0) was used to calculate DT_{50} and DT_{90}. A diagram of the model is given in Figure 7.2.2.1/46.	
4.2.2.	Concentration values	The concentration of Flufenoxuron at each sampling interval is given in Table 7.2.2.1/94.	
4.3.	**Specification of the transformation products**	Carbon dioxide and bound residues were the major transformation products. The 2,6-difluorobenzamide was not found and no volatiles other than CO_2 were detected.	

Section A7.2.2.1 **Rate and route of degradation**

BPD Annex Points IIIA, VII.4, XII.1.1, XII.1.4 7.2.2.1 Aerobic degradation in soil

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1. Materials and methods

The study was conducted according to SETAC and OECD 307 guidelines with no significant deviations. [amide ring- ^{14}C]-Flufenoxuron was applied to three UK soils at a rate of 0.15µg/g and incubated aerobically using a flow through system with ethandiol and 2%parrafin in xylene to trap volatiles and NaOH to trap $^{14}CO_2$. The incubation was in the dark at 20 ±2ºC for 0, 2, 7, 14, 30, 59, 90, or 120 days. Soil samples were extracted with acetonitrile, which was analyzed by HPLC and TLC. The soil was combusted to determine unextracted radiocarbon.

5.2. Results and discussion

5.2.1. Material balance

The overall mass balance ranged from 103.2% to 96.4% with an average of 99.3%. The extractable radiocarbon decreased from 100% on day 0 to 52, 22, and 38% for the Chapel Hill, Newhaven, and Baylam soils respectively at 120 days. The unextractable radiocarbon increased to 21 to 25% by the end of the study, with 23 to 52% mineralized to CO_2.

5.2.2. DT_{50}/DT_{90}

At experimental conditions (20°C), the following results were obtained:

	Chapel Hill Farm clay loam	Newhaven Cottage clay loam	Baylam sandy loam
DT_{50} (days)	124	36	64
DT_{90} (days)	432	191	449

At a reference temperature of 12°C the following dissipation times were calculated using the equation DT_{50} (12°C) = DT_{50} (20°C) x e (0.08 x (T-T12)):

	Chapel Hill Farm clay loam	Newhaven Cottage clay loam	Baylam sandy loam
DT_{50} (days)	235	68	121
DT_{90} (days)	819	362	852

5.2.3. Transformation products

Carbon dioxide and bound residues were the major transformation products. The 2,6-difluorobenzamide was not found (see Table 7.2.2.1/94)

5.3. Conclusion

This study meets the essentials of SETAC and OECD guidelines for an aerobic soil metabolism study. The study shows that the DT_{50} of flufenoxuron in laboratory soils ranges from 68 to 235 days (36 days to 124 days at experimental conditions). Carbon dioxide and bound residues were the major transformation products. The 2,6-difluorobenzamide was not found.

5.3.1. Reliability 1

5.3.2. Deficiencies No X

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/02/2005
Materials and Methods	Applicant's version is acceptable providing the inclusion of the following amendments: - 3.1.7. Further relevant properties: The entry should be read as: "*The solubility of Flufenoxuron in water is* [1.86 µg/l] *at pH 4,* [1.36 µg/l] *at pH 7 and* [3.69 µg/l] *at pH 9,* [(see Doc IIIA, section 3.5)]. -3.4.1 Test system: Change to "[Three] *soils (See Table 7.2.2.1/91) were treated* […].
Results and discussion	Applicant's version is acceptable providing the inclusion of the following amendments: 4.1 Material balance: amend the entry as follow: "*The overall mass balance ranged from 103.2% to 96.4% with an average of 99.3%* [(expressed as the mean of 2 replicates). Individual value ranged from 94% TAR to 106.5% TAR (Baylam sandy loam). See Table *7.2.2.1/94*]"
Conclusion	Applicant's version is acceptable providing the inclusion of the following amendments: 5.3.2 Deficiencies: the OECD Draft Guideline 307 was used with the following exceptions - Biomass was determined prior to dosing and at the termination of the study only. - Volatiles traps were changed when units to which they were connected were removed for analysis or every ca. 30 to 40 days which aver was the sooner. - Bulk density, textural class (FAO) and moisture capacity at pF 2.0 were not determined. - The study was conducted at soil moisture content of 45% of MWHC. - No validation of the analytical method was provided.
Reliability	2 (study has retained as key study)
Acceptability	Acceptable The study is acceptable and will be retained as key study for aerobic degradation in soil for Flufenoxuron in association with the results obtained in reference 6.
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*

Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.2.2.1/91 Soil Characteristics

Source	Chapel Hill Farm, Empingham, Rutland, UK	Newhaven Cottage, Hartington Upper Quarter, Derbyshire, UK	Baylam, Ipswich, Suffolk, UK
Soil Name	SK 960087	SK 15556090	PT 103
UK particle size distribution Sand % (2000-63 um) Silt % (63-2 µm) Clay % (<2µm) Textural Class	 33 35 32 Clay loam	 23 57 20 Clay loam	 71 14 15 Sandy loam
BBA particle size distribution Sand % (2000-63 um) Silt % (63-2 µm) Clay % (<2µm) Textural Class	 33 35 32 schwach toniger Lehm	 23 57 20 schluffiger Lehm	 71 14 15 stark lehmiger Sand
USDA particle size distribution Sand % (2000-63 um) Silt % (63-2 µm) Clay % (<2µm) Textural Class	 35 33 32 Clay loam	 24 56 20 Silt loam	 72 13 15 Sandy loam
Organic Carbon %	2.7	4.5	1.4
Organic Matter %	4.7	7.8	2.4
pH in H_2O	8.0	6.7	5.5
pH in 1M KCl	7.2	6.2	4.9
C.E.C. meq/100g	19.6	17.4	8.3
Water Holding Capacity at pF0 (0.001 bar) %	56.6	107.7	47.6
Water Holding Capacity at pF2.5 (0.33 bar) %	25.0	48.5	16.2
Dry Matter %	81.2	69.1	83.2
Disturbed Bulk Density (g/cm^3)	0.89	0.51	1.04
Biomass (start of study) µg C/g	526.5	604.8	434.9
Biomass (end of study) µg C/g	500.1	654.1	226.1

Table 7.2.2.1/92 HPLC Conditions

Hardware		
Gilson 305 and 306 pumps, 811C or 881B dynamic mixer and 231 or 231 XL injector with Lablogic β-ram Radiodetector and Applied Biosystems 759A Absorbance detector.		
Jasco PU-980 pump and LG-980-02 Gradient Unit with a Gastor 6T-103 Degasser, Gilson 401C Diluter and 231XL, 720 injector, Lablogic β-ram Radiodetector, and Jasco UV-975 Absorbance detector		
Method 1 – purity check and Day 0 extracts		
Column:	HiChrom RPB C18 (250 x 4.6 mm id)	
Mobile Phase A:	Water	
Mobile Phase B:	Acetonitrile	
Mobile Phase Program:	0 min. 10 min. 15 min. 20 min. 21 min. 30 min. 31 min. 35 min. 40 min.	5% B 40% B 60% B 80 % B 80% B 90% B 100% B 5% B 5% B
Flow Rate:	1 mL/min	
UV Detector Wavelength:	254 nm	
Method 2 – Day 1 and subsequent extracts		
Column:	HiChrom RPB C18 (250 x 4.6 mm id)	
Mobile Phase A:	Water	
Mobile Phase B:	Acetonitrile	
Mobile Phase Program:	0 min. 10 min. 15 min. 20 min. 21 min. 30 min. 31 min. 35 min. 40 min.	20% B 40% B 60% B 80 % B 80% B 90% B 100% B 20% B 20% B
Flow Rate:	1 mL/min	
UV detector wavelength:	254 nm	
Retention Times:	Flufenoxuron – 28 min. 2,6-difluorobenzamide – 5 min.	

Table 7.2.2.1/93 TLC Conditions

Plates	Whatman Silica Gel KF6
Method 1 – determination of radiopurity	
Solvent:	Hexane:diethyl ether:ammonia (33:66:0.2, by volume)
Method 1 – analysis of selected soil extracts	
Solvent:	Ethyl acetate:toluene (1:1, by volume)
Rf:	Flufenoxuron – 0.69 to 0.72 2,6-difluorobenzamide – 0.40 to 0.41

Table 7.2.2.1/94 Recovery of radioactivity and distribution of metabolites after application of benzamide-^{14}C-Flufenoxuron to soil and incubation under aerobic conditions (mean of two replicates) [%total applied radioactivity]

DAT	$^{14}CO_2$	extractable			NER	material balance
		total	Flufenoxuron	unknown		
Chapel Hill Farm						
0	-	100.5	100.0	0.4	2.3	102.7
2	0.3	95.8	95.1	0.7	3.3	99.4
7	1.4	91.5	91.1	0.3	4.8	97.6
14	2.8	89.5	89.5	-	8.2	100.5
30	5.5	83.2	83.1	-	9.2	97.9
59	10.1	70.5	70.2	0.3	14.9	97.2
90	18.5	58.8	58.6	0.2	19.1	98.6
120	23.2	52.0	51.6	0.4	21.3	98.5
Newhaven Cottage						
0	-	101.5	101.0	0.5	1.7	103.2
2	14	97.2	96.5	0.7	3.4	101.9
7	5.4	85.9	85.6	0.3	8.6	100.8
14	13.3	69.1	69.1	-	14.1	97.1
30	21.9	56.3	56.2	0.1	17.8	97.4
59	34.7	37.8	37.6	0.2	24.1	98.4
90	46.0	24.9	24.7	0.1	26.5	99.5
120	52.5	22.1	22.0	0.1	25.2	101.6
Baylam						
0	-	99.6	99.1	0.5	1.1	100.6
2	1.2	96.8	96.2	0.7	3.8	101.8
7	6.1	82.4	82.1	0.2	9.3	98.4
14	10.8	73.7	73.4	0.2	13.0	98.1
30	19.5	60.5	60.3	0.2	18.7	100.2
59	24.3	50.7	50.5	0.2	19.7	96.4
90	30.1	47.1	46.8	0.3	20.1	98.7
120	36.4	38.5	38.3	0.1	22.6	97.4

NER = non-extractable residues

Figure 7.2.2.1/43 Pattern of decline of [^{14}C]-Flufenoxuron and formation of degradates in Chapel Hill soil

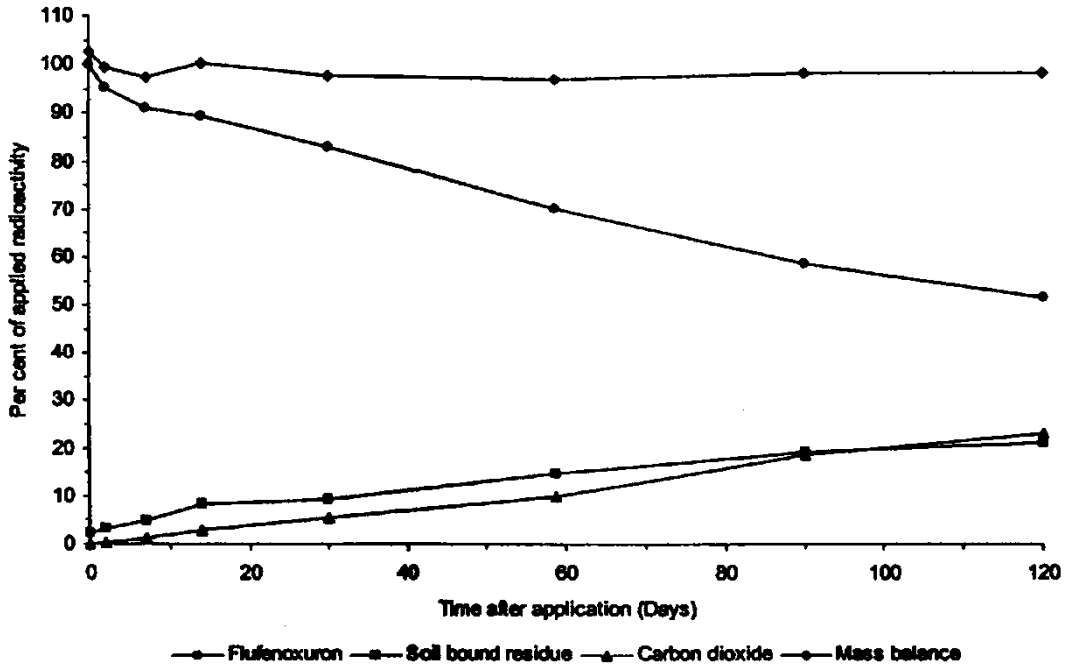


Figure 7.2.2.1/44 Pattern of decline of [^{14}C]-Flufenoxuron and formation of degradates in Newhaven Cottage soil

Figure 7.2.2.1/45 Pattern of decline of [^{14}C]-Flufenoxuron and formation of degradates in Baylam soil

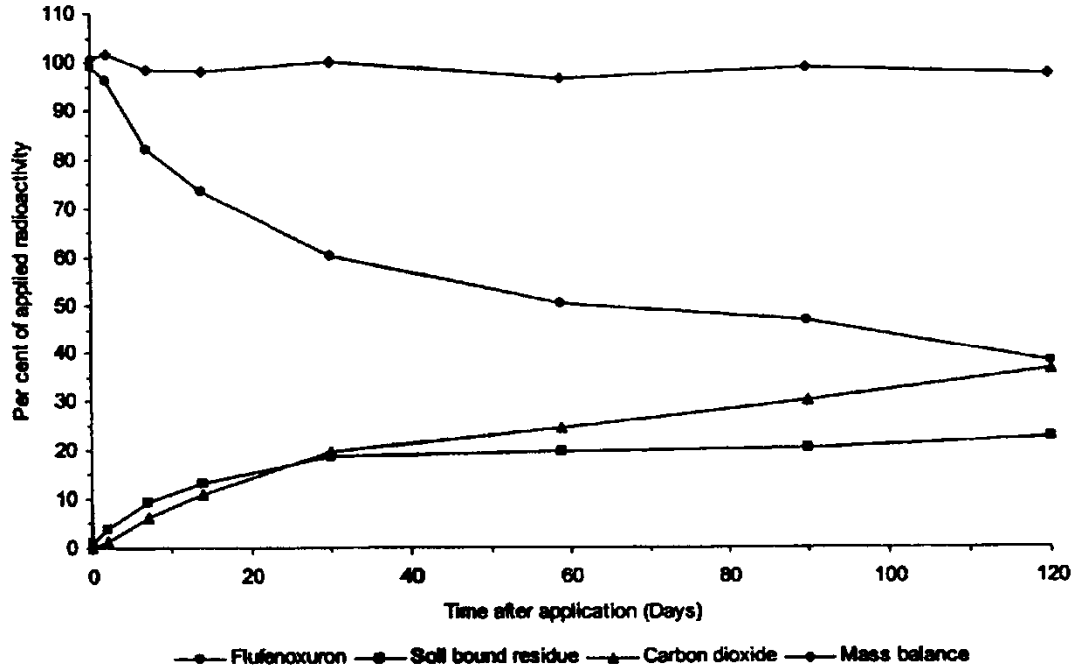
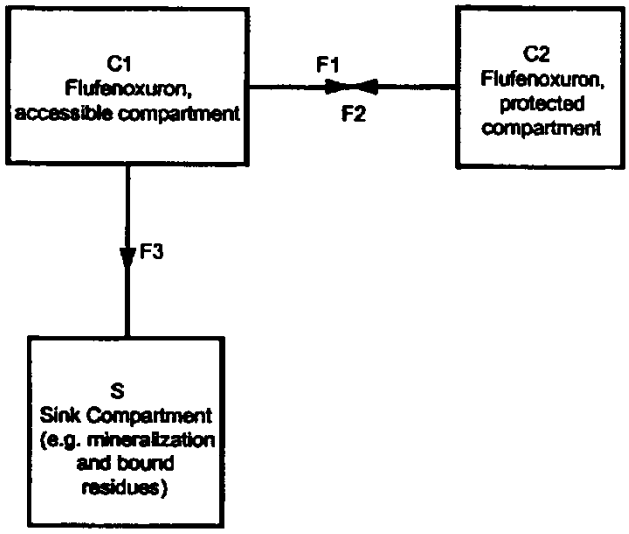

Per cent of applied radioactivity
110
100
90
80
70
60
50
40
30
20
10
0
0
20
40
60
80
100
120
Time after application (Days)
Flufenoxuron
Soil bound residue
Carbon dioxide
Mass balance

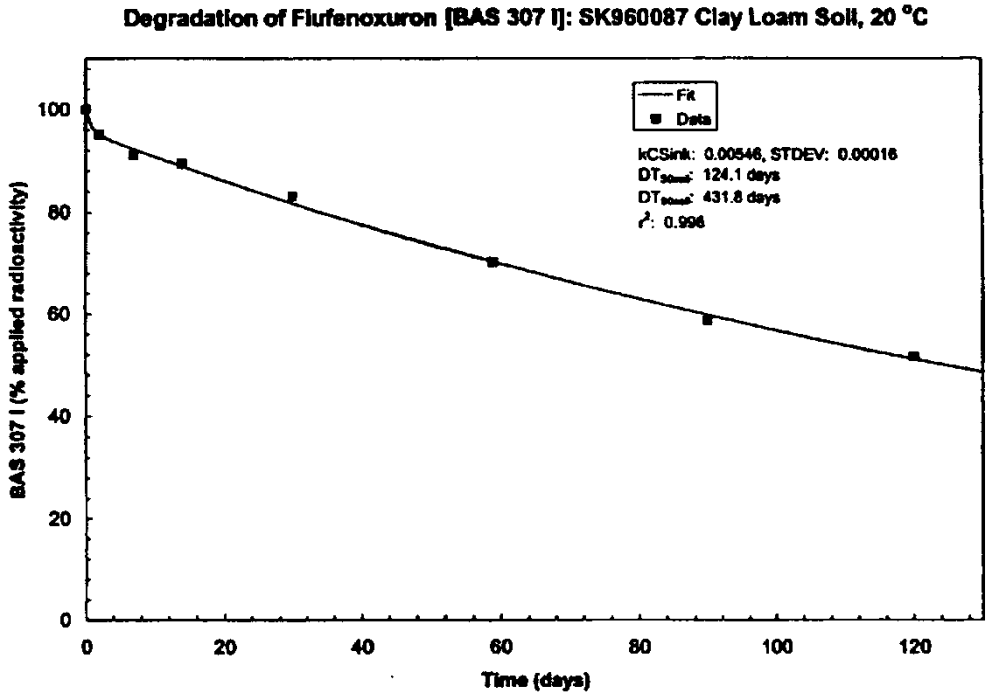
Figure 7.2.2.1/46 Compartmental Model for Dissipation of [^{14}C]-Flufenoxuron



Definitions

Compartment: C1 Unconditional **Flufenoxuron, accessible compartment** **dC1/dt = -F1+F2-F3 Initial Value = Cinitial**	**Compartment: C2 Unconditional** **Flufenoxuron, protected compartment** **dC2/dt = +F1-F2 Initial Value = 0.0**
Flow: F1 Unconditional **Flow from Compound to C Protected** **F1 = kCP * C1**	**Flow: F2 Unconditional** **Flow from C Protected to Compound** **F2 = kPC * C2**
Flow: F3 Unconditional **Flow from Compound to Sink** **F3 = KCSink * C1**	**Compartment: S Unconditional** **Sink Compartment (e.g. mineralization and bound residues). dS/dt = +F3 Initial Value = 0.0**

Figure 7.2.2.1/47 Degradation rate for Flufenoxuron in Chapel Hill soil determined using the Compartmental Model



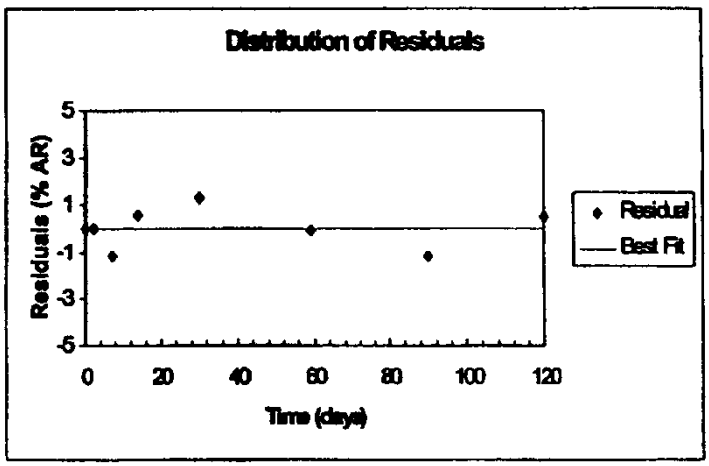
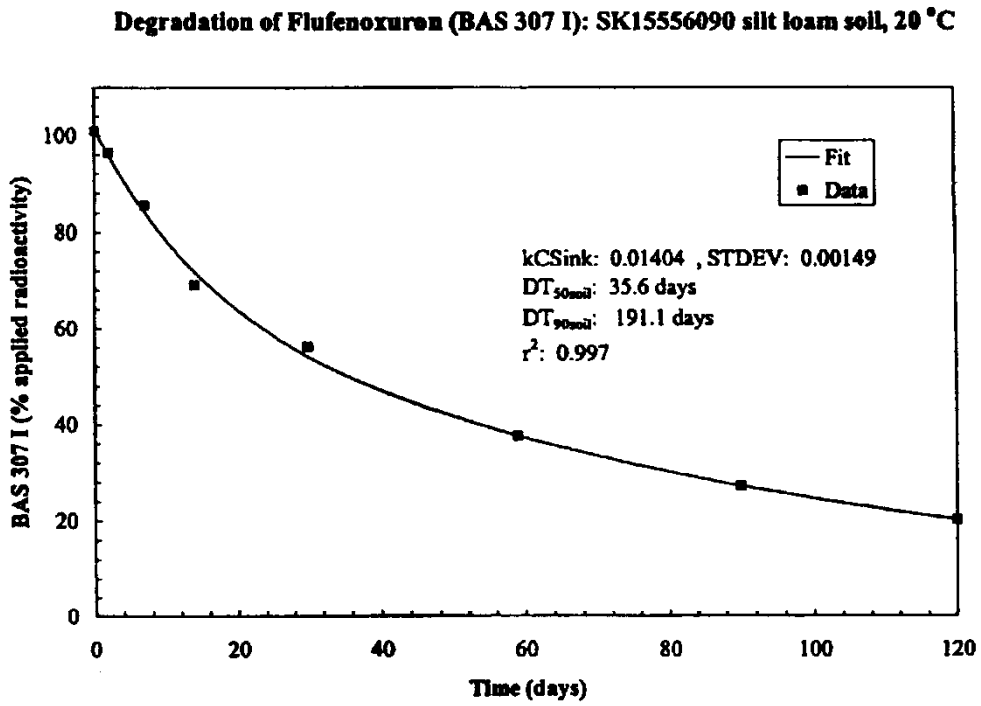


Figure 7.2.2.1/48 Degradation rate for Flufenoxuron in Newhaven Cottage soil determined using the Compartmental Model



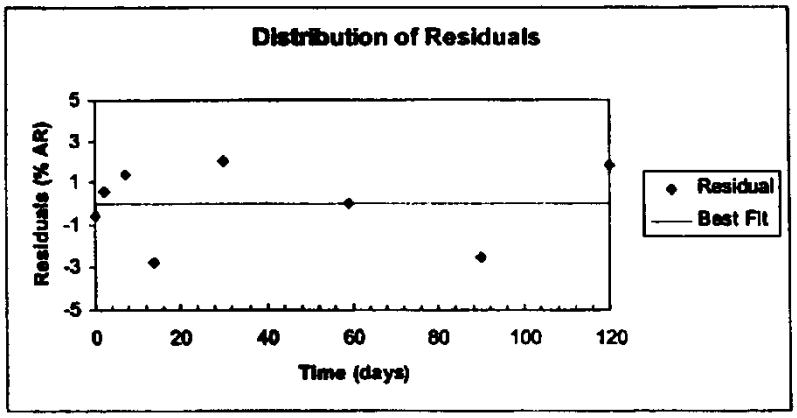
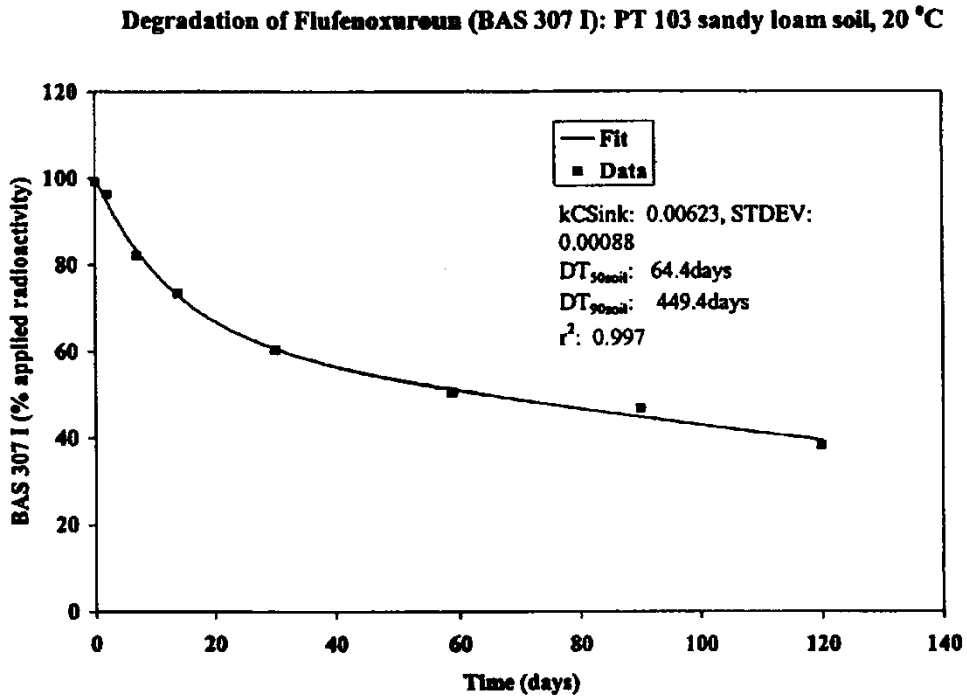
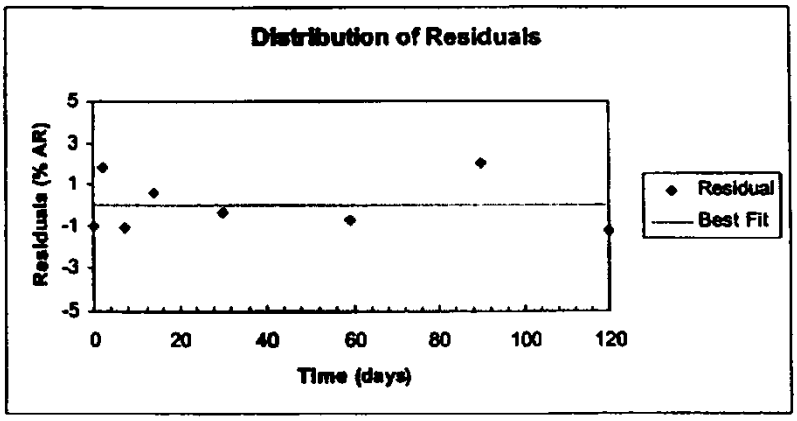


Figure 7.2.2.1/49 Degradation rate for Flufenoxuron in Baylam soil determined using the Compartmental Model





Section A7.2.2.1 **Aerobic Degradation in Soil**

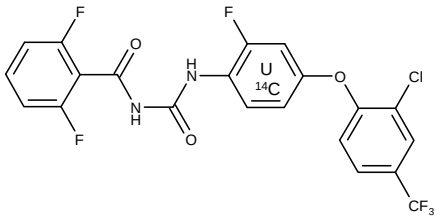
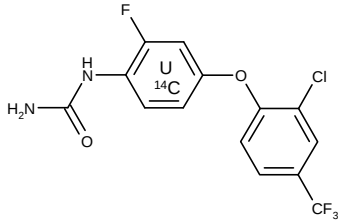
BPD Annex Points IIIA, VII.4, XII.1.1, XII.1.4 7.2.2.1 Aerobic degradation in soil

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**5) Stephan A & Ebert D (2003)** Degradation rates of BAS 307 I (Flufenoxuron) and Reg. No. 4064702 (CL932338) under aerobic conditions in different soils (DT_{50}/DT_{90}) XXXX. unpublished XXXX	
1.2.	**Data protection**	Yes	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I authorisation.	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Yes, BBA Guideline Part IV, 4-1; SETAC, Procedures for assessing the environmental fate and ecotoxicity of pesticides, March 1995; OECD Guideline 307, Aerobic and anaerobic transformation in soil	
2.2.	**GLP**	Yes (laboratory certified by Landesamt fuer Umweltschutz und Gewerbeaufsicht, Mainz, Germany)	
2.3.	**Deviations**	No	

Section A7.2.2.1 **Aerobic Degradation in Soil**

BPD Annex Points IIIA, VII.4, XII.1.1, XII.1.4 7.2.2.1 Aerobic degradation in soil

3. MATERIALS AND METHODS

3.1.	**Test materials**	[aniline-^{14}C]-Flufenoxuron and [aniline-^{14}C]-Reg.No. 4064702	
3.1.1.		[aniline-^{14}C]-Flufenoxuron	
3.1.1.1.	Lot/Batch number	XXXX	
3.1.1.2.	Purity	99.9% radiopure by HPLC	
3.1.1.3.	Specific activity	3.89MBq/mg	
3.1.1.4.	Radiolabeling		
3.1.1.5.	Further relevant properties	The solubility of Flufenoxuron in water is 186 µg/l at pH 4, 136 µg/l at pH 7 and 369 µg/l at pH 9.	X
3.1.2.		[aniline-^{14}C]-Reg.No. 4064702	
3.1.2.1.	Chemical name	N-{4-[2-chloro-4-(trifluoromethyl)phenoxy]-2-fluorophenyl}urea	
3.1.2.2.	Lot/Batch number	CFQ12161	
3.1.2.3.	Purity	98.7% radiopure by HPLC	
3.1.2.4.	Specific activity	3.48 MBq/mg	
3.1.2.5.	Radiolabeling		
3.2.	**Reference materials**	Reg. No. 241208 (CL 359882), XXXX, purity 99% was used as reference standard for HPLC identification of metabolites of Reg. No 4064702.	
3.3.	**Test solution**	About 1.2 mg of ^{14}C-Flufenoxuron was dissolved in 24 mL of acetonitrile. The concentration of the solution was determined by LSC to be 0.052 µg/µL. About 2.25 mg of ^{14}C-Reg. No. 4064702 was dissolved in 40 mL of acetonitrile. The concentration of the solution was determined by LSC to be 0.055 µg/µL	
3.4.	**Testing procedure**		

Section A7.2.2.1 **Aerobic Degradation in Soil**

BPD Annex Points IIIA, VII.4, XII.1.1, XII.1.4 7.2.2.1 Aerobic degradation in soil

3.4.1.	Test system	Four soils were used in this study (SeeTable 7.2.2.1/95). All four were treated with ^{14}C-Reg. No. 4064702. Additionally, Bruch West and Li35b soil were treated with ^{14}C-flufenoxuron in separate experiments. The soils were adjusted to 40% MWC and aliquots equivalent to 100g dry weight were weighed into glass bottles. Soils were treated with a nominal application rate of 0.05mg/kg dry soil (96 µL of ^{14}C-flufenoxuron or 91 µL of ^{14}C-Reg No. 4064702). The soils were homogenized by shaking and placed in the incubator. The samples were aerated with a slight stream of moistened, CO_2 free air. Volatiles were trapped by NaOH, ethylene glycol, and H_2SO_4 traps in series. The soil moisture content was maintained by frequent weighing and adding water if needed.	
3.4.2.	Temperature	20 ± 2 ºC.	
3.4.3.	Duration of the test	Up to 119 days after dosing.	
3.4.4.	Number of replicates	A single replicate of each soil was analyzed at each interval.	
3.4.5.	Analytical methods	Samples were extracted three times with 190 mL of acetonitrile, the extracts were analyzed by LSC, combined, concentrated to dryness and redissolved in methanol for HPLC analysis under the conditions in Table 7.2.2.1/96. The extracted soils were air dried and combusted to determine the non-extractable residues.	
3.5.	**Transformation products**	Flufenoxuron degradates were identified by HPLC with reference compounds.	
		4. RESULTS	
4.1.	**Material balance**	The mean ^{14}C-mass accountability was 99% and ranged from 92% to 106% for the Flufenoxuron metabolism. For the Reg. No. 4064702 the mean was 97% and the range from 90% to 106% (See Table 7.2.2.1/97 and Table 7.2.2.1/98).	
4.1.1	Extractability	Acetonitrile-extractable ^{14}C-residues were 95.9% and 97.9% at day) for flufenoxuron and decreased to 57.1% and 50.0% by day 119 with a corresponding increase in the unextractables. The day 0 extractability for Reg. No. 4064702 ranged from 92.0% to 94.1% and decreased to 17.6% to 25.5% by day 119. Mineralization to $^{14}CO_2$ was observed in only two soils, accounting for 2% or 7.8% of the dose at 119 days.	X
4.2.	**DT_{50}/DT_{90}**	The DT_{50} values for Flufenoxuron at experimental temperature conditions were 122 and 115 days. The DT_{50} values for Reg.No. 4064702 ranged from 47 to 59 days. The DT_{50} values were recalculated to a reference temperature of 12°C using the equation DT(12°C) = DT50 (T) x e (0.08 x (T - 12)). The DT_{50} values for Flufenoxuron were 218 and 231 days. The DT_{50} values for	

Section A7.2.2.1 **Aerobic Degradation in Soil**

BPD Annex Points IIIA, VII.4, XII.1.1, XII.1.4 7.2.2.1 Aerobic degradation in soil

		Reg. No. 4064702 ranged from 89 to 112 days. See Table 7.2.2.1/99.	X
4.2.1.	Concentration values	The concentrations of Flufenoxuron and its metabolites as percentage of the initial dose at each interval are shown in Table 7.2.2.1/97 and Table 7.2.2.1/98). The results are shown graphically with the fitted curves in Figure 7.2.2.1/51 to Figure 7.2.2.1/55.	
4.2.2.	Kinetic order	Pseudo first order	
4.3.	**Specification of the transformation products**	Reg. No 4064702 was the only metabolite identified in the Flufenoxuron metabolism experiment reaching a maximum of 8.3% at 30 days in the Li35b soil. No other components accounted for more than 1% of the dose. In the Reg. No. 4064702 metabolism experiment, only two products were found at 2% each. One was identified as Reg. No. 241208.	
		5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1.	**Materials and methods**	Four soils were used in this study. All four were treated with Reg. No. 4064702. In additional experiments, Bruch West and Li35b soil were treated with flufenoxuron. The soils were adjusted to 40% MWC and aliquots equivalent to 100g dry weight were weighed into glass bottles. Soils were treated with a nominal application rate of 0.05mg/kg dry soil (96 µL of 0.052 µg/µL ^{14}C-flufenoxuron in acetonitrile or 91 µL of 0.055 µg/µL ^{14}C-Reg No. 4064702 in acetonitrile). The soils were homogenized by shaking and placed in the incubator in the dark at 20 ± 2ºC for up to 119 days. The samples were aerated with a slight stream of moistened, CO_2 free air. Volatiles were trapped by NaOH, ethylene glycol, and H_2SO_4 traps in series. The soil moisture content was maintained by frequent weighing and adding water if needed. Samples were extracted three times with 190 mL of acetonitrile, the extracts were analyzed by LSC, combined, concentrated to dryness and redissolved in methanol for HPLC. The extracted soils were air dried, combusted, and counted to determine unextractables. Model Maker 3.0.4 was used to derive rate constants for the degradations.	
5.2.	**Results and discussion**		
5.2.1.	Material balance	The average material balance was 98% with a range from 90% to 106%.	
5.2.2.	DT_{50}/DT_{90}	The DT_{50} values for Flufenoxuron were 122 and 115 days. The DT_{50} values for Reg.No. 4064702 ranged from 47 to 59 days. See Table 7.2.2.1/99. The DT50 values were recalculated to a reference temperature of 12°C. The DT_{50} values for Flufenoxuron were then 218 and 231 days. The DT_{50} values for Reg. No. 4064702 ranged from 89 to 112 days.	
5.2.3.	Transformation products	Reg.No. 4064702 was the only metabolite identified in the Flufenoxuron metabolism experiment reaching a maximum of 8.3% at 30 days in the Li35b soil. No other components accounted for more than 1% of the dose. In the Reg. No. 4064702 metabolism experiment, only	

Section A7.2.2.1	**Aerobic Degradation in Soil**
BPD Annex Points IIIA, VII.4, XII.1.1, XII.1.4	7.2.2.1 Aerobic degradation in soil

		two products were found at 2% each. One was identified as Reg. No. 241208.
5.3.	**Conclusion**	Flufenoxuron was aerobically degraded in soil with a half-life of 115 to 122 days with Reg. No.4064702 as the only significant metabolite, accounting for a maximum of 8% of the dose. Reg.No. 4064702 itself was degraded with a half-life of 47 to 59 days. The DT50 values were recalculated to a reference temperature of 12°C. The DT_{50} values for flufenoxuron were 218 and 231 days. The DT_{50} values for Reg. No. 4064702 ranged from 89 to 112 days.
5.3.1.	Reliability	1
5.3.2.	Deficiencies	No

Section A7.2.2.1 **Aerobic Degradation in Soil**

BPD Annex Points IIIA, VII.4, XII.1.1, XII.1.4 7.2.2.1 Aerobic degradation in soil

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/02/2005
Materials and Methods	Applicant's version is acceptable providing the inclusion of the following amendments: - 3.1.7. Further relevant properties: The entry should be read as: "*The solubility of Flufenoxuron in water is* [1.86 µg/l] *at pH 4,* [1.36 µg/l] *at pH 7 and* [3.69 µg/l] *at pH 9,* [(see Doc IIIA, section 3.5)].
Results and discussion	Applicant's version is acceptable providing the inclusion of the following amendments: 4.2 DT_{50}/DT_{90}: Table 7.2.2.1/18: add a footnote to DT_{90} values for Flufenoxuron: [* not reliable, too far extrapolated]. 4.1.1 Extractability: Add at the end of the paragraph: "[The bound residues reached levels of 65 – 80% TAR at the end of incubation in all four soils.]".
Conclusion	Applicant's version is acceptable providing the inclusion of the following amendments: 5.3.2 Deficiencies - Flufenoxuron was tested on only two soils. - Only one replicate was analyzed. - As one replicate was analyzed, the recovery rate and the repeatability of the analytical method cannot be evaluated as recommended in the OECD guideline n°307
Reliability	2 (study has retained as key study)
Acceptability	Acceptable The study is acceptable and will be retained as key study for aerobic degradation in soil for Flufenoxuron (in association with the results obtained in reference 5) and for its metabolite Reg. No.4064702.
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*

Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.2.2.1/95 Soils used to investigate the degradation rate of Flufenoxuron and its "urea" metabolite (Reg.No. 4064702, CL 932338)

Soil designation and origin	Bruch West, Limburgerhof, RP, Germany	Li35b, Limburgerhof, RP, Germany	LUFA 2.2, Speyer, RP, Germany	LUFA 3A, Altlussheim, BW, Germany
DIN Particle size distribution [%]				
sand 0.063 – 2 mm	62.8	76.2	84.8	47.2
silt 0.002 – 0.063 mm	36.8	21.3	13.4	46.0
clay < 0.002 mm	0.5	2.6	1.8	6.8
textural class	silty sand	silty sand	silty sand	silty sand
Organic C [%]	2.3	0.9	2.4	2.4
pH [H_2O]	7.8	7.1	6.6	8.1
pH [1M KCl]	7.0	6.3	5.9	7.4
cation exchange capacity [mEq/100g]	14.0	7.4	9.7	19.6
water holding capacity [g/100 g dry weight]	30.4	27.7	39.4	42.8
microbial biomass [mg C/100 g dry weight]	30.2	16.2	36.1	67.8

Table 7.2.2.1/96 HPLC Equipment and Conditions

Pumps	2 Kontron HPLC pumps 422
Auto Sampler	Kontron AS 465
UV detector	Kontron 430
Radiodetector	Berthold, LB 507A
Software	Dionex chromeleon V4.30, build 382
Column	Phenomenex, ultracarb 7 ODS (30), 250 x 4.6mm, 7 µm
Mobile Phase	A: water:acetonitrile:acetic acid (900:100:1) B: acetonitrile:acetic acid (1000:1)
Flow Rate	1 mL/min
Gradient	Time (min) %B 0 10 5 10 45 95 45 100 46 100 46.1 95 51 10 60 10

Table 7.2.2.1/97 Recovery of radioactivity and distribution of metabolites after application of fluoroaniline-^{14}C-Flufenoxuron to soil and incubation under aerobic conditions [% TAR]

DAT	$^{14}CO_2$	extractable				Unextracted	material balance
		total	Flufenoxuron	"urea" CL932338	others		
Bruch West							
0	n.d.	95.9	95.9			4.1	100.0
3	0.0	95.9	95.9			4.1	100.0
7	0.0	98.0	95.9	2.0		6.1	104.1
14	0.0	93.9	91.8	2.0		10.2	104.1
30	0.0	81.6	77.6	4.1		14.3	95.9
57	0.0	79.6	77.6	2.0		20.4	100.0
91	0.0	55.1	53.1	2.0		36.7	91.8
119	0.0	57.1	51.0	4.1	0.0	38.8	95.9
Li35b							
0	n.d.	97.9	97.9			2.1	100.0
3	0.0	93.8	93.8			4.2	98.0
7	0.0	89.6	87.5	2.1		6.3	95.9
14	0.0	89.6	85.4	4.2		10.4	100.0
30	0.0	93.3	75.0	8.3		22.9	106.2
57	0.0	70.8	66.7	4.2		25.0	95.8
91	0.0	60.4	56.3	4.2		35.4	95.8
119	0.0	50.0	45.8	4.2	0.0	43.8	93.8

Table 7.2.2.1/98 Recovery of radioactivity and distribution of metabolites after application of fluoroaniline-^{14}C-Reg.No. 4064702 (CL932338) to soil and incubation under aerobic conditions [%TAR]

DAT	$^{14}CO_2$	extractable				unextractable	material balance
		total	"urea" CL932338	"amine" CL359882	others		
Bruch West							
0	n.d.	92.0	92.0			8.0	100.0
3	0.0	88.0	88.0			10.0	98.0
7	0.0	84.0	84.0			14.0	98.0
14	0.0	80.0	80.0			18.0	98.0
30	0.0	76.0	76.0			20.0	96.0
57	0.0	44.0	42.0	2.0		52.0	96.0
91	2.0	30.0	28.0	0.0	0.0	68.0	100.0
119	2.0	24.0	22.0		2.0	80.0	106.0
Li35b							
0	n.d.	94.1	94.1			5.9	100.0
3	0.0	86.3	86.3			9.8	96.1
7	0.0	82.4	82.4			15.7	98.1
14	0.0	78.4	78.4			19.6	98.0
30	0.0	66.7	66.7			33.3	100.0
57	0.0	45.1	45.1			45.1	90.2
91	0.0	27.5	25.5	2.0	0.0	74.5	102.0
119	0.0	25.5	23.5	0.0	0.0	72.5	98.0
Lufa 2.2							
0	n.d.	92.2	92.2			7.8	100.0
3	0.0	88.2	88.2			7.8	96.0
7	0.0	88.2	88.2			9.8	98.0
14	0.0	76.5	76.5			17.6	94.1
30	0.0	68.6	86.6			29.4	98.0
57	0.0	47.1	45.1	2.0		49.0	96.1
91	0.0	35.3	33.3	2.0	0.0	56.9	92.2
119	0.0	23.5	21.6	2.0	2.0	72.5	96.0
Lufa 3A							
0	n.d.	92.2	92.2			7.8	100.0
3	0.0	86.3	86.3			11.8	98.1
7	0.0	78.4	78.4			15.7	94.1
14	0.0	68.6	68.6			25.5	94.1
30	2.0	54.9	54.9			33.3	90.2
57	3.9	37.3	37.3			54.9	96.1
91	5.9	27.5	27.5		0.0	62.7	96.1
119	7.8	17.6	15.7	0.0	0.0	64.7	90.0

Table 7.2.2.1/99 DT_{50} and DT_{90} for Flufenoxuron and "urea" metabolite (Reg. No. 4064702, CL 932338)

Compound	Soil	DT_{50}	DT_{90}	r^2
Experimental conditions T = 20°C				
Flufenoxuron	Bruch West	122	407	0.95
	Li35b	115	381	0.98
"urea" Reg. No. 4064702 CL 932338	Bruch West	57	190	0.97
	Li35b	56	186	0.99
	Lufa 2.2	59	196	0.99
	Lufa 3a	47	156	0.99
Reference temperature = 12°C				
Flufenoxuron	Bruch West	231	772	0.95
	Li35b	218	723	0.98
"urea" Reg. No. 4064702 CL 932338	Bruch West	108	360	0.97
	Li35b	106	353	0.99
	Lufa 2.2	112	372	0.99
	Lufa 3a	89	296	0.99

Figure 7.2.2.1/50 Experimental data and calculated degradation curve for flufenoxuron in Bruch West soil

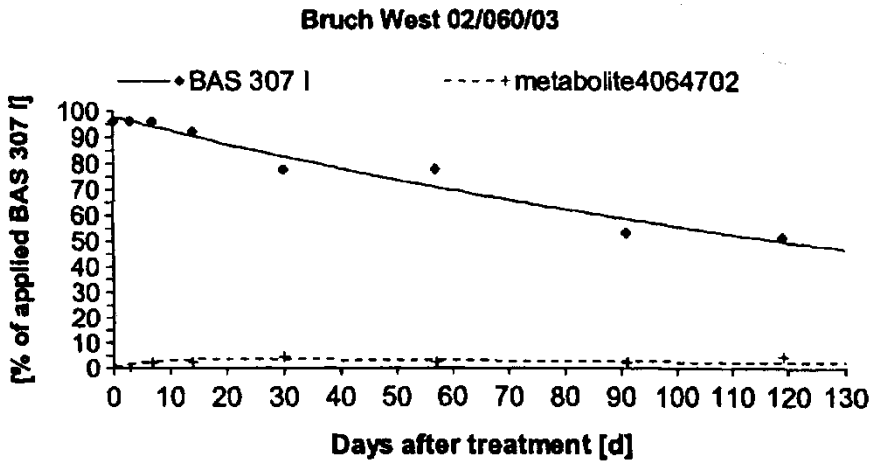


Figure 7.2.2.1/51 Experimental data and calculated degradation curve for flufenoxuron in Li35b soil

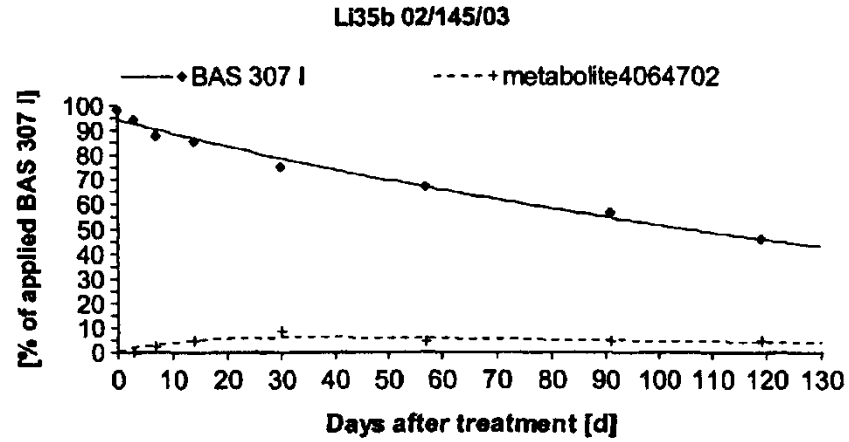


Figure 7.2.2.1/52 Experimental data and calculated degradation curve for Reg. No. 4064702 in Bruch West soil

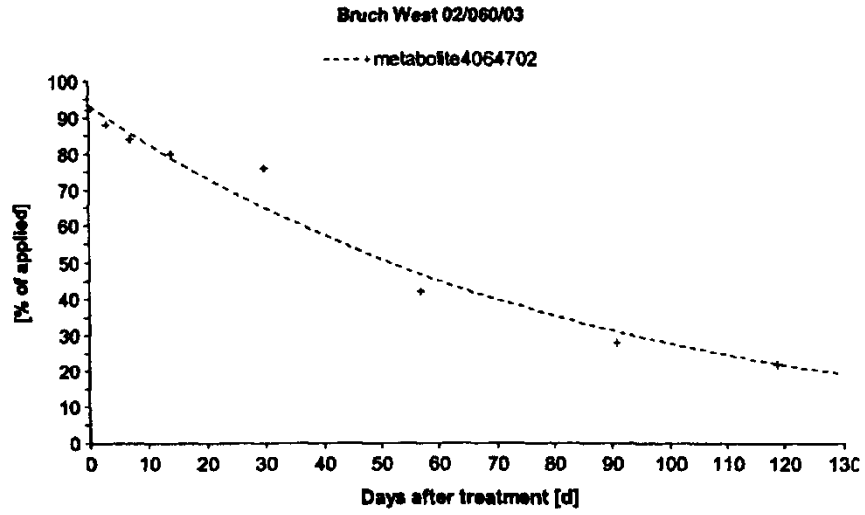


Figure 7.2.2.1/53 Experimental data and calculated degradation curve for Reg. No. 4064702 in Li35b soil

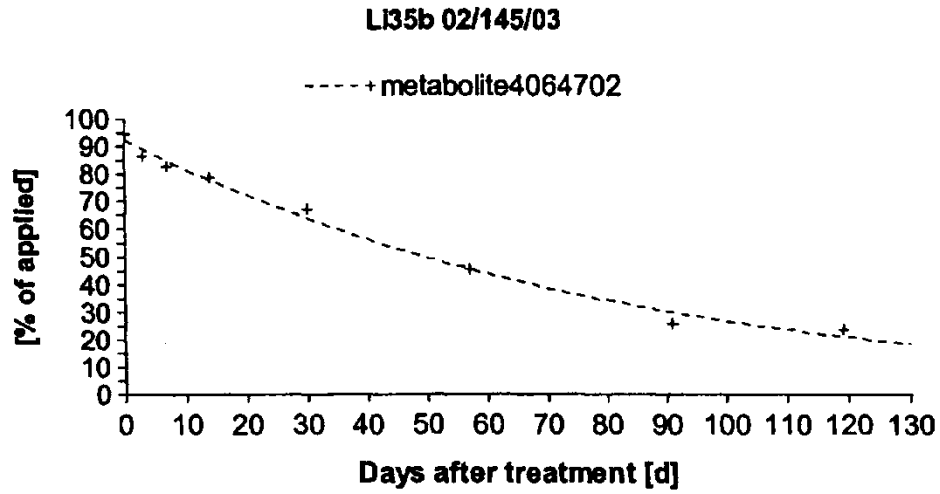


Figure 7.2.2.1/54 Experimental data and calculated degradation curve for Reg. No. 4064702 in Lufa 2.2 soil

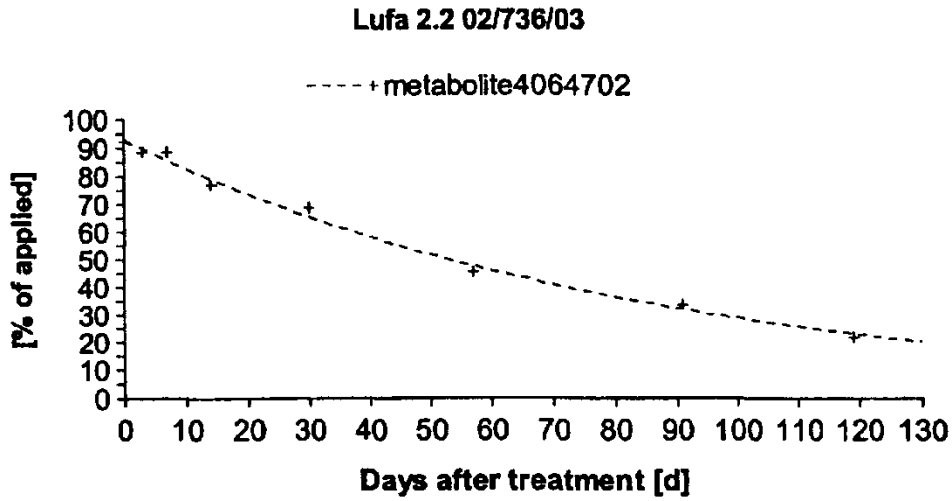
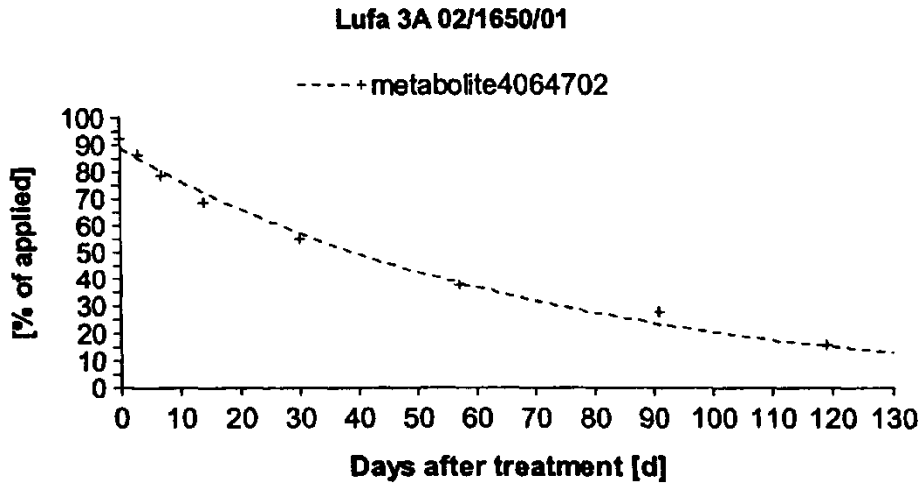


Figure 7.2.2.1/55 Experimental data and calculated degradation curve for Reg. No. 4064702 in Lufa 3a soil



Section A7.2.2.1 **Rate and route of degradation**

BPD Annex Point IIIA, VII.4, XII.1.1, XII.1.4 IIIA 7.2.2.1 Aerobic degradation in soil

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1. REFERENCE

1.1.	**Reference**	**6) Beigel C. (2004)** Calculation of the DT_{50} values at 10ºC of BAS 307 I (Flufenoxuron) and Reg. No. 4064702 (CL 932338) in Different Soils under Aerobic Conditions. XXXX unpublished XXXX
1.2.	**Data protection**	Yes
1.2.1.	Data owner	BASF
1.2.2.	Companies with letter of access	XXXX
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I authorisation.

2. GUIDELINES AND QUALITY ASSURANCE

2.1.	**Guideline study**	No
2.2.	**GLP**	Not applicable, calculation only
2.3.	**Deviations**	No

3. MATERIALS AND METHODS

3.1.	**Test materials**	Not applicable
3.2.	**Testing procedure**	
3.2.1.	Calculations	The DT_{50}values for Flufenoxuron and its degradation product Reg. No. 4064702 at 10ºC in various soils was calculated from the values determined at 20ºC in the aerobic metabolism study by Stephan and Ebert (2003, A7.2.2.1(04)). The rate constants were calculated using the relationship; $$k_{10^\circ C} = \frac{k_{20^\circ C}}{e^{\left(\frac{E_A}{R}\right)\left(\frac{1}{283}-\frac{1}{293}\right)}}$$ and the DT_{50} values were calculated from the rate constant as follows: $$DT_{50(10^\circ C)} = k_{10^\circ C}/\ln 2$$

4. RESULTS

4.1.	**DT_{50}**	The DT_{50} values for Flufenoxuron at 20ºC and the calculated DT_{50} at 10ºC are given in Table 7.2.2.1/100.

Section A7.2.2.1	**Rate and route of degradation**
BPD Annex Point IIIA, VII.4, XII.1.1, XII.1.4	IIIA 7.2.2.1 Aerobic degradation in soil

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1.	**Materials and methods**	The DT_{50} values for Flufenoxuron and Reg. No. 4064702 in various soils at 10ºC were calculated from the experimentally determined values at 20ºC using the Arrhenius equation.
5.2.	**Results and discussion**	
5.2.1.	DT_{50}/DT_{90}	The DT_{50} values for Flufenoxuron at 20ºC and the calculated DT_{50} at 10ºC are given in Table 7.2.2.1/100.
5.3.	**Conclusion**	The calculated DT_{50} for Flufenoxuron at 10ºC was 267 or 252 days. The calculated DT_{50} for Reg. No. 4064702 at 10ºC was 103 to 129 days.
5.3.1.	Reliability	1
5.3.2.	Deficiencies	No

Evaluation by Competent Authorities

Use separate "evaluation boxes" to provide transparency as to the comments and views submitted

EVALUATION BY RAPPORTEUR MEMBER STATE

Date	01/02/2005
Materials and Methods	Applicant’s version is acceptable.
Results and discussion	Applicant’s version is acceptable. Calculations made by RMS are of the same order, although slightly lower.
Conclusion	Applicant’s version is acceptable.
Reliability	1
Acceptability	acceptable
Remarks	

COMMENTS FROM ...

Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.2.2.1/100First–order DT_{50} values for Flufenoxuron and Reg. No. 4064702 in various soils

Substance	Soil	DT_{50}	
		20ºC Stephan and Ebert (2003)	10ºC Calculated
Flufenoxuron	Bruch West	122	267
	Li35b	115	252
Reg. No 4064702	Bruch West	57	125
	Li35b	56	123
	Lufa 2.2	59	129
	Lufa 3A	47	103

Section A7.2.2.2	**Rate and route of degradation in soil**
BPD Annex Point IIIA, XII.1.1, Annex VI, para 85	7.2.2.2 Field soil dissipation and accumulation

Official use only

		1. REFERENCE
1.1.	**Reference**	**Smalley R (2003)** Field Soil dissipation of BAS 307 I in the formulation BAS 307 QA I on bare soil in France (S) and Spain XXXX unpublished XXXX
1.2.	**Data protection**	Yes
1.2.1.	Data owner	BASF
1.2.2.	Companies with letter of access	XXXX
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I authorisation
		2. GUIDELINES AND QUALITY ASSURANCE
2.1.	**Guideline study**	Yes, SETAC Procedures for assessing the environmental fate and ecotoxicity of pesticides (March 1995) and ECPA Guidance Document on Field Dissipation Studies
2.2.	**GLP**	Yes (laboratory certified by the Department of Health of the Governement of the United Kingdom, United Kingdom)
2.3.	**Deviations**	No
		3. MATERIALS AND METHODS
3.1.	**Test material**	
3.1.1.	Lot/Batch number	XXXX
3.1.2.	Specification	See below
3.1.3.	Purity	Flufenoxuron was applied as a DC formulation containing 100 g as/L
3.1.4.	Further relevant properties	None
3.2.	**Reference substances**	The analytical standards used for the soil analyses were: Flufenoxuron, Lot No. AC 7467-005, Purity 99.3%, Expiry Date 29 0ct. 2006 XXXX Purity 95%, Expiry Date 15 Aug 2003.
3.3.	**Test solution and application**	Flufenoxuron was applied once to each plot at a target rate of 400 g a.s./ha using boom sprayers. See Table 7.2.2.2/ 1 for equipment details and Table 7.2.2.2/ 2 for application details.
3.4.	**Testing procedure**	

Section A7.2.2.2	**Rate and route of degradation in soil**
BPD Annex Point IIIA, XII.1.1, Annex VI, para 85	7.2.2.2 Field soil dissipation and accumulation

3.4.1.	Study design	Flufenoxuron was applied as a DC formulated product to four bare soil plots at each of two locations in Spain (ALO 27/01 and ALO 28/01) and two locations in southern France (FTL/23/01 and FBD/21/01). Petri dishes with 50 g of soil were placed in the plots during application to verify application. Soil cores (25-30 cm) were collected at intervals up to approximately one year after application, divided into 0-10, 10-20, and 20+ cm segments, pooled by depth, and analyzed for Flufenoxuron and CL 932338 (Reg.No. 4064702).
3.4.2.	Test site	The study was conducted at two sites in Spain and two sites in southern France. The characteristics of the soil are given in Table 7.2.2.2/ 3.
3.4.3.	Temperature and Rainfall	Weather data was collected at stations 8 km or less from the test sites. Data are given in the report.
3.4.4.	Duration of the test	Samples were collected up to 364 days after application.
3.4.5.	Number of replicates	At each sampling, five cores were taken from each of four plots and pooled for one analytical sample.
3.4.6.	Sampling	Samples were collected at 0, 14, 30, 60, 100, 180, and 360 days after application. Samples were immediately frozen and kept frozen at less than –18ºC, except for brief periods due to mechanical failures. The stability of flufenoxuron in frozen soil samples was shown.
3.4.7.	Analytical methods	Samples were analyzed at CEM Analytical Services Ltd. using BASF method RLA 12637V (Detailed of the method if given under IIIA 4.2)
3.5.	**Transformation products**	Transformation products tested: Yes
3.5.1.	Method of analysis for transformation products	BASF method RLA 12637V (Detailed of the method if given under IIIA 4.2)
		4. RESULTS
4.1.	**Application verification**	The application verification results showed 63 to 73% of the target rate of 400 g a.s./ha Table 7.2.2.2/ 4).
4.2.	**DT_{50}/DT_{90}**	DT_{50} values ranged from 6.1 to 66.8 days and DT_{90} values ranged from 20 to 222 days (Table 7.2.2.2/ 9). The DT_{50} and DT_{90} values were determined from first order rate constants estimated with Model Maker version 3.0.4. For the French sites the low DAT 0 values were replaced by values calculated from the application verification samples. The data and fitted curves are shown in Figure 7.2.2.2/ 1 to Figure 7.2.2.2/ 4 and, residuals from the fit are shown in Figure 7.2.2.2/ 5 to Figure 7.2.2.2/ 8.
4.2.1.	Concentration values	The total residues of flufenoxuron and CL 932338 (Reg.No. 4064702) at each interval at each of the sites are presented in Table 7.2.2.2/ 5 to Table 7.2.2.2/ 8.

Section A7.2.2.2	**Rate and route of degradation in soil**
BPD Annex Point IIIA, XII.1.1, Annex VI, para 85	7.2.2.2 Field soil dissipation and accumulation

4.2.2.	Leaching	Residues of Flufenoxuron were found only in the top two layers of soil, indicating no tendency to leach.
4.2.3.	Kinetic order	Pseudo first order
4.3.	**Specification of the transformation products**	Residues of CL 932338 (0.01 mg/kg) were found only in trial FBD/21/01 in the 0-10 cm layer at 176 days after application.

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1.	**Materials and methods**	Flufenoxuron was applied as a DC formulation to bare soil plots in Spain and France at a target rate of 400 g as/ha. Soil cores (25-30 cm) were collected up to approximately one year after application, sectioned into 10 cm segments, pooled, homogenized, and analyzed for residues of Flufenoxuron and CL 932338 (Reg.No. 4064702). Petri dishes with soil were placed in the plots during application to verify the application rate. The results of the soil core analyses were analyzed by Model Maker version 3.0.4 to give first order rate constants, which were used to calculate DT_{50} and DT_{90} values.
5.2.	**Results and discussion**	Application verification samples showed that the application reached 63 to 73% of the target rate of 400 g as/ha. Residues of Flufenoxuron declined from initial values of 0.12 to 0.39 mg/kg immediately after application to <0.01 to 0.04 mg/kg at 1 year after application. Flufenoxuron was found only in the top two layers of soil, indicating no tendency to leach. CL932338 was found at 0.01 mg/kg only in the top layer of soil at one interval of one trial.
5.2.1.	DT_{50}/DT_{90}	DT_{50} values ranged from 6.1 to 66.8 days and DT_{90} values ranged from 20 to 222 days.
5.2.2.	Leaching	Residues of flufenoxuron were found only in the top two layers of soil, indicating no tendency to leach.
5.3.	**Conclusion**	A field soil dissipation was conducted with Flufenoxuron according to SETAC and ECPA guidelines. This study shows that Flufenoxuron is degraded under field conditions with a half-life of 6.1 to 66.8 days. The "urea"-metabolite (CL 932338, Reg.No. 4064702) was detected only in one interval of one site at the limit of detection of 0.01 ppm.
5.3.1.	Reliability	1
5.3.2.	Deficiencies	No

Section A7.2.2.2	**Rate and route of degradation in soil**
BPD Annex Point IIIA, XII.1.1, Annex VI, para 85	7.2.2.2 Field soil dissipation and accumulation

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/02/2005
Materials and Methods	Applicant's version is acceptable.
Results and discussion	Applicant's version is acceptable.
Conclusion	Applicant's version is acceptable.
Reliability	1
Acceptability	acceptable
Remarks	
	COMMENTS FROM ...
Date	Give date of comments submitted
Materials and Methods	Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion. Discuss if deviating from view of rapporteur member state
Results and discussion	Discuss if deviating from view of rapporteur member state
Conclusion	Discuss if deviating from view of rapporteur member state
Reliability	Discuss if deviating from view of rapporteur member state
Acceptability	Discuss if deviating from view of rapporteur member state
Remarks	

Table 7.2.2.2/ 1 Application Equipment

Trail No.	Swath Width (m)	No. of Nozzles	Nozzle Spacing (cm)	Nozzle Size
ALO/27/01	2.0	4	50	LU 90-02
ALO/28/01	2.0	4	50	Unknown
FBD/21/01	3.0	12	25	XR 110-01
FTL/23/01	3.0	9	33.3	110 04

Table 7.2.2.2/ 2: Application Details

Trial No.	Plot No	Date of Application	Rate (g as/ha)	Appl. Volume (L/ha)
ALO/27/01	2	5 June 2001	399	303
	3	5 June 2001	417	317
	4	5 June 2001	421	320
	5	5 June 2001	417	317
ALO/28/01	2	14 June 2001	417	317
	3	14 June 2001	413	313
	4	14 June 2001	382	290
	5	14 June 2001	391	297
FBD/21/01	2	27 July 2001	421	316
	3	27 July 2001	436	327
	4	27 July 2001	414	310
	5	27 July 2001	421	316
FTL/23/01	2	14 June 2001	436	327
	3	14 June 2001	432	324
	4	14 June 2001	404	303
	5	14 June 2001	424	318

Table 7.2.2.2/ 3 Soil Characteristics

	ALO/27/01	ALO/28/01	FBD/21/01	FTL/23/01
pH (1:2.5 in water)	6.8	7.8	6.9	7.3
pH (0.1 N KCl)	6.5	7.2	6.1	6.7
Organic matter (%)	0.5	0.9	1.5	2.1
Organic carbon (%)	0.3	0.5	0.8	1.2
Sand (%)	90	63	60	49
Silt (%)	5	11	22	35
Clay (%)	5	26	18	16
USDA Classification	Sand	Sandy clay loam	Sandy loam	Loam
CEC (meq/100g)	2.1	13.7	9.5	9.0
WHC (%)	4.2	23.2	19.4	23.0
Dry bulk density (g/L)	1205	1074	1077	987

Table 7.2.2.2/ 4 Application Verification Results

Trial No.	Plot No	Dose Verification Results (mg/kg)	Dose Verification Results (g as/ha)	Mean Result (g as/ha)	Standard Deviation (%)
ALO/27/01	2	8.44, 8.42	373, 373	303	54.1
	3	7.12, 5.25	315, 232		
	4	5.65, 7.57	250, 335		
	5	6.23, 6.14	276, 272		
ALO/28/01	2	5.91, 5.24	262, 232	252	43.1
	3	5.34, 5.54	236, 245		
	4	4.16, 6.79	184, 300		
	5	5.33, 7.30	236, 323		
FBD/21/01	2	4.49, 7.68	199, 340	310	105.2
	3	10.97, 6.94	485, 307		
	4	3.81, 9.31	169, 412		
	5	7.15, 5.72	316, 253		
FTL/23/01	2	6.65, 9.51	294, 421	298	92.8
	3	6.75, 8.03	299, 355		
	4	4.61, 6.47	204, 286		
	5	8.71, 3.14	385, 139		

Table 7.2.2.2/ 5 Flufenoxuron and CL 932338 residues in soil from Trial ALO/27/01

Sampling Interval (DALA)	Flufenoxuron (mg/kg)	CL 932338 (mg/kg)
0-	<0.01	<0.01
0+	0.39	<0.01
14	0.06	<0.01
31	0.05	<0.01
59	0.02	<0.01
100	0.02	<0.01
182	0.01	<0.01
358	<0.01	<0.01

Table 7.2.2.2/ 6 Flufenoxuron and CL 932338 residues in soil from Trial ALO/28/01

Sampling Interval (DALA)	Flufenoxuron (mg/kg)	CL 932338 (mg/kg)
0-	<0.01	<0.01
0+	0.24	<0.01
14	0.10	<0.01
30	0.07	<0.01
60	0.07	<0.01
102	0.07	<0.01
179	0.04	<0.01
364	0.02	<0.01

Table 7.2.2.2/ 7 Flufenoxuron and CL 932338 residues in soil from Trial FBD/21/01

Sampling Interval (DALA)	Flufenoxuron (mg/kg)	CL 932338 (mg/kg)
0-	<0.01	<0.01
0+	0.12[1]	<0.01
14	0.14	<0.01
31	0.11	<0.01
61	0.12	<0.01
101	0.07	<0.01
176	0.09	0.01
362	0.04	<0.01

[1] This value not used. A value of 0.288, calculated from the petri dish results was used instead.

Table 7.2.2.2/ 8 Flufenoxuron and CL 932338 residues in soil from Trial FTL/23/01

Sampling Interval (DALA)	Flufenoxuron (mg/kg)	CL 932338 (mg/kg)
0-	<0.01	<0.01
0+	0.13[1]	<0.01
15	0.16	<0.01
32	0.14	<0.01
60	0.11	<0.01
103	0.10	<0.01
180	0.07	<0.01
361	0.02	<0.01

[1] This value not used. A value of 0.303, calculated from the petri dish results was used instead.

Table 7.2.2.2/ 9 DT_{50}/DT_{90} Values for Flufenoxuron

Trial No	DT_{50} (days)	DT_{90} (days)	r^2	Remarks
ALO/27/01	6.1	20.1	0.98	Optimization C_{ini} and k
ALO/28/01	30.6	101.5	0.70	Optimization C_{ini} and k
FBD/21/01	61.5	204.3	0.81	Optimization C_{ini} and k Petri dish value for DAT 0
FTL/23/01	66.8	222.0	0.83	Optimization C_{ini} and k Petri dish value for DAT 0

Figure 7.2.2.2/ 1 Residues of Flufenoxuron and fitted curve – trial ALO/27/01

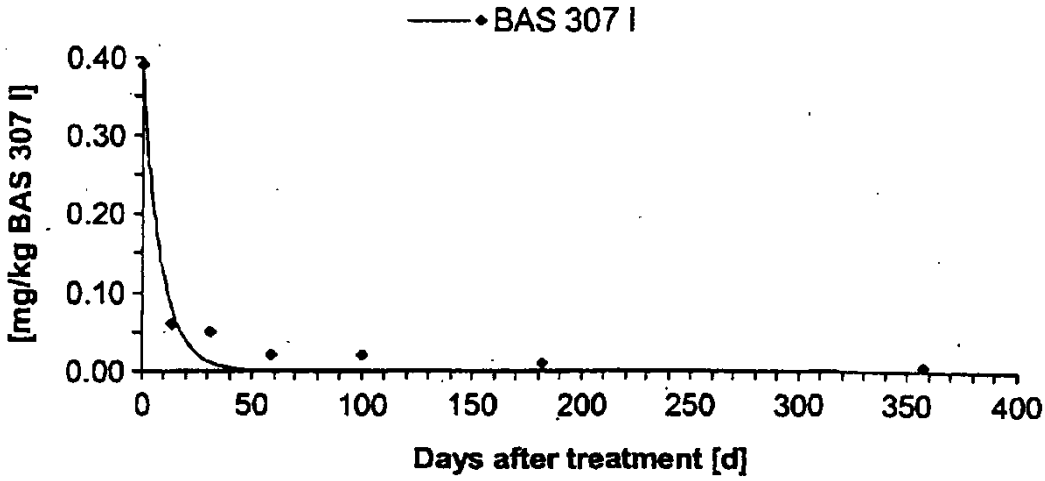


Figure 7.2.2.2/ 2 Residues of Flufenoxuron and fitted curve – trial ALO/28/01

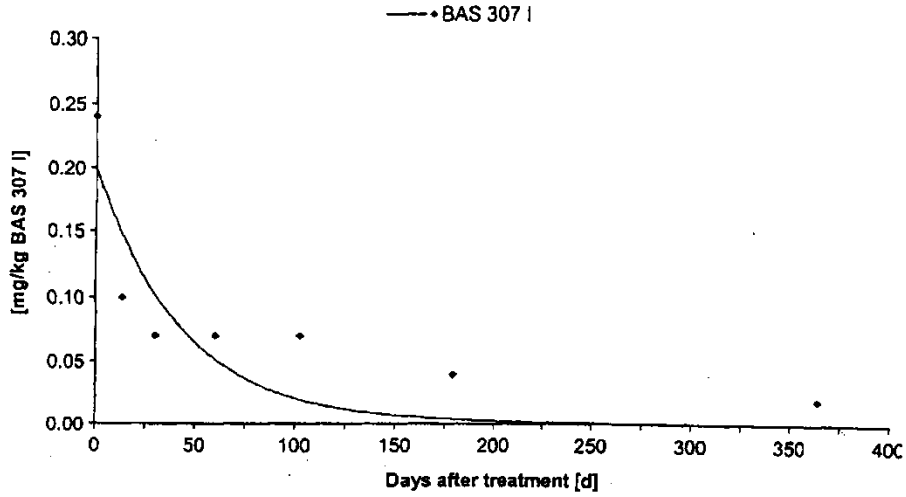


Figure 7.2.2.2/ 3 Residues of Flufenoxuron and fitted curve – trial FDB/21/01

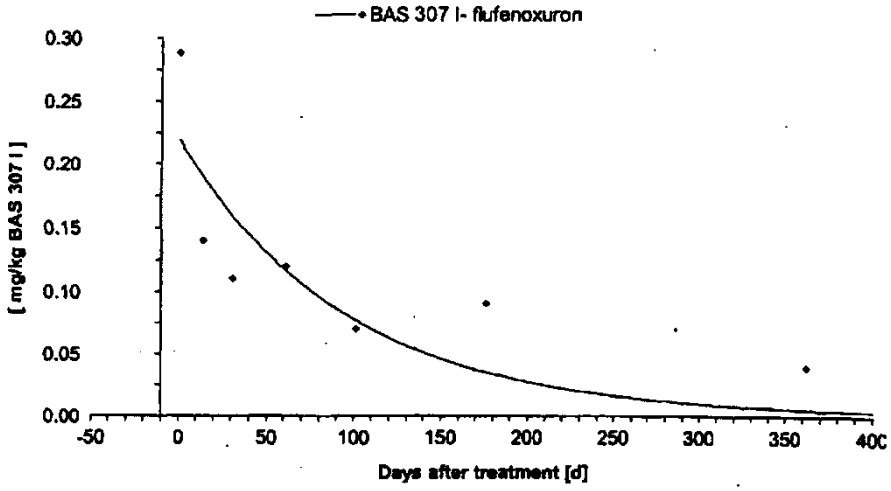


Figure 7.2.2.2/ 4 Residues of Flufenoxuron and fitted curve – trial FTL/23/01

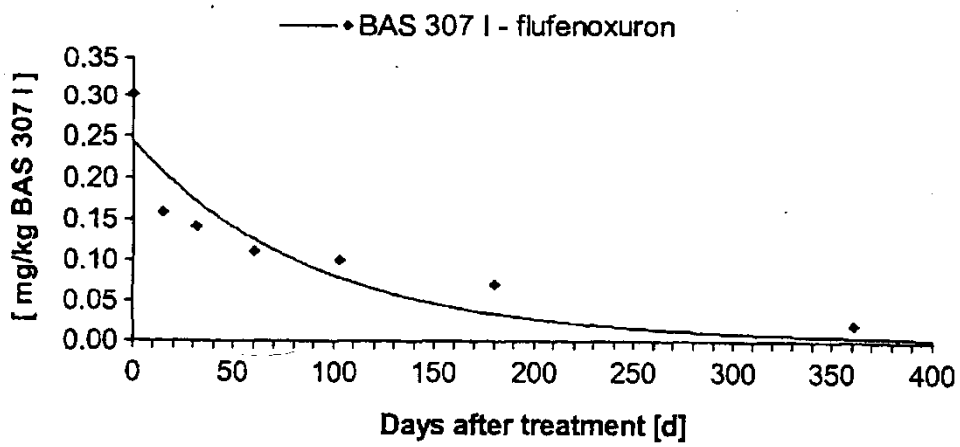


Figure 7.2.2.2/ 5 Plot of residuals – Trial ALO/27/01

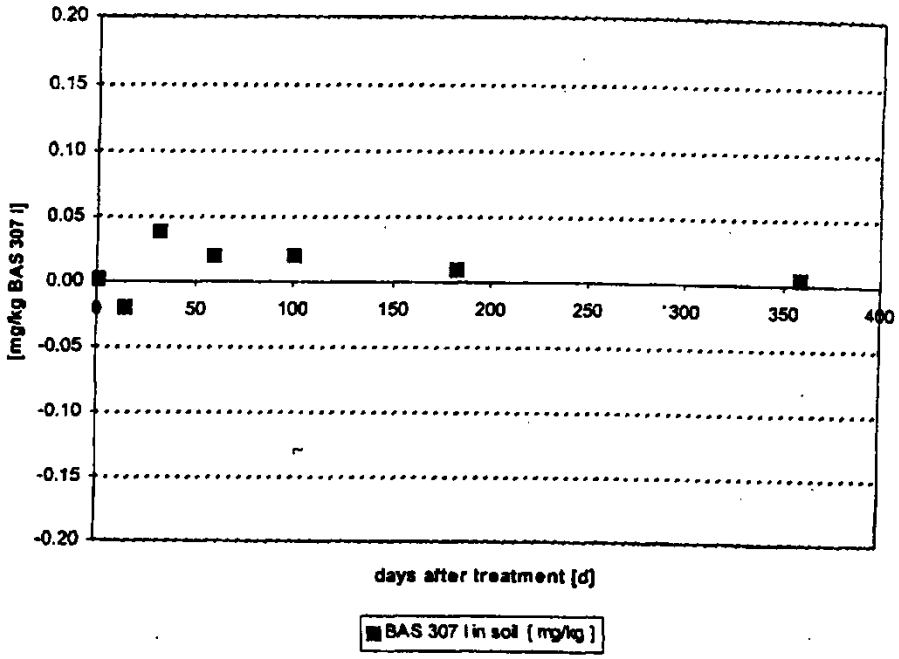


Figure 7.2.2.2/ 6 Plot of residuals – Trial ALO/28/01

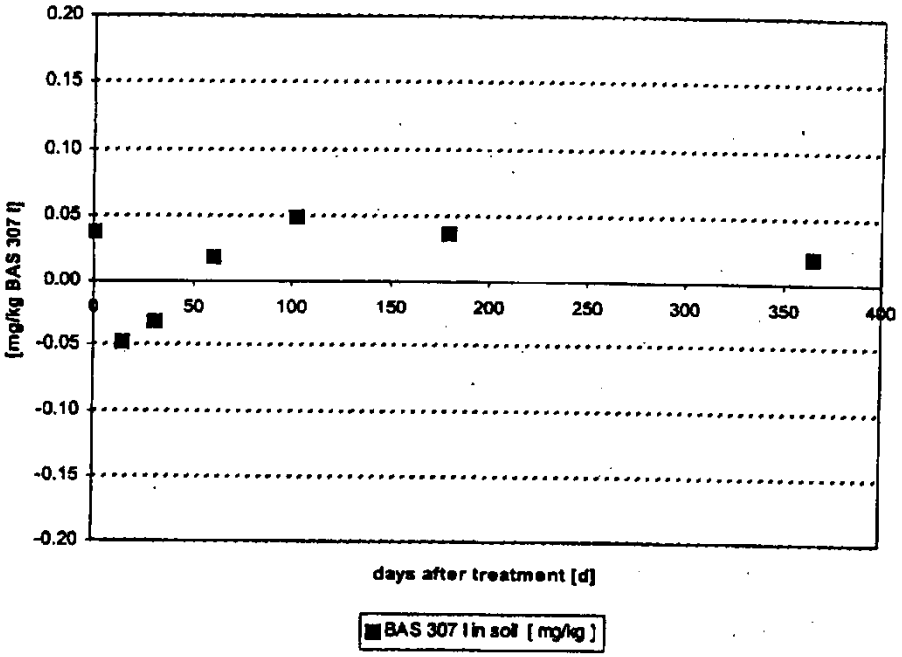


Figure 7.2.2.2/ 7 Plot of residuals – Trial FDB/21/01

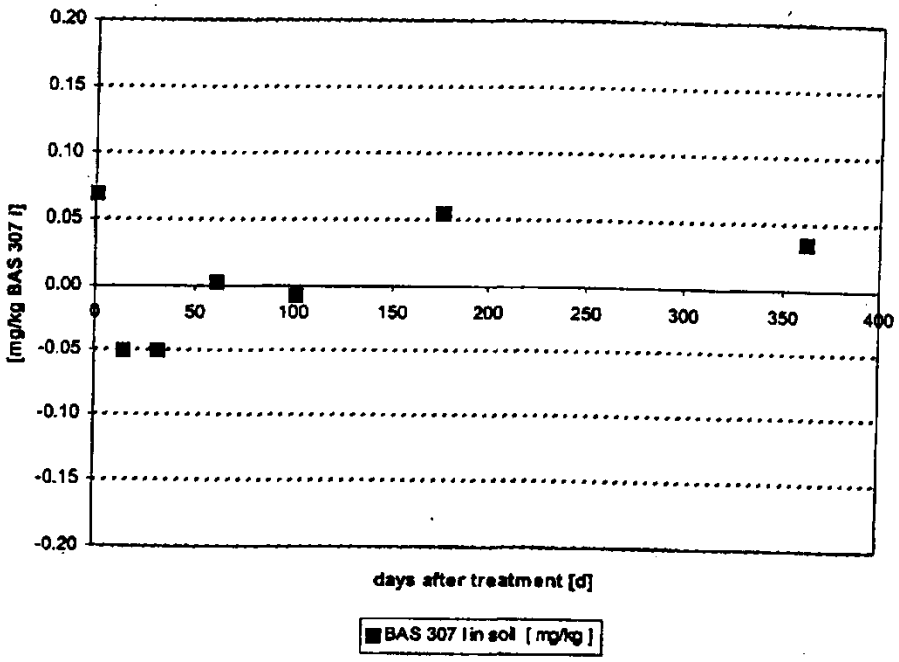
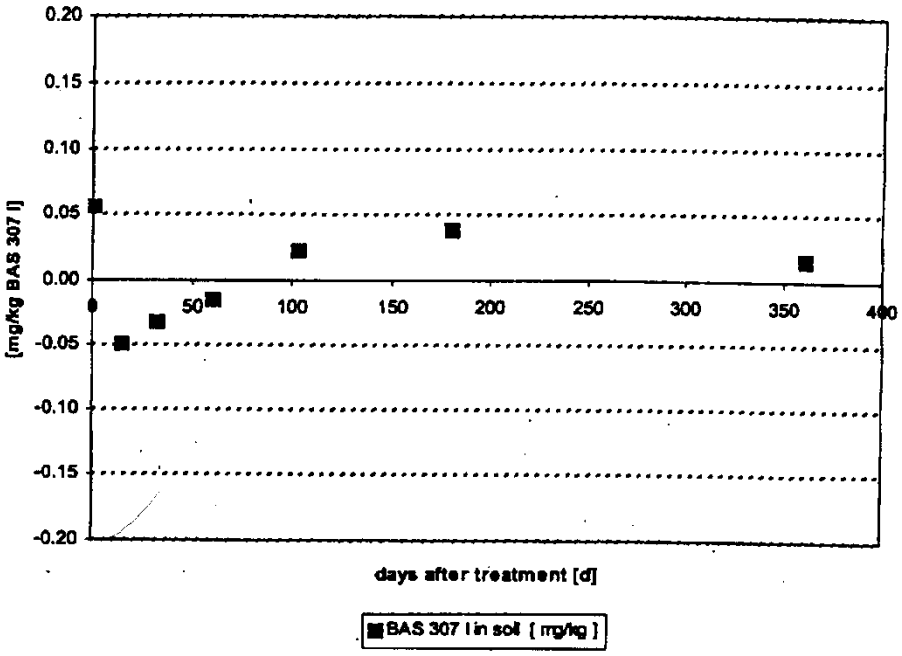


Figure 7.2.2.2/ 8 Plot of residuals – Trial FTL/23/01



Section A7.2.2.3	**Rate and route of degradation in soil**
BPD Annex Points IIIA, XII.1.4	IIIA 7.2.2.3 Extent and Nature of Bound Residues

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**1) Standen M & Hill A (1993)** CASCADE (WL 115110): A comparison of the degradation of [aniline-^{14}C]- and [toluyl-^{14}C]-CASCADE in soil under aerobic and anaerobic conditions. XXXX unpublished XXXX	
1.2.	**Data protection**	Yes	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Yes, BBA Guideline, Part IV, 4-1 (Dec. 1986)	
2.2.	**GLP**	Yes (laboratory certified by the Department of Health of the Government of the United Kingdom, United Kingdom)	
2.3.	**Deviations**	No	
		3. MATERIALS AND METHODS	
3.1.	**Test material**	See Section A7.2.2.1-3	
3.2.	**Testing procedure**		
3.2.1.	Test system	See Section A7.2.2.1-3	
3.2.2.	Analytical methods	After extraction with acetonitrile: water, the unextractable residues in the 150 day samples (both aerobic and anaerobic and both labels) were further characterized by separation into fulvic, humic, and humin fractions. The samples were washed with 0.5M HCl, then extracted by shaking with 0.5M NaOH for 19 hours at room temperature. The extracted soil was combusted to determine radiocarbon in the humin fraction. The extract was acidified to pH 1 with conc. HCl, precipitating the humic acids. After centrifugation and decanting through filters, the fulvic acid solution was radioassayed by LSC. The fulvic fractions from only the aerobic samples had sufficient radiocarbon to warrant further work. These samples were partitioned with dichloromethane and then ethyl acetate and the organic phases were combined, radioassayed, and concentrated for TLC analysis. The humic fraction was redissolved in 0.5M NaOH and partitioned with ethyl acetate, acidified to pH 2, and the suspension of reprecipitated humics was extracted with dichloromethane. The organic phases were dried, combined, radioassayed, and	

Section A7.2.2.3	**Rate and route of degradation in soil**
BPD Annex Points IIIA, XII.1.4	IIIA 7.2.2.3 Extent and Nature of Bound Residues

concentrated for TLC analysis.

3.3.	**Transformation products**	Transformation products tested: Yes
3.3.1.	Method of analysis for transformation products	Flufenoxuron degradates were identified by TLC and HPLC cochromatography with reference standards.

4. RESULTS – BOUND RESIDUES

(Results for extractable residues are given in Sections A7.2.2.1-3 and A7.2.2.4-3)

4.1.	**Material balance**	Soil bound residues accounted for 45.7% and 46.3% of the total applied radioactivity (TAR) for aerobic soils and 15.0% and 16.9% TAR in the anaerobic soils as determined by combustion of the previously solvent-extracted soils. The totals of the fulvic, humic and humin fractions gave excellent agreement with these numbers. See Table 7.2.2.3/ 1.
4.2.	**Specification of the transformation products**	The acid prewash recovered 0.1 to 1.1% TAR and the fulvic acid fractions contained 4.7 to 7.1% TAR with negligible percentages in the anaerobic samples. The humic fraction contained 18.6 to 21.8% TAR (sum of organo-soluble and aqueous phase) in the aerobic experiment, and 6-7% TAR in the anaerobic experiment. The insoluble humin fraction contained 18-20% TAR in the aerobic and about 8% TAR in the anaerobic experiment. Unchanged flufenoxuron was the only component identified in organic extracts but accounted for less than 2% TAR for all samples.

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1.	**Materials and methods**	This study was conducted according to BBA Guideline, Part IV, 4-1. [Aniline-^{14}C]- and [Toluyl-^{14}C]-Flufenoxuron were applied to a clay loam soil as a formulated material at 0.5mg/kg. Samples were incubated in the dark at 22ºC using an open system. Anaerobic samples were incubated aerobically for 30 days then amended with lucerne meal and flooded and flushed with nitrogen immediately. Aerobic and anaerobic samples were analyzed at 150 days after application had approximately 46% and 16% (respectively) of the original radiocarbon remaining extraction with acetonitrile water. The bound radiocarbon was further characterized by KOH extraction and separation into fulvic, humic and humin fractions. The fulvic and humic acid fractions were partitioned with dichloromethane and TLC.
5.2.	**Results and discussion**	
5.2.1.	Transformation products	The bound residues of Flufenoxuron are associated primarily with the humic and humin fractions of the soil. Unchanged Flufenoxuron is the primary component of organo-extractable portions of both fractions, but constituted less than 2% of the original dose.

Section A7.2.2.3	**Rate and route of degradation in soil**
BPD Annex Points IIIA, XII.1.4	IIIA 7.2.2.3 Extent and Nature of Bound Residues

5.3.	**Conclusion**	The study meets the requirements of BAA Guideline, Part IV, 4-1. Bound residues of Flufenoxuron are primarily associated with the humin and humic fractions. Flufenoxuron is the only identified component of organic extracts of these fractions, but is always <2% TAR.
5.3.1.	Reliability	1
5.3.2.	Deficiencies	No

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/02/2005
Materials and Methods	Applicant's version is acceptable provided the following amendments: 3.1.7 and 3.2: see section IIIA 7.2.2.1. 3.4.1 Method of analysis for transformation products*: Change to: "Flufenoxuron degradates* [WL115096 and WL129183] *were identified by TLC and HPLC cochromatography with reference standards*.
Results and discussion	Applicant's version is acceptable.
Conclusion	Applicant's version is acceptable providing the inclusion of the following amendments: 5.4.2 Deficiencies: add the following points - Degradation was tested in only one soil. - Certificates of analysis of the reference substances are not enclosed in the study report.
Reliability	2
Acceptability	Acceptable

Section A7.2.2.3	**Rate and route of degradation in soil**
BPD Annex Points IIIA, XII.1.4	IIIA 7.2.2.3 Extent and Nature of Bound Residues

Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.2.2.3/ 1 Soil Bound Residue Fractionation

soil sample	HCl pre-wash	fulvic acids organo-soluble	fulvic acids aqueous phase	humic acids organo-soluble	humic acids aqueous phase**	insoluble humin fraction	total
150 day, aerobic, aniline	1.1	2.3	2.4	4.8	17.0	18.1	45.7
150 day, aerobic, toluyl	0.8	5.1	2.0	4.6	14.0	19.8	46.3
150 day, anaerobic, aniline	0.06	-*	-*	2.4	3.9	7.6	15.0
150 day, anaerobic, toluyl	0.1	-*	-*	3.2	3.9	8.4	16.8

* not performed because of too low radioactivity
** > 85% of this radioactivity was precipitated with the humic acids on the second acidification step

Section A7.2.2.3	**Rate and route of degradation in soil**
BPD Annex Points IIIA, XII.1.4	IIIA 7.2.2.3 Extent and nature of bound residues

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**2) Goodyear A & Gross R (2001)** [^{14}C]-Flufenoxuron (BAS 307 I): Aerobic Soil Rate of Degradation in Three Soils. XXXX unpublished XXXX	
1.2.	**Data protection**	Yes	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I.	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Yes, SETAC (March 1995) Part 1, Section 1.1 Aerobic Degradation and OECD 307 Aerobic and Anaerobic Transformation in Soil (August 2000)	
2.2.	**GLP**	Yes (laboratory certified by the Department of Health of the Government of the United Kingdom, United Kingdom)	
2.3.	**Deviations**	No	
		3. MATERIALS AND METHODS	
3.1.	**Test material**	Materials and methods are described in Section A7.2.2.1-4	
3.1.1.	Analytical methods	Soils were extracted by shaking 30 minutes with acetonitrile (4 x 100 ml). The unextracted radioactivity was determined by combustion and the soil was further extracted with water. Fractionation into humic acids, fulvic acids, and humin was done for the 120 day samples only.	
3.2.	**Transformation products**	Transformation products in humic substances tested: No	
		4. RESULTS – BOUND RESIDUES (Results for extractable residues are given in Sections A7.2.2.1-4)	
4.1.	**Material balance**	Unextracted residues in the samples investigated accounted for 25.7 to 20.4% of the total applied radioactivity (TAR).	X

Section A7.2.2.3	**Rate and route of degradation in soil**
BPD Annex Points IIIA, XII.1.4	IIIA 7.2.2.3 Extent and nature of bound residues

4.2.	**Characterization of the bound residues**	The humin fraction contained 9 to 13 % TAR, humic acids 2 to 8%, and the fulvic acids 6 to 10 % TAR (Table 7.2.2.3/ 2).

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1.	**Materials and methods**	The study was conducted according to SETAC and OECD 307 guidelines with no significant deviations. [amide ring- ^{14}C]-Flufenoxuron was applied to three UK soils at a rate of 0.15µg/g and incubated aerobically for 120 days. Radiocarbon remaining in the soil after acetonitrile extraction was extracted with water and separated into humic acid, fulvic acid, and humin fractions.
5.2.	**Results and discussion**	The humin fraction contained 9 to 13 % TAR, humic acids 2 to 8%, and the fulvic acids 6 to 10 % TAR.
5.3.	**Conclusion**	The majority of the unextractable radioactivity resulting from aerobic soil metabolism of flufenoxuron was in the humin fraction in two of the tested soils (12 –13%) and in the fulvic acids fraction in the third (10.3%).
5.3.1.	Reliability	1
5.3.2.	Deficiencies	No

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	*01/02/2005*
Materials and Methods	See section A7.2.2.1-4. Applicant's version is acceptable.

Section A7.2.2.3	**Rate and route of degradation in soil**
BPD Annex Points IIIA, XII.1.4	IIIA 7.2.2.3 Extent and nature of bound residues

Results and discussion	See section A7.2.2.1-4. Applicant's version is acceptable. 4.1 Material balance: add "[After 120 days incubation,] *unextracted residues in the samples investigated accounted for 25.7 to 20.4% of the total applied radioactivity (TAR)."*
Conclusion	Applicant's version is acceptable.
Reliability	2 (study has retained as key study)
Acceptability	Acceptable
Remarks	

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.2.2.3/ 2 Soil bound residue fractionation of 120 day samples

	% of applied radioactivity		
	Chapel Hill	**Newhaven Cottage**	**Baylam**
Unextracted residues	20.4	25.7	25.2
Fulvic acids fraction	5.7	5.3	10.3
Humic acids fraction	2.5	7.5	6.1
Humin fraction	12.2	12.9	8.8

Section A7.2.2.4 **Rate and Route of Degradation in Soil**

BPD Annex Point IIIA, XII.1.1. IIIA 7.2.2.4 Anaerobic degradation in soil

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**1) Richardson K (1990)** A comparison of the degradation of [aniline-^{14}C] WL115110 in soil under aerobic and anaerobic conditions. XXXX unpublished XXXX **2) Richardson K (1990)** A comparison of the degradation of [aniline-^{14}C] WL115110 in soil under aerobic and anaerobic conditions (corrigendum). XXXX unpublished XXXX)	
1.2.	**Data protection**	No	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	No data protection claimed	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	No specific guideline referenced. Although no specific guidelines are referenced, the study meets the essentials of an anaerobic soil degradation study.	
2.2.	**GLP**	Yes (laboratory certified by Department of Health of the Government of the United Kingdom, United Kingdom)	
2.3.	**Deviations**	No	
		3. MATERIALS AND METHODS	
3.1.	**Test Materials**	Materials and methods are described in Section A7.2.1.1-1 & -2	
		4. RESULTS – ANAEROBIC PORTION (Results for the aerobic portion are summarized in Section A7.2.1.1-1 & -2)	
4.1.	**Material balance**	Total recoveries of radioactivity varied from 99.8 to 92.7% of the dose for the anaerobic portion of the study, with the lowest recoveries found at the earliest periods. This is attributed to	

Section A7.2.2.4	**Rate and Route of Degradation in Soil**
BPD Annex Point IIIA, XII.1.1.	IIIA 7.2.2.4 Anaerobic degradation in soil

		resuspension of the milled product in the floodwater and losses in transfer. The floodwater contained 13.6% of the applied dose on day 0, 1% on day 15, and 0.1 to 0.2 % thereafter.
4.1.1	Extractability	The amount of extractable radioactivity in the anaerobic portion of the study varied from 79.0 to 96.8 % of the applied dose with the earliest intervals being the lowest due to Flufenoxuron remaining in the flood water. Unextracted radiocarbon slowly increased from 0.1% to 5.6% of the dose at 152 days. No volatiles or CO_2 were found.
4.2.	**DT_{50}**	The DT_{50} was not reached in the anaerobic portion of the study. After 152 days of incubation 88% of the Flufenoxuron remained.
4.2.1.	Concentration values	The concentration of Flufenoxuron decreased from 92.6% of the applied dose (0.5 mg/kg) to 87.6% at 152 days after application. See Table 7.2.2.4/ 1
4.3.	**Specification of the transformation products**	"Urea" degradate under anaerobic conditions, accounted for only 2.4% of the dose at 152 days after treatment. "Amine" degradate was detected only at 152 days and less than 1% of the dose. (See Table 7.2.2.4/ 1 and Table 7.2.2.4/ 2).

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1.	**Materials and methods**	Although no specific guideline is referenced, this study was conducted according to the general principles of aerobic and anaerobic soil degradation studies, the exception being that the test substance was applied as a suspension instead of a solution or formulated material and the anaerobic samples were flooded immediately instead of after an aerobic incubation period. [Aniline-^{14}C]-Flufenoxuron was applied to a silty clay loam at 0.5 mg/kg using a closed system with periodic flushing with either moist, CO_2 free air (aerobic) or nitrogen (anaerobic). Polyurethane foam and KOH were used to trap volatiles and CO_2 respectively. Anaerobic samples were amended with lucerne meal and flooded and flushed with nitrogen immediately after application. Soil samples were analyzed at dosing and after 15, 30, 61, 90, and 152 days of incubation in the dark at 25ºC. Soil samples were analyzed by extraction with acetonitrile: water and partition with dichloromethane. The extracts were analyzed by liquid scintillation counting, and the dichloromethane phase by normal phase TLC.
5.2.	**Results and discussion**	
5.2.1.	Material balance	Total recoveries of radioactivity varied from 99.8 to 92.7% of the dose for the anaerobic portion of the study, with the lowest recoveries found at the earliest periods.
5.2.2.	DT_{50}	The DT_{50} was not reached in the anaerobic portion of the study. After 152 days of incubation 88% of the Flufenoxuron remained.
5.2.3.	Transformation products	"Urea" degradate, under anaerobic conditions, accounted for only 2.4% of the dose at 152 days after treatment. "Amine" degradate was detected only at 152 days and less than 1% of the dose.

Section A7.2.2.4	**Rate and Route of Degradation in Soil**
BPD Annex Point IIIA, XII.1.1.	IIIA 7.2.2.4 Anaerobic degradation in soil

5.3.	**Conclusion**	Flufenoxuron is anaerobically degraded slowly in soil with 88% remaining after 152 days. "Urea" degradate accounted for only 2.4% of the dose 152 days. Unextractable residues accounted for 5.6% of the dose at the end of the study, and no volatiles or CO_2 were found.
5.3.1.	Reliability	1
5.3.2.	Deficiencies	No

Section A7.2.2.4	**Rate and Route of Degradation in Soil**
BPD Annex Point IIIA, XII.1.1.	IIIA 7.2.2.4 Anaerobic degradation in soil

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	Evaluation by Rapporteur Member State
Date	02/01/2005
Materials and Methods	See section A7.2.2.1.
Results and discussion	Applicant's version is acceptable.
Conclusion	Applicant's version is acceptable provided the following amendments: - 5.3.2: deficiencies: - Only one soil was examined. - the test substance was labelled on one site only, - the test substance was applied as a suspension instead of a solution or formulated material - the anaerobic samples were flooded immediately instead of after an aerobic incubation period - Certificates of analysis of the reference substances are not enclosed in the study report. - A statement on the validity of the study are not provided in view of the validity criteria proposed in OECD Guideline.
Reliability	2
Acceptability	acceptable Results from this study are acceptable despite the deficiencies cited above: Flufenoxuron is degraded very slowly in anaerobic soil. This study will not be retain as key study, as reference 3 was realised with labeling on two sites
Remarks	
	Comments from ...

Date	**Give date of comments submitted**
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.2.2.4/ 1: Distribution of radioactivity in Flufenoxuron treated soil under anaerobic conditions

Recovery of radioactivity and distribution of metabolites after application of aniline-^{14}C-Flufenoxuron to soil and incubation under anaerobic conditions [%TAR]

DAT	$^{14}CO_2$	water for flooding (saturation water)	extractable residues (total)	water phase after DCM partitioning of soil extracts*	unextracted	material balance
0	-	13.6	79.0	-	0.1	92.7
15	0.0	1.0	90.9	1.5	1.2	93.1
30	0.0	0.1	96.8	0.3	1.7	98.6
61	0.0	0.1	94.8	2.7	2.2	97.1
90	0.0	0.2	95.3	12.9	3.1	98.6
152	0.0	0.1	94.1	7.1	5.6	99.8

* does not count for material balance (included in total extractable residues)

Results of TLC analysis of soil extracts after application of aniline-^{14}C-Flufenoxuron to soil and incubation under anaerobic conditions [%TAR]

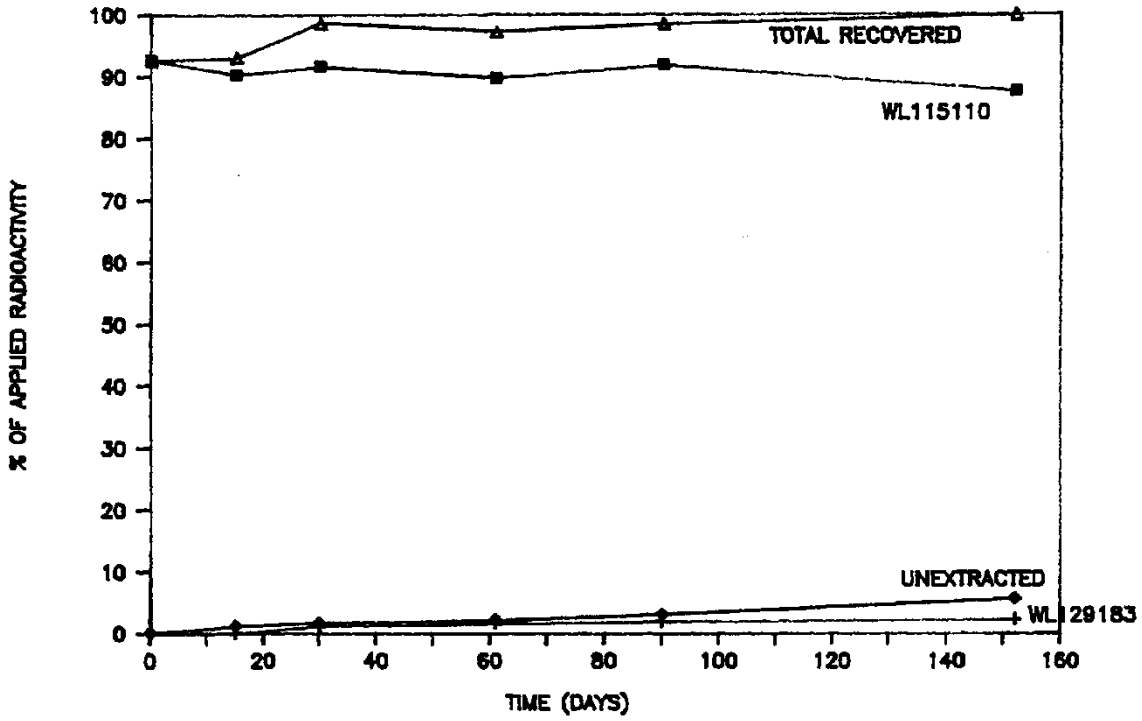
DAT	water for flooding (saturation water) *	Flufenoxuron WL115110 (total, including *)	"urea" WL129183 CL932338	"amine" WL115096 CL359882	others	water phase after DCM partitioning*
0	*13.6*	92.6	-	-	-	-
15	*1.0*	90.2	0.0	0.0	0.1	*1.5*
30	*0.1*	91.7	1.2	0.0	3.9	*0.3*
61	*0.1*	89.8	1.6	0.0	0.7	*2.7*
90	*0.2*	91.9	1.9	0.0	1.4	*12.9*
152	*0.1*	87.6	2.4	0.5	3.7	*7.1*

* all radioactivity attributed to unchanged Flufenoxuron

Table 7.2.2.4/ 2 Specification and amount of transformation products

Lab/Report Code, and/or IUPAC* Chemical Name*(s)	**Amount [%] of parent compound measured**
WL 129183, CL 932338, Reg No 4064702 N-{4-[2-chloro-4-(trifluoromethyl)phenoxy]-2-fluoromethyl}urea	Max. 2.4% at 152 days
WL 115096, CL 359882, Reg NO. 241208 4-[2-chloro-4-(trifluoromethyl)phenoxy]-2-fluorobenezenamine	<1%

Figure 7.2.2.4/ 1 Degradation of 14C-Flufenoxuron in anaerobic soil



Section A7.2.2.4	**Rate and Route of Degradation in Soil**
BPD Annex Points IIIA, XII.1.1	IIIA 7.2.2.4 Anaerobic degradation in soil

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**3) Standen M & Hill A (1993)** CASCADE (WL 115110): A comparison of the degradation of [aniline-^{14}C]- and [toluyl-^{14}C]-CASCADE in soil under aerobic and anaerobic conditions. unpublished XXXX	
1.2.	**Data protection**	No	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	No data protection claimed	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Yes, BBA Guideline, Part IV, 4-1 (Dec. 1986)	
2.2.	**GLP**	Yes (laboratory certified by the Department of Health of the Government of the United Kingdom, United Kingdom)	
2.3.	**Deviations**	No	
		3. MATERIALS AND METHODS	
3.1.	**Test material**	See Section A7.2.2.1-3	
3.2.	**Testing procedure**		
3.2.1.	Test system	See Section A7.2.2.1-3	
3.2.2.	Analytical methods	See Section A7.2.2.1-3	
3.3.	**Transformation products**	Transformation products tested: Yes	
3.3.1.	Method of analysis for transformation products	Flufenoxuron degradates were identified by TLC and HPLC cochromatography with reference standards.	
		4. RESULTS – ANAEROBIC PORTION (Aerobic results are given in Section A7.2.2.1-3)	
4.1.	**Material balance**	Mass balance for the anaerobic samples ranged from 99.8% and 99.1% (for the aniline and toluyl labels, respectively) at day 60 to 101.3% and	

Section A7.2.2.4	**Rate and Route of Degradation in Soil**
BPD Annex Points IIIA, XII.1.1	IIIA 7.2.2.4 Anaerobic degradation in soil

		101.2% on day 150 (see Table 7.2.2.4/ 3).
4.1.1.	Extractability	For the anaerobic soils, the amount of radiocarbon extractable with acetonitrile: water and the unextractable radiocarbon changed little after establishment of anaerobic conditions, with about 85% extractable and 15% unextractable.
4.2.	**DT_{50}**	The DT_{50} for Flufenoxuron in anaerobic soil was not reached during this study. At the end of the 150 day study, about 75% of the Flufenoxuron remained with no significant degradation after establishing anaerobic conditions (see Table 7.2.2.4/ 4).
4.2.1.	Concentration values	At the end of the 150-day study, about 75% the Flufenoxuron remained with no significant degradation after establishing anaerobic conditions. The amounts of Flufenoxuron and its metabolites in aerobic soil at each sampling interval are shown in Table 7.2.2.4/ 3.
4.3.	**Specification of the transformation products**	No metabolite exceeded 10% of the applied dose at any time during the study. "Urea" degradate reached a maximum of 5.1% at 60 days after treatment (equivalent to preflooding value) and slowly declined to 3.5% by the end of the study. "Benzenamine" degradate was also detected, but at <1% of the applied dose.
	5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1.	**Materials and methods**	This study was conducted according to BBA Guideline, Part IV, 4-1. [Aniline-^{14}C]- and [Toluyl-^{14}C]-Flufenoxuron were applied to a clay loam soil as a formulated material at 0.5mg/kg. Samples were incubated in the dark at 22ºC using an open system. Separate samples were incubated in a closed system (biometer flasks) with periodic flushing with air to maintain aerobic conditions and flush $^{14}CO_2$ into KOH traps. Anaerobic samples were incubated aerobically for 30 days then amended with lucerne meal and flooded and flushed with nitrogen immediately. Aerobic soil samples were analyzed at dosing and after 30, 60, 91, and 150 days. Anaerobic samples were analyzed at 60, 91, and 150 days after application. Soil samples were analyzed by extraction with acetonitrile: water and partition with dichloromethane. The extracts were analyzed by liquid scintillation counting, and the dichloromethane phase by HPLC and normal phase TLC.
5.2.	**Results and discussion**	
5.2.1.	Material balance	Mass balance for the anaerobic samples ranged from 99.8% and 99.1% (for the aniline and toluyl labels, respectively) at day 60 to 101.3% and 101.2% on day 150 (See Table 7.2.2.4/ 3).
5.3.	**DT_{50}**	The DT_{50} for Flufenoxuron in anaerobic soil was not reached during this study. At the end of the 150-day study, 77.9% and 74.9% of the Flufenoxuron remained with no significant degradation after establishing anaerobic conditions.
5.3.1.	Transformation products	No metabolite exceeded 10% of the applied dose at any time during the study.

Section A7.2.2.4	**Rate and Route of Degradation in Soil**
BPD Annex Points IIIA, XII.1.1	IIIA 7.2.2.4 Anaerobic degradation in soil

5.4.	**Conclusion**	The study meets the requirements of BAA Guideline, Part IV, 4-1. The study shows that Flufenoxuron is degraded very slowly under anaerobic conditions in soil. No mineralization to CO_2 was observed, and unextractables accounted for about 15% of the dose at 60 through 150 days.
5.4.1.	Reliability	1
5.4.2.	Deficiencies	No

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/02/2005
Materials and Methods	See Doc IIIA 7.2.2.1
Results and discussion	Applicant's version is acceptable.
Conclusion	Applicant's version is acceptable providing the inclusion of the following amendments: - 5.4: Conclusion: add the following statement "*there was no significant differences between the anerobic degradation rate of both labels. Additionally, there were no difference in the amount and type of degradation products formed between the aniline and toluyl labels*. " 5.4.2 Deficiencies: add the following points - Degradation was tested on only one soil. - Certificates of analysis of the reference substances are not enclosed in the study report. - A statement on the validity of the study was not provided in view of the validity criteria proposed in OECD Guideline.
Reliability	2
Acceptability	acceptable Despite the deficiencies cited above, the outcomes of this study are acceptable.
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.2.2.4/ 3 Distribution of radiocarbon in anaerobic soil (% of applied dose)

	[aniline-^{14}C]			[toluyl-^{14}C]		
Days after treatment	**60**	**91**	**150**	**60**	**91**	**150**
Flood water	0.1	0.1	0.1	0.2	0.1	0.1
Extracted with acetonitrile:water	84.0	84.2	86.1	86.2	85.4	84.2
Dichloromethane soluble	83.8	84.1	86.1	86.1	85.3	84.2
Water soluble	0.2	0.1	0	0.1	0.1	0
Unextracted	15.6	17.0	15.1	12.7	13.9	16.9
Total	99.8	101.3	101.3	99.1	99.4	101.2

Table 7.2.2.4/ 4 Identity of radiocarbon extracted from anaerobic soils

	Aniline			**Toluyl**		
	60	**91**	**150**	**60**	**91**	**150**
Flufenoxuron	75.8	74.9	77.9	77.7	76.1	74.9
"Urea" (CL 932338, WL 129183, Reg. No. 4064702)	5.1	4.2	3.5	5.1	4.5	3.3
"benzeneamine" (CL 359882, WL 115096, Reg No. 241208)	0.6	0.8	0.0	0.6	0.7	0.0
Others	2.3	4.3	4.6	2.8	4.1	6.1

Table 7.2.2.4/ 5 Specification and amount of transformation products

Lab/Report Code, and/or IUPAC Chemical Name*(s)*	**Amount [%] of parent compound measured**
WL 129183 N-{4-[2-chloro-4-(trifluoromethyl)phenoxy]-2-fluoromethyl}urea	Max. 5.1% at 60 days 3.3 to 3.5% at 150 days
WL 115096 4-[2-chloro-4-(trifluoromethyl)phenoxy]-2-fluorobenezenamine	<1%

Section A7.2.2.4 Rate and Route of Degradation in Soil

BPD Annex Point IIIA, XII.1.1 IIIA 7.2.2.4 Anaerobic degradation in soil

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**4) Lewis CJ, Gross R (2001)** 14C-Flufenoxuron: Soil photolysis under artificial sunlight. XXXX. unpublished XXXX	
1.2.	**Data protection**	Yes	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Yes, SETAC Europe March 1995	
2.2.	**GLP**	Yes (laboratory certified by Department of Health of the Government of the United Kingdom, United Kingdom)	
2.3.	**Deviations**	No	
		3. MATERIALS AND METHODS	
3.1.	**Test material**	[Amide ring-^{14}C] and [Benzotrifluoride ring-^{14}C]-Flufenoxuron	
3.1.1.	Lot/Batch number	[XXXX	
3.1.2.	Specification	See below	
3.1.3.	Purity	[Amide ring-^{14}C]-Flufenoxuron - 95.6% radiopure [Benzotrifluoride ring-^{14}C]-Flufenoxuron - 96.8% radiopure	
3.1.4.	Radiolabeling	[Amide ring-^{14}C]-Flufenoxuron [Benzotrifluoride ring-^{14}C]-Flufenoxuron	
3.1.5.	UV/VIS absorption spectra and absorbance value	See Figure 7.2.2.4/ 2.	
3.1.6.	Further relevant properties	Flufenoxuron was rapidly degraded in aqueous photolysis studies, with predicted environmental half-lives of 12 to 40 days depending on season and latitude.	
3.2.	**Reference substances**	Reference substances used for co-chromatography are given in Table 7.2.2.4/ 6.	

Section A7.2.2.4 Rate and Route of Degradation in Soil

BPD Annex Point IIIA, XII.1.1 IIIA 7.2.2.4 Anaerobic degradation in soil

3.3.	**Test solution**	A stock solution of [amide ring-^{14}C]-Flufenoxuron was prepared by dissolving ca. 4.6 mg in 3 mL of acetone. The application solution was prepared by evaporating a 50 µL aliquot of the stock and redissolving in 4.2 ml of acetonitrile. A stock solution of [benzotrifluoride ring-^{14}C]-Flufenoxuron was prepared by dissolving ca 12 mg in 1.5 mL of acetone. The application solution was prepared by evaporation of a 180 µL aliquot of the stock solution and redissolving in 1.0 mL of acetonitrile.	X
3.4.	**Testing procedure**		
3.4.1.	Test system	Soil layers (ca. 2 mm), formed by spreading a slurry (equivalent to 4g dry weight) in water on metal trays and allowing the soil to dry, were treated with Amide-^{14}C- and benzotrifluoride-^{14}C-labeled Flufenoxuron. The characterization of the soil is given in Table 7.2.2.4/ 7. Aliquots of the test substances in acetonitrile solutions were added dropwise to the surface of the soil samples and allowed to evaporate. The final concentration was 0.6 µg/4 g dry soil. Samples were continuously irradiated using a Hanau Suntest CPS Accelerated Exposure machine equipped with a 1.5 kW xenon arc lamp as light source. Wavelengths of <290 nm were filtered off to give ultraviolet and visible light with a spectral distribution close to that of natural sunlight. Samples for irradiation were maintained at 20 ± 3°C in the Exposure Machine by circulating water through a cooling block on which the soil trays were located. The cooling chamber was sealed with a quartz glass lid and had an air inlet and outlet to allow passage of air to trapping solutions. Dark control samples were housed in a sealed common chamber maintained also at 20 ± 3°C in the dark. Carbon dioxide-free air was drawn through the chambers and through a series of six traps for possible polar or non-polar organic volatiles and CO_2.	
3.4.2.	Determination of irradiance	The spectral properties and intensity of the xenon lamp were measured at the position of the soil surface using a LI-1800 spectroradiometer. It was calculated that 12 hours of irradiation is equal to one day of UK summer sunlight.	
3.4.3.	Temperature	20 ± 3°C	
3.4.4.	Duration of the test	Samples were irradiated continuously for up to 16 days.	
3.4.5.	Number of replicates	Duplicate samples were taken at day 0 and single samples at all other intervals.	
3.4.6.	Sampling	Samples were taken at 0, 3, 6, 13, and 16 days of continuous irradiation for the amide-label and 0, 3, 6, 10, and 15 days of continuous irradiation for the benzotrifluoride-label.	
3.4.7.	Analytical methods	The soil samples were extracted 3 x with acetonitrile/water (7:3 v:v) and supernatants were removed after centrifugation. The combined extract	

Section A7.2.2.4 Rate and Route of Degradation in Soil

BPD Annex Point IIIA, XII.1.1 IIIA 7.2.2.4 Anaerobic degradation in soil

		was diluted with water, partitioned with dichloromethane, concentrated by rotary evaporation and then analyzed by TLC. Selected samples were also analyzed by HPLC to confirm test compound and degradation products (Table 7.2.2.4/ 8 and Table 7.2.2.4/ 9).
3.5.	**Transformation products**	Transformation products tested: Yes
3.5.1.	Method of analysis for transformation products	Transformation products were identified and quantitated by TLC and HPLC.
		4. RESULTS
4.1.	**Controls**	No degradation of Flufenoxuron was observed in the dark controls.
4.2.	**Photolysis data**	
4.2.1.	Concentration values	The distribution of the radiocarbon in the irradiated samples and dark controls is presented in Table 7.2.2.4/ 10 for the amide label and in Table 7.2.2.4/ 11 for the benzotrifluoride label. The degradation of Flufenoxuron and the fitted curves are shown in Figure 7.2.2.4/ 3 and Figure 7.2.2.4/ 4.
4.2.2.	Mass balance	Mass balance was greater than 96% for all intervals except for the 15 day interval of the benzotrifluoride label which was 82%. This interval was not used in the statistical analysis.
4.2.3.	DT_{50}	The DT_{50} expected under bright summer sunlight in Harrowgate, UK (ca. 54ºN) was 147 days for the amide label and 166 days for the benzotrifluoride label.
4.3.	**Specification of the transformation products**	2,6-diflourobenzamide was the only product found, accounting for a maximum of <3% of the radiocarbon dose.
		5. APPLICANT'S SUMMARY AND CONCLUSION
5.1.	**Materials and methods**	The photolysis of Flufenoxuron on soil was studied according to SETAC guidelines using two forms of ^{14}C labeled Flufenoxuron. The test substances were applied to thin layers of soil in acetonitrile solutions and irradiated continuously at 20ºC for up to 16 days under a xenon lamp. At intervals, samples were extracted with acetontirlie: water and analyzed by LSC, TLC, and HPLC.
5.2.	**Results and discussion**	Flufenoxuron was degraded slowly with 80% (amide label) remaining after 16 days of artificial irradiation. The extrapolated DT_{50} under UK summer sunlight (ca. 54ºN) was 147 to 166 days. 2,6-difluorobenzamide was the only metabolite.
5.3.	**Conclusion**	Photolysis is not likely to be significant route of degradation of Flufenoxuron in soil.
5.3.1.	Reliability	1

Section A7.2.2.4 Rate and Route of Degradation in Soil

BPD Annex Point IIIA, XII.1.1 IIIA 7.2.2.4 Anaerobic degradation in soil

5.3.2. Deficiencies No

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/02/2005
Materials and Methods	Applicant's version is acceptable, providing the following ammendments: - 3.3 Test solution: Second paragraph, first sentence, change to " *A stock solution of [benzotrifluoride ring-^{14}C]-Flufenoxuron was prepared by dissolving ca* [0.12 mg] *in 1.5 mL of acetone."*
Results and discussion	Applicant's version is acceptable.
Conclusion	Applicant's version is acceptable.
Reliability	1
Acceptability	acceptable
Remarks	
	COMMENTS FROM ...
Date	Give date of comments submitted
Materials and Methods	Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion. Discuss if deviating from view of rapporteur member state
Results and discussion	Discuss if deviating from view of rapporteur member state

Section A7.2.2.4 Rate and Route of Degradation in Soil

BPD Annex Point IIIA, XII.1.1

IIIA 7.2.2.4 Anaerobic degradation in soil

Conclusion	Discuss if deviating from view of rapporteur member state
Reliability	Discuss if deviating from view of rapporteur member state
Acceptability	Discuss if deviating from view of rapporteur member state
Remarks	

Table 7.2.2.4/ 6 Reference substances used for co-chromatography

Name/No.	**Lot. No.**	**Purity**
Flufenoxuron, unlabeled	XXXX	99.3%
2,6-difluorobenzamide	XXXX	100%
CL 359882	XXXX	99%
CL 932338	XXXX	95%

Table 7.2.2.4/ 7 Soil used to investigate the soil photolysis of Flufenoxuron

Soil designation sample code	Newhaven Cottage (used for amide-label) CS16/00-628	Newhaven Cottage (used for benzo-trifluoride-label) CS32/00-333
Textural class (BBA scheme)	silty loam	silty loam
Origin	near Newhaven Cottage, Hartington Upper Quarter, Derbyshire, UK	
Particle size distribution [%] (BBA-scheme): 0.063 – 2 mm 0.002 – 0.063 mm < 0.002 mm	 23 57 20	 23 57 20
Organic C [%]	4.5	4.5
cation exchange capacity [mval/100g dry soil]	17.4	17.8
pH [KCl] pH [H2O]	6.2 6.7	6.2 6.7
Biomass (fumigation-extraction method) [ug C/g]	604.77	620.57
maximum water holding capacity at pF 2.5 [g H_2O/100g dry soil]	48.5	34.7

Table 7.2.2.4/ 8 HPLC Conditions

Column	HiChrom RPB C18 (25 x 4.6mm id)
Solvent A	water
Solvent B	acetonitrile
Gradient	Time (min) %B 0 80 1 80 9 90 10 95 19.9 80 30 80
Flow rate	1 mL/min
UV detection	ABI Model 759A absorbance detector at 254 nm
^{14}C detection	β-ram flow through radioactivity monitor
Retention time	Flufenoxuron – 17.6 min CL932338 - 11.7 min CL 211558 – 3.5 min CL 359882 – 15.2 min

Table 7.2.2.4/ 9 TLC conditions

Stationary phase	Whatman Silica Gel KF6
Mobile phase	Toluene:ethyl acetate:ammonia (50:50:0.2)
R_f	Flufenoxuron – 0.57 CL932338 – 0.09,0.17 CL359882 – 0.57 CL211558 – 0.32
Plates were developed in glass chambers and imaged with a Fujix BAS 1500 imager using TINA 2.09g analysis software.	

Table 7.2.2.4/ 10 Recovery and distribution of radioactivity during soil photolysis of amide-^{14}C-Flufenoxuron [% TAR]

DAT	$^{14}CO_2$	Flufenoxuron	2,6-diflouro-benzamide CL211558	others	aqueous phase after partitioning	unextracted	material balance
irradiated							
0	-	95.3	n.d.	1.0	1.9	3.1	101.3
3	2.0	87.8	1.7	1.9	3.6	5.4	102.4
6	2.0	82.6	2.4	2.3	1.8	6.0	97.1
10	2.3	86.6	1.4	1.0	2.0	5.2	98.8
13	3.0	82.9	1.2	1.5	1.6	5.7	96.2
16	4.0	80.4	2.7	1.5	1.7	6.4	96.9
dark control							
0	-	95.3	n.d.	1.0	1.9	3.1	101.3
3	0.6	94.8	n.d.	1.6	2.5	2.7	102.2
6	1.5	91.8	n.d.	2.0	1.8	3.0	100.1
10	1.7	96.2	n.d.	0.5	2.6	3.2	104.4
13	3.6	95.0	n.d.	1.4	1.9	2.5	104.6
16	5.9	93.8	n.d.	1.4	1.5	2.2	105.1

nd = not detected

Table 7.2.2.4/ 11 Recovery and distribution of radioactivity during soil photolysis of benzotrifluoride-^{14}C-Flufenoxuron [% TAR]

DAT	$^{14}CO_2$	Flufenoxuron	others	aqueous phase after partitioning	unextracted	material balance
irradiated						
0	-	98.3	0.9	1.1	1.3	101.6
3	0.3	94.5	0.4	0.9	4.1	100.4
6	0.8	88.5	1.5	1.3	4.9	97.9
10	1.2	93.1	0.6	1.2	5.1	101.5
*15**	*1.8*	*76.0*	*n.d.*	*0.7*	*3.4*	*82.2*
dark control						
0	-	98.3	0.9	1.1	1.3	101.6
3	n.d.	98.0	1.2	n.d.	1.5	100.7
6	n.d.	97.3	0.7	n.d.	1.7	99.7
10	n.d.	99.5	0.4	n.d.	2.2	102.1
15	0.6	97.0	1.1	n.d.	2.2	100.9

nd = not detected; * this value not included in analysis due to poor mass balance

Figure 7.2.2.4/ 2 UV-vis adsorption spectrum of Flufenoxuron

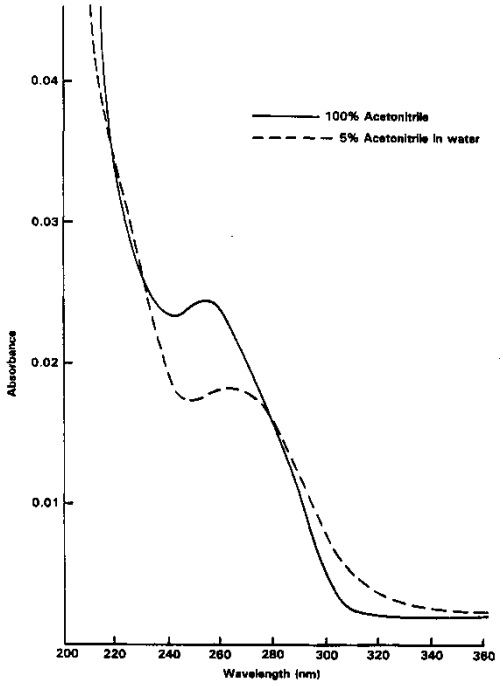


Figure 7.2.2.4/ 3 Photodegradation of Flufenoxuron from a soil surface -Amide label

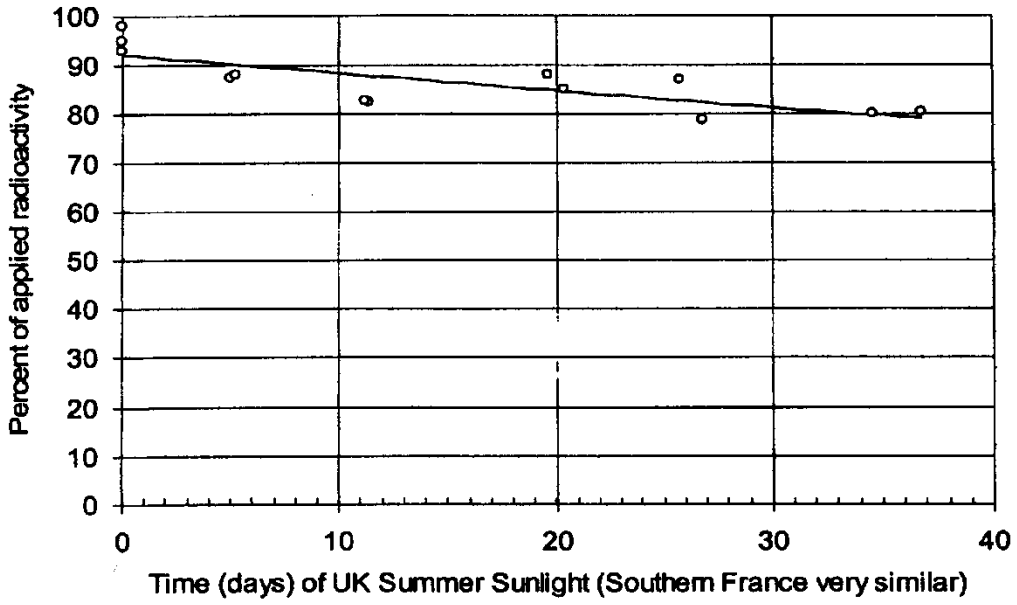
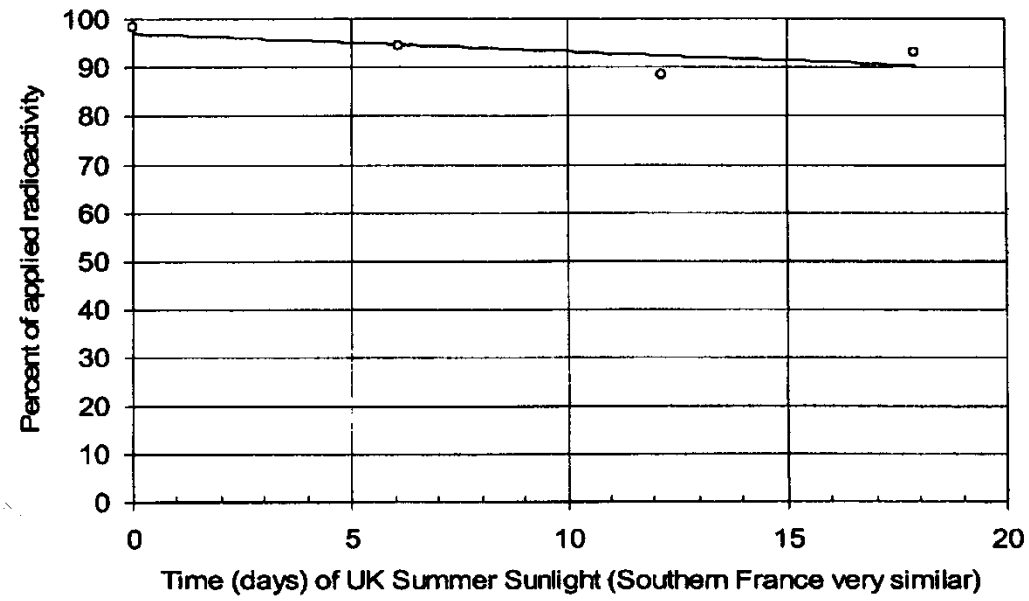


Figure 7.2.2.4/ 4 Photodegradation of Flufenoxuron from a soil surface -Benzotrifluoride label



Section A7.2.3.1	**Adsorption and Mobility in soil**
BPD Annex Point IIIA, XII.1.2	7.2.3.1 Adsorption and desorption studies (parent)

0. Justification of the choice of the key study

RMS Comment (01/02/05):

TNG data requirements for section 7.2.3 is an adsorption/desorption study in at least three soils and where relevant the adsorption and desorption of metabolites and degradation product.

Three studies were submitted: The notifier did not provide any justification for the choice of a key study for Flufenoxuron.

Reference 1 (see page 246; comments on page 250) is an adsorption/desorption study on 3 soils, where the active substance was labelled on only one site ([carbonyl-^{14}C]-Flufenoxuron). Degradation products were not tested. Organic carbon percentages were 0.6%, 1.8%, and 3.1%.

Reference 2 (see page 258) is an adsorption/desorption study on 3 soils, where the active substance was labelled on only one site ([amide-^{14}C]-Flufenoxuron). Due to poor mass balance, one soil was not further analyzed. Degradation products did not occur under the condition of this test. Organic carbon percentages were 4.7%, 2.9%, and 3.9%.

Reference 3 is an adsorption/desorption study on 5 soils, where metabolite Reg. No. 4064702 was studied.

The whole values from reference 1 and 2 are proposed by RMS to be key values for risk assessment

Section A7.2.3.1 Adsorption and Mobility in soil

BPD Annex Point IIIA, XII.1.2 7.2.3.1 Adsorption and desorption studies (parent)

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**1) Hill AD, Standen ME (1993)** [Carbonyl-14C] WL115110 (Cascade): Adsorption/desorption in three soils. XXXX. unpublished XXXX	
1.2.	**Data protection**	No	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	No data protection claimed	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Yes, OECD 106	X
2.2.	**GLP**	Yes (laboratory certified by the Department of Health of the Government of the United Kingdom, United Kingdom)	
2.3.	**Deviations**	No	
		3. MATERIALS AND METHODS	
3.1.	**Test material**	[Carbonyl-^{14}C]-Flufenoxuron	
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	See below	
3.1.3.	Purity	98.3% radiopure	
3.1.4.	Radiolabeling	[Carbonyl-^{14}C]-Flufenoxuron	
3.1.5.	Specific Activity	109 µCi/mg	
3.1.6.	Further relevant properties	The solubility in water for Flufenoxuron is 186 µg/l at pH 4, 136 µg/l at pH 7 and 369 µg/l at pH 9. Flufenoxuron is hydrolytically stable under neutral and acidic conditions.	X
3.1.7.	Method of analysis	All analyses were by LSC supplemented with TLC determination of purity and confirmation of the stability of the test substance during the test.	
3.2.	**Degradation products**	Degradation products tested: No	
3.2.1.	Method of analysis for degradation	Not applicable.	

Section A7.2.3.1 **Adsorption and Mobility in soil**

BPD Annex Point IIIA, XII.1.2 7.2.3.1 Adsorption and desorption studies (parent)

	products		
3.3.	**Reference substance**	No	
3.3.1.	Method of analysis for reference substance	Not applicable.	
3.4.	**Soil types**	Characteristics of the three UK soils used in this study are given in Table 7.2.3.1/ 1.	X
3.5.	**Testing procedure**		
3.5.1.	Test system	The tests were conducted in 35 mL stoppered glass centrifuge tubes.	
3.5.2.	Test solution and Test conditions	Flufenoxuron (0.055 mg) was dissolved in 550 µL of acetone to yield a solution of ca. 0.1 µg/µL. Nominal 0.2, 0.5, 1.0, and 2.0 µg/L solutions were prepared by injecting 2 - 20 µL of the acetone solution into 1 L of 0.01 M $CaCl_2$ solution. Moisture saturated soil, equivalent to 0.25 g dry weight, was weighed into the centrifuge tubes and 25 mL of solutions were added for a soil/solution ratio of 1:100. LSC was done with a Packard 2200 CA liquid scintillation counters and combustion using a Packard 306M sample oxidizer. TLC conditions for the purity and stability checks are given in Table 7.2.3.1/ 2.	
3.6.	**Test performance**		
3.6.1.	Preliminary test	According to (a)"OECD 106": Yes Preliminary tests were conducted to confirm solubility, determine adsorption to containers, and to determine equilibrium time. For the solubility test, solutions were prepared in $CaCl_2$ as for the adsorption test, centrifuged at 11000 G, and requantitated by LSC. **For the container test, polycarbonate and glass centrifuge tubes were compared by adding Flufenoxuron in CaCl2 solution and assaying by LSC after 6 and 24 hours on a wrist shaker and after 29 hours of standing at room temperature.** Godstone soil (0.25g) was used for the equilibrium test. 25 mL of the highest concentration solution was added and the soil-solution and a solution only blank were mixed on a rotary mixer. Duplicate samples were analyzed by LSC after 2, 4, 8, 24, and 48 hours.	
3.6.2.	Screening test: Adsorption	According to (a)"OECD 106": Yes The preliminary test showed equilibration in 8 hours, but 22 hours was used for convenience. Samples were mixed on Mathum blood suspension rotary mixers and centrifuged at 2500 rpm for 15 minutes. The aqueous phase was removed and quantitated by LSC. In order to determine the amount of test substance adsorbed onto the	

Section A7.2.3.1 **Adsorption and Mobility in soil**

BPD Annex Point IIIA, XII.1.2 7.2.3.1 Adsorption and desorption studies (parent)

		glass surface versus the soil, a second set of soil samples was prepared and equilibrated. The solutions were removed and quantitated by LSC and the soil plugs were removed, dried and extracted with water:acetonitrile, which was analyzed by LSC. Radiocarbon remaining on the glassware was determined by shaking with 10 mL of acetonitrile and LSC.	
3.6.3.	Screening test: Desorption	According to (a)"OECD 106": Performed **Blank calcium chloride solution was added to the soil plugs and shaken to break up the plug, then mixed, centrifuged, and quantitated as above. The desorption was repeated a second time, and the soil was dried in a vacuum oven and analyzed by combustion and LSC. Because of poor efficiency in combustion, these values were not used, but the results of acetonitrile extraction of the soil (see above) were used to calculate the percentage of the test substance recovered at each desorption.**	
		4. RESULTS	
4.1.	**Preliminary test**	The solubility test suggested that ca. 75% of Flufenoxuron was present as a fine suspension instead of a solution. Despite this indication, reproducibility of the Kd indicates most was in solution. No results are presented for the container adsorption test, but glass tubes were used in the main test and an additional experiment was added to assess the Flufenoxuron remaining on the container after the adsorption step. Results of the equilibration test are shown in Table 7.2.3.1/ 3. The results showed equilibrium was reached in about 8 hours and the solution only blank showed that the test substance was significantly absorbed onto the container surface.	X
4.2.	**Screening test: Adsorption**	The results of the adsorption test are summarized in Table 7.2.3.1/ 4. Flufenoxuron was strongly adsorbed to the soils. The amount of test substance adsorbed was 98.1 to 93.8% of the total available after correcting for that on the glass. A linear relationship was found for all three soils by plotting the concentrations adsorbed onto soil against the respective concentrations in the aqueous phase at equilibrium. The slope of the graph lines (1/n) was 1.156, 0.995 and 1.06 for Woodstock, Elm Farm, and Godstone soils, respectively. Adsorption isotherms are shown in Figure 7.2.3.1/ 1, Figure 7.2.3.1/ 2 and Figure 7.2.3.1/ 3.	X
4.3.	**Screening test: Desorption**	The amount of Flufenoxuron recovered in the first desorption step varied from 1.22% to 4.63% for the first desorption and from 1.21 to 4.19 for the second with the Woodstock soil in the lower range and the Godstone in the upper range (Table 7.2.3.1/ 5)	
Calculations			

Section A7.2.3.1 **Adsorption and Mobility in soil**

BPD Annex Point IIIA, XII.1.2 7.2.3.1 Adsorption and desorption studies (parent)

4.3.1.	K_d	K_d, was calculated only for the adsorption step. The adsorption coefficient is the ratio (x/m)/(b/c) where x is the amount of test substance on the mass m of soil, B is the total test substance in the solution, and C is the solution volume. Values varied from 1470 to 4835, with the Godstone soil lower than the other two soils.	
4.3.2.	K_{OC}	Adsorption coefficients corrected for the organic carbon content of the soil varied from 345407 to 126772.	
Degradation product(s)		No degradation of the test substance occurred under the conditions of the test.	
		5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1.	**Materials and methods**	The adsorption and desorption of Flufenoxuron on three soils was studied using [carbonyl-^{14}C]-Flufenoxuron. Four different concentrations (0.1, 0.5, 1.0 and 2.0 µg/l) of the ^{14}C-labelled test item in 0.01 M $CaCl_2$ solutions were tested. The ratio of soil versus test solution was 1:100. The methods are consistent with OECD 106. Significant adsorption to the glass containers used in this study made it necessary to correct for loss to the glassware when calculating $K_{d,ads}$, and the recovery in the desorption steps included Flufenoxuron recovered from the containers.	
5.2.	**Results and discussion**	The results show that Flufenoxuron is very strongly adsorbed to and not readily desorbed from soil. Flufenoxuron is not expected to be mobile in soil.	
5.2.1.	Adsorbed a.s. [%]	The amount of test substance adsorbed was 98.1 to 93.8% of the total available after correcting for that on the glass.	
5.2.2.	K_d	K_d, was calculated only for the adsorption step. Average values were 4250, 3206, and 1738 for the Woodstock, Elm Farm, and Godstone soils, respectively.	
5.2.3.	K_{OC}	The average adsorption coefficients corrected for the organic carbon content of the soil were 137104, 178 093, and 289747 for Woodstock, Elm Farm, and Godstone, respectively.	
5.2.4.	Desorption	The amount of Flufenoxuron recovered in each desorption step was 1 - 4%, indicating that Flufenoxuron is strongly held by the soil.	
5.2.5.	Degradation products (% of a.s.)	Flufenoxuron was stable under the conditions of the test.	
5.3.	**Conclusion**	This study meets the criteria of OECD 106 except for using only three soils and not determining desorption coefficients. The results show that Flufenoxuron is very strongly adsorbed to and not readily desorbed from soil. With an average K_{oc} of 201648 in the three soils, Flufenoxuron is classified as non-mobile in the UK Soil Survey and Land Research Centre Pesticide Mobility Classification.	
5.3.1.	Reliability	1	X

Section A7.2.3.1	**Adsorption and Mobility in soil**
BPD Annex Point IIIA, XII.1.2	7.2.3.1 Adsorption and desorption studies (parent)

5.3.2. Deficiencies	No	X

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/02/2005
Materials and Methods	Applicant's version is acceptable providing the inclusion of the following amendments: -2.1: Specify "*Yes, OECD 106* [(1981)]" - 3.1.6. Further relevant properties: The entry should be read as: "*The solubility of Flufenoxuron in water is* [1.86 µg/l] *at pH 4,* [1.36 µg/l] *at pH 7 and* [3.69 µg/l] *at pH 9,* [(see Doc IIIA, section 3.5)]. *Flufenoxuron is hydrolytically stable under neutral and acidic conditions.*
Results and discussion	Applicant's version is acceptable providing the inclusion of the following amendments: - 4.1 preliminary test; table 7.2.3.1/3: correct value after 48 h mixing time/solution only is 0.38 instead of 0.36. - 4.2 Screening test: adsorption; table 7.2.3.1/4: It should be specified that "*Adsorption coefficients were calculated using data from the glass adsorption study*."
Conclusion	Applicant's version is acceptable providing the inclusion of the following amendments: - 5.3.2: deficiencies: Change "No" to "Yes"; add: - Only three soils were studied, instead of 5 as recommended in OECD guideline 106 (2000); - Desorption coefficients were not determined (recommended in OECD guideline 106 (2000)); - Certificates of analysis of the reference substances are not enclosed in the study report. - No indication on the validity of analytical methods was provided. - PH of the 3 soils were not representative of different soil conditions.
Reliability	2
Acceptability	Acceptable Despite the deficiencies reported above, the results were considered acceptable as complementary data to reference 2.
Remarks	
	COMMENTS FROM ...

Section A7.2.3.1	**Adsorption and Mobility in soil**
BPD Annex Point IIIA, XII.1.2	7.2.3.1 Adsorption and desorption studies (parent)

Date	Give date of comments submitted
Materials and Methods	Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion. Discuss if deviating from view of rapporteur member state
Results and discussion	Discuss if deviating from view of rapporteur member state
Conclusion	Discuss if deviating from view of rapporteur member state
Reliability	Discuss if deviating from view of rapporteur member state
Acceptability	Discuss if deviating from view of rapporteur member state
Remarks	

Table 7.2.3.1/ 1: Classification and physico-chemical properties of soils used as adsorbents

	Godstone	**Elm Farm**	**Woodstock**
Classification	Sand	Sandy loam	Silty Clay
Sand [%]	91	58	18
Silt [%]	5	27	46
Clay [%]	4	15	36
Organic carbon [%]	0.6	1.8	3.1
pH (1:2.5 H_2O)	6.7	7.1	6.8
Cation exchange capacity (MEQ/100 g)	1.0	10.9	25.7

Table 7.2.3.1/ 2 TLC Conditions

Merck F254 0.25 mm plates	Flufenoxuron R_f
diethyl ether/hexane 1:1	0.63
ethyl acetate/toluene 1:1	0.80

Table 7.2.3.1/ 3 Results of equilibrium test

Mixing Time	Flufenoxuron in aqueous (µg/L)	
	Soil/Solution(1:100)	Solution only
0	2.08	2.08
2	0.35	0.81
4	0.21	0.64
8	0.12	0.60
24	0.14	0.76
48	0.13	0.36

Table 7.2.3.1/ 4 Adsorption test results - K_d and K_{OC} Determination

Nominal concentration of test solution (µg/L)	0.2	0.5	1.0	2.0
Initial concentration of test solution (mg/l)	0.19	0.43	0.90	1.76
Total test material in 50 mL[1] solution (ng)	9.6	21.6	45.0	88.0
Woodstock				
Weight of dry soil	0.495	0.505	0.499	0.517
Total in adsorption solution (ng)	nd	0.5	1.04	1.64
Volume of adsorption solution (mL)	48.0	48.5	48.0	48.0
Adsorbed on glass (ng)	0.23	0.64	0.87	0.95
Available test substance (ng)	9.37	20.96	44.13	87.05
% test substance adsorbed	100	97.6	97.6	98.1
Quantity test substance adsorbed	9.37	20.46	43.09	85.41
Adsorption coefficient (K_d)	ERR	3930	3986	4835
Organic Carbon	3.1			
K_{OC}	ERR	126772	128565	155975
Elm Farm				
Weight of dry soil	0.515	0.500	0.512	0.512
Total in adsorption solution (ng)	0.26	0.64	1.26	2.47
Volume of adsorption solution (mL)	49.0	48.5	49.0	49.0
Adsorbed on glass (ng)	0.29	0.72	1.51	2.02
Available test substance (ng)	9.31	20.88	43.49	85.98
% test substance adsorbed	97.2	96.9	97.1	97.1
Quantity test substance adsorbed	9.05	20.24	42.23	83.51
Adsorption coefficient (K_d)	3312	3068	3208	3236
Organic Carbon	1.8			
K_{OC}	183989	170424	178199	179761
Godstone				
Weight of dry soil	0.503	0.502	0.50	0.507
Total in adsorption solution (ng)	0.54	1.04	1.9	4.33
Volume of adsorption solution (mL)	49.0	49.0	49.0	48.0
Adsorbed on glass (ng)	0.91	1.81	2.92	8.14
Available test substance (ng)	8.69	19.79	42.08	79.86
% test substance adsorbed	93.8	94.7	95.5	94.6
Quantity test substance adsorbed	8.15	18.75	40.18	75.53
Adsorption coefficient (K_d)	1470	1760	2072	1651
Organic Carbon	0.6			
K_{OC}	245042	293298	345407	275241

[1] Replicate pairs were summed

Table 7.2.3.1/ 5 Desorption test results

Sample Code	Amount of test substance adsorbed to both glass and soil (ng)	Amount of test substance in supernatant after			
		Desorption 1		Desorption 2	
		ng	%	ng	%
W 0.2	9.61	--	--	--	--
W 0.5	20.41	0.32	1.57	0.26	1.27
W 1.0	44.67	0.58	1.30	0.54	1.21
W 2.0	88.77	1.08	1.22	1.08	1.22
EF 0.2	9.09	--	--	--	--
EF 0.5	20.16	0.34	1.69	0.32	1.59
EF 1.0	44.03	0.95	2.16	0.86	1.95
EF 2.0	86.53	1.48	1.71	1.61	1.86
G 0.2	9.09	0.38	4.18	0.30	3.30
G 0.5	9.71	0.45	4.63	0.38	3.91
G 1.0	39.74	1.8	4.09	1.58	3.98
G 2.0	76.84	3.5	4.55	3.22	4.19

Figure 7.2.3.1/ 1 Adsorption isotherm for Woodstock soil

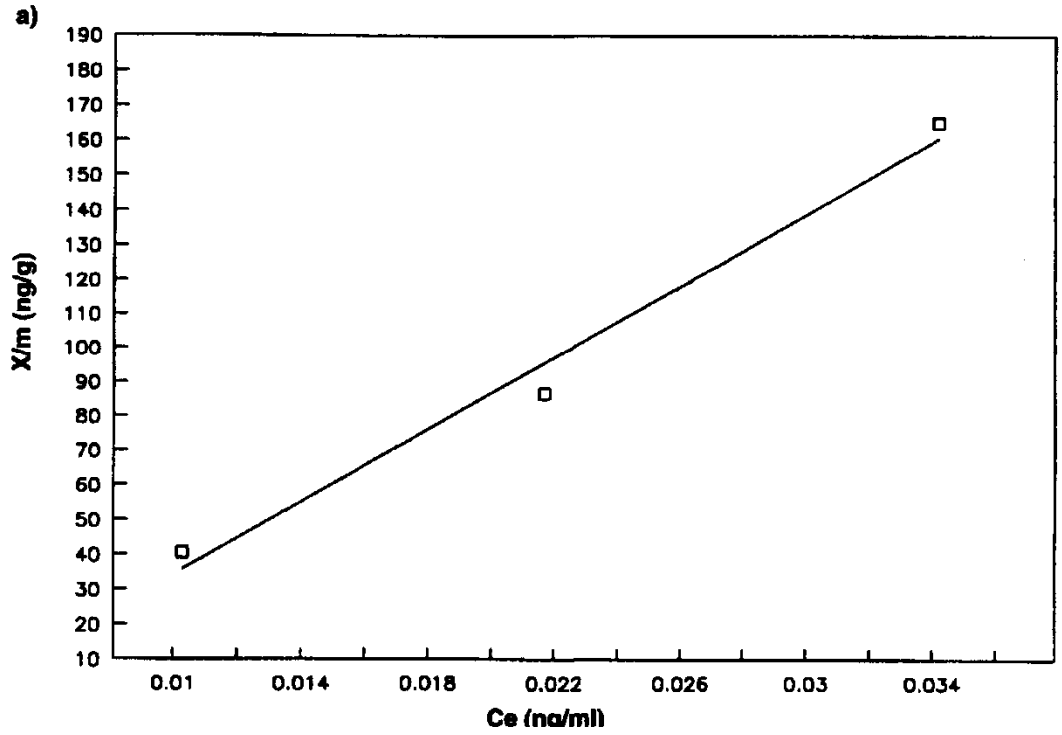


Figure 7.2.3.1/ 2 Adsorption isotherm for Elm Farm soil

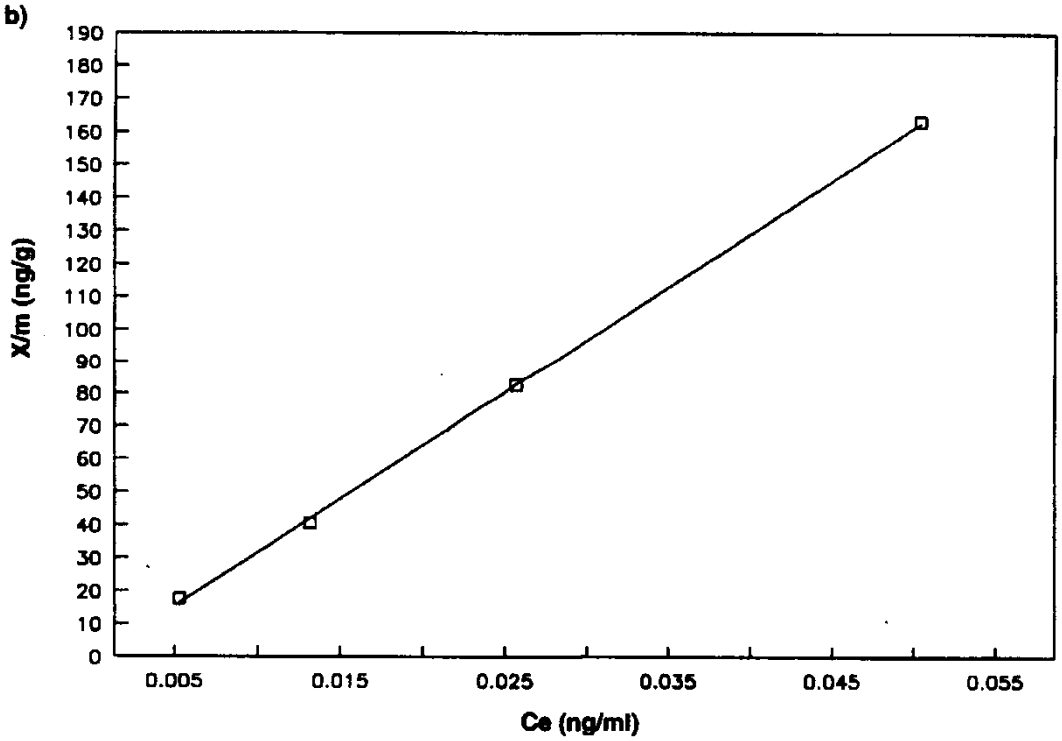
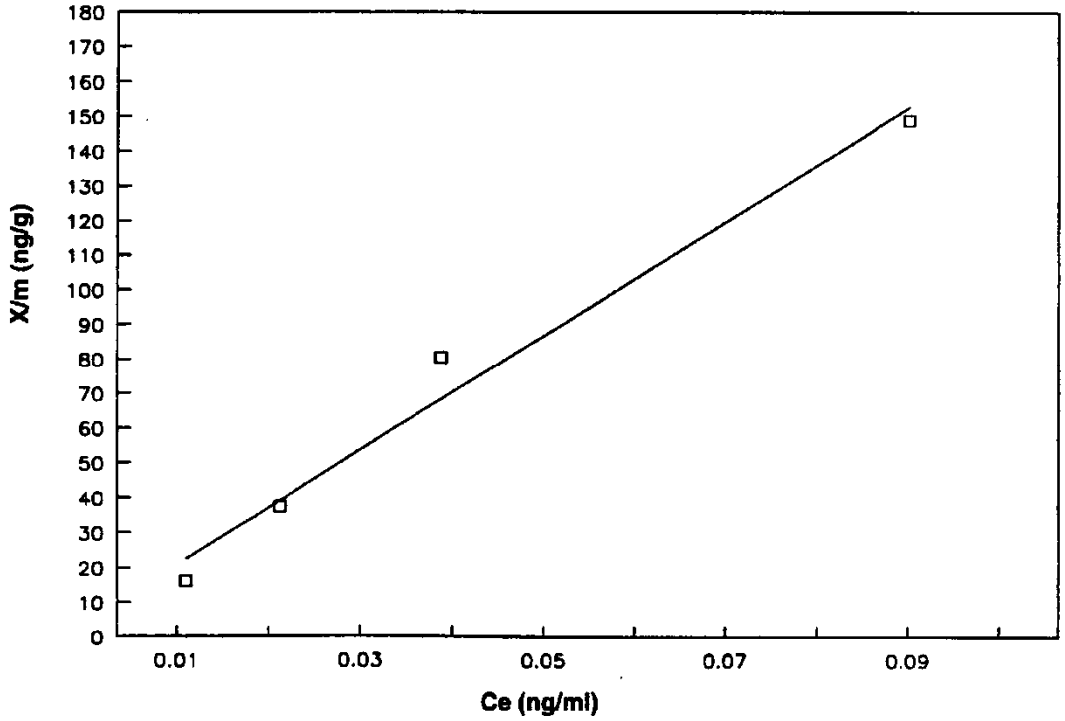


Figure 7.2.3.1/ 3 Adsorption isotherm for Godstone soil



Section A7.2.3.1 Adsorption and Mobility in soil

BPD Annex Point IIIA XII.1.2 7.2.3.1 Adsorption and desorption studies (parent)

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**2) Rosenwald J (2002)** Adsorption/Desorption of [^{14}C]-Flufenoxuron (BAS 307 I) in Three Soils. XXXX. unpublished XXXX	
1.2.	**Data protection**	Yes	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Yes, OECD 106	
2.2.	**GLP**	Yes (laboratory certified by Ministerium fuer Umwelt und Naturschutz, Landwirtschaft und Verbraucherschutz des Landes Nordrhein-Westfalen, 40190 Düsseldorf)	
2.3.	**Deviations**	No	
		3. MATERIALS AND METHODS	
3.1.	**Test material**	[Amide ring-^{14}C]-Flufenoxuron	
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	See below	
3.1.3.	Purity	95.6% radiopurity	
3.1.4.	Radiolabeling	The test substance was labeled with ^{14}C in the amide ring.	
3.1.5.	Specific Activity	32.36 µCi/mg	
3.1.6.	Further relevant properties	The solubility in water for Flufenoxuron at pH 4 is 1.9 µg/l Flufenoxuron is hydrolytically stable under neutral and acidic conditions.	X
3.1.7.	Method of analysis	All analyses were by LSC, with HPLC confirmation of the stability of the test substance.	
3.2.	**Degradation products**	No degradation of Flufenoxuron occurred under the conditions of this test.	
3.3.	**Reference substances**	Unlabeled Flufenoxuron (Lot No. XXXX and 2,6-difluorobenzamide (Lot No. XXXX) were used for co-	

Section A7.2.3.1 **Adsorption and Mobility in soil**

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		chromatography.	
3.4.	**Soil types**	Three soils from the UK, two clay loams and a silty clay loam, were used in this study. However, due to poor mass balance, the Chapel Hill farm soil was not further analyzed. The characteristics of the soils are given in Table 7.2.3.1/ 6.	X
3.5.	**Testing procedure**		
3.5.1.	Test system	The tests were conducted in 500 mL polypropylene co-polymer (PPCO) centrifuge containers (Nalgene).	
3.5.2.	Test solution and Test conditions	^{14}C-Flufenoxuron (ca. 0.96 mg) was dissolved in 1 mL acetonitrile to yield a solution of ca. 960 mg/L. A 104 µL aliquot was diluted to 10 mL with acetonitrile to give an 11.2 µg/mL solution. An aliquot of this solution was diluted to 0.9 µg/mL. An aliquot of the acetone solution was diluted with acetonitrile to 16.8 µg/mL and this was diluted to 1.0 µg/mL in acetonitrile. Aliquots of 12 to 64 µL of the acetonitrile solutions were applied directly to the surface of the $CaCl_2$ solutions (0.01 M, 250 mL) already in the test vessels with the soils (2.5g dry weight) to give total applications of 0.02, 0.0625, 0.125, 0.25, or 0.5 µg. The vessels were shaken at 250 rpm on an orbital shaker at 20 ± 3ºC in the dark for 48 hr for the adsorption phase and 24 hours for the desorption phase. The test vessels were centrifuged at 400 rpm for 100 min and the supernatant was decanted and extracted 3 x with 100 mL of dichloromethane, which was concentrated and analyzed by LSC. For the adsorption study, soils were analyzed by combustion and LSC. In the desorption study soils were extracted with water:acetonitrile, which was partitioned with dichloromethane and analyzed by LSC. The extracted soils were analyzed by combustion and LSC. Dichloromethane extracts from stability samples and the high level desorption soils were analyzed by HPLC (See Table 7.2.3.1/ 7) to show stability of the test substance.	X X
3.6.	**Test performance**		
3.6.1.	Preliminary test	According to (a)"OECD 106": Yes <u>Soil/Solution ratio</u> This test was not performed. Previous study (IIIA 7.2.3.1-1) had shown that Flufenoxuron is strongly adsorbed by soil and a ratio of 1:100 was used. <u>Solubility test</u> Two test vessels were filled with 250 mL $CaCl_2$ solution and spiked with Flufenoxuron in acetonitrile to give ca. 2 µg/L. After brief shaking aliquots were taken for direct LSC. The samples were split and either centrifuged or filtered, extracted with dichloromethane, and quantitated by LSC. The test vessels were rinsed with acetone followed by a surfactant and the rinses were analyzed by LSC.	

Section A7.2.3.1 **Adsorption and Mobility in soil**

BPD Annex Point IIIA XII.1.2 7.2.3.1 Adsorption and desorption studies (parent)

		Adsorption to containers Air-dried samples (2.5g) of all three soil types were equilibrated with $CaCl_2$ solution (250 mL) by shaking overnight. The solution was exchanged for fresh $CaCl_2$ solution, and Flufenoxuron in acetonitrile stock solution was added to give a concentration of 2 µg/L. A control sample without soil was also spiked and blank vessels with soil and no test substance were prepared. After shaking and centrifuging, the supernatant was extracted with dichloromethane, which was concentrated and analyzed by LSC. The soil was air dried, milled and combusted. The test vessels were rinsed with dichloromethane, which was concentrated and analyzed by LSC. Equilibrium Time Duplicate test units at the highest test concentration were prepared for each soil and sampling interval. After 6, 24, or 48 hours of shaking, samples were removed and centrifuged. The supernatant was extracted with dichloromethane, which was concentrated and analyzed by LSC, and the soil was combusted and analyzed by LSC. The desorption equilibrium time was determined using a similar set of samples. After equilibrating and centrifuging, the $CaCl_2$ was replaced with fresh and samples were analyzed as above after 24, 48, or 96 hours of shaking. Stability test The stability of Flufenoxuron under the conditions of the test was checked with two 48 hour adsorption samples dosed at 4 µg/L (higher than the test dose to allow HPLC analysis). After 48 hours of adsorption, the samples were centrifuged and the soil was extracted with acetonitrile:water followed by diethyl ether. The combined extracts were reduced and analyzed by HPLC and LSC. The other phases (soil residue, vessel rinse, and supernatant extract) were analyzed by LSC.	X
3.6.2.	Screening test: Adsorption	According to (a)"OECD 106": Yes The test vessels were shaken on an orbital shaker at 250 rpm for 48 hours at 20 ± 2ºC in the dark. Each concentration was tested in duplicate along with a blank for each soil type and a spiked control sample without soil. After shaking, the samples were centrifuged at 4700 rpm for 100 minutes. The supernatant was decanted and extracted 3 x with 100 mL of dichloromethane. The dichloromethane was concentrated to ca. 5 mL by rotary evaporator and analyzed by LSC. The soil was combusted and the vessel was rinsed with dichloromethane and analyzed by LSC.	
3.6.3.	Screening test: Desorption	According to (a)"OECD 106": Performed A separate set of samples was prepared for the desorption phase and equilibrated as for the adsorption samples. After centrifugation and removal of the $CaCl_2$ solution, fresh $CaCl_2$ solution was added and shaken for 24 hours. After centrifuging, the supernatants were extracted and analyzed by LSC as above, and the soil was extracted with acetonitrile: water, which was partitioned with dichloromethane and analyzed by LSC and, in the case of the highest concentrations, by HPLC.	

Section A7.2.3.1 **Adsorption and Mobility in soil**

BPD Annex Point IIIA XII.1.2 7.2.3.1 Adsorption and desorption studies (parent)

4. RESULTS

4.1. Preliminary test

Results of the solubility test are shown in Table 7.2.3.1/ 8. The test showed that counting in the $CaCl_2$ solution was very low efficiency and that the dichloromethane extract recovered all radioactivity and it was not lost during concentration. The centrifuge test showed the Flufenoxuron to be in solution, and the losses in the filtration test are attributed to adsorption on the filter and/or glassware.

The vessel adsorption test showed that Flufenoxuron was strongly bound to the glassware in the absence of soil, but only at 6 to 11% of the applied radiocarbon with the soils. This was considered acceptable. Results are shown in Table 7.2.3.1/ 9.

The results of the adsorption equilibrium experiment are shown in

Table 7.2.3.1/ 10. The adsorption equilibrium time was determined to be 48 hours. The results of the desorption equilibrium experiment are shown in Table 7.2.3.1/ 11. The desorption equilibrium time was determined to be 24 hours.

4.2. Screening test: Adsorption

Results of the adsorption test are shown in Table 7.2.3.1/ 12 for the Chelmorton soil and Table 7.2.3.1/ 14 for the Kenslow Farm soil. The Chelmorton soil adsorbed 76 to 91% of the applied radiocarbon and the Kenslow Farm soil adsorbed 80 to 90%.

4.3. Screening test: Desorption

Results of the desorption test are shown in Table 7.2.3.1/ 13 for the Chelmorton soil and Table 7.2.3.1/ 15 for the Kenslow Farm soil. The desorption for both soils was less than 3% except for the lowest concentration samples which were in the range of 5 to 13%.

Calculations

4.3.1. $K_{d,ads}$, $K_{d,des}$

The average adsorption coefficient and standard deviation was 2756 ± 1282 for the Chelmorton soil and 3441 ± 1782 for the Kenslow Farm soil. The average desorption coefficient and standard deviation was 4020 ± 1884 for the Chelmorton soil and 5895 ± 5023 for the Kenslow Farm soil.

4.3.2. Ka_{oc} , Kd_{oc}

The average $K_{a,OC}$ value and standard deviation was 95030 ± 44220 for the Chelmorton soil and 88240 ± 45700 for the Kenslow Farm soil. Desorption coefficients corrected for organic carbon were not given.

Degradation product(s) Not applicable

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1. Materials and methods

The adsorption and desorption of Flufenoxuron on two soils was studied. A third was not reported because of poor mass balance. The study meets the requirements of OECD 106 except for including only two soils. Aliquots of soil (2.5 g) were equilibrated with 250 mL of 0.01 M

Section A7.2.3.1	**Adsorption and Mobility in soil**
BPD Annex Point IIIA XII.1.2	7.2.3.1 Adsorption and desorption studies (parent)

		$CaCl_2$ spiked with 0.02 to 0.5 µg of ^{14}C-Flufenoxuron by shaking for 48 hours in polypropylene co-polymer centrifuge tubes. After centrifugation, the supernatant was extracted with dichloromethane and analyzed by LSC and the soil was dried, combusted, and analyzed by LSC. A second set of samples was equilibrated as for the adsorption phase, but the supernatant was discarded and an equal volume of fresh $CaCl_2$ solution was added equilibrated and analyzed as above.
5.2.	**Results and discussion**	Flufenoxuron was stable during the test and mass balance for the adsorption phase was 85 to 105%. Flufenoxuron was strongly adsorbed to soil and not readily released. For both adsorption and desorption, a statistically significant fit could not be found for the Freundlich isotherms. This may be due to the variation in the lower concentrations, which were near the limit of quantitation.
5.2.1.	Adsorbed a.s. [%]	Results of the adsorption test showed that 76 to 91% of the applied radiocarbon was adsorbed to the soil. Less than 3% was desorbed, except for the lowest concentration samples, which released up to 13%.
5.2.2.	K_a	The average adsorption coefficient was 2756 for the Chelmorton soil and 3441 for the Kenslow Farm soil.
5.2.3.	K_d	The average desorption coefficient was 4020 for the Chelmorton soil and 5895 for the Kenslow Farm soil.
5.2.4.	Ka_{oc}	The average $K_{a,OC}$ value was 95030 for the Chelmorton soil and 88240 for the Kenslow Farm soil.
5.2.5.	Degradation products (% of a.s.)	No degradation of Flufenoxuron occurred under the test conditions.
5.3.	**Conclusion**	The study meets the criteria of OECD 106 and the results show that Flufenoxuron is strongly adsorbed to soil and not readily released. With an average K_{oc} of 91635 in the three soils, Flufenoxuron is classified as non-mobile in the UK Soil Survey and Land Research Centre Pesticide Mobility Classification.
5.3.1.	Reliability	1
5.3.2.	Deficiencies	No

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/03/2005
Materials and Methods	Applicants version is acceptable with the following amendments:

Section A7.2.3.1	**Adsorption and Mobility in soil**
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	- 3.1.6 Further relevant properties: add at the end of the first sentence*: "The solubility in water for Flufenoxuron at pH 4 is 1.9 µg/l* [and 1.5 µg/l at pH 7 at 25°C.]" - 3.4 Soils types: Add after the first sentence: "they meet the requirements of the OECD guideline 106 for the OECD soils 2, 3, and 4. In table 7.2.3.1/6, add a footnote on the pH value of the Kenslow farm (5.7): [value just outside the OECD soil requirement (pH optimum in the range of 4.0 – 5.5)]. - 3.5.2 Test solution and test conditions: amend the following sentence "*The vessels were shaken at 250 rpm on an orbital shaker at* [20 ± 2ºC] *in the dark for 48 hr for the adsorption phase and 24 hours for the desorption phase. The test vessels were centrifuged at* [4700 rpm] *for 100 min and* […]*"* 3.6.1 Preliminary test / stability test: the stability test was performed using two different soils: Chelmorton silt loam (low organic carbon and low clay content) and Kenslow Farm loam (high organic carbon and high clay content). The second step of OECD guideline was not performed. Validation of the analytical method was not provided.
Results and discussion	Applicant's version is acceptable.
Conclusion	Applicant's version is acceptable.
Reliability	2
Acceptability	Acceptable The results are acceptable in complement to the results of reference 1.
Remarks	

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.2.3.1/ 6 Characterization of soils used for adsorption/desorption of Flufenoxuron

Soil		**Organic C**	**pH**		**Particle size distribution (%)***			**CEC**
Origin	**Type***	**(%)**	**$CaCl_2$**	**H_2O**	**< 2 µm (clay)**	**2-63 µm (silt)**	**63-2000 µm (sand)**	**(mVal/100 g)**
Chapel Hill Farm	Clay loam	4.7	7.6	n.d.	35	28	37	26.4
Chelmorton	Silty clay loam	2.9	6.1	n.d.	19	64	17	12.0
Kenslow Farm	Clay loam	3.9	5.7	n.d.	21	47	32	14.2

Table 7.2.3.1/ 7 HPLC Conditions

HPLC System	Merck pump, Abimed injector, Packard-Radiodetector, Waters-UV-Detector
Column	Spherisorb 5 ODS 2,5µm, 250 x 4.6 mm
Solvent A	Glacial acetic acid (0.5% in deionized water)
Solvent B	Acetonitrile
Gradient	Time (min) %B 0 68 20 68 25 100 30 100 31 68 35 68
Flow rate	1 mL/min
UV detection	254 nm
^{14}C detection	Packard Flow Scintillation Analyzer

Table 7.2.3.1/ 8 Solubility test results

Sample description	**%AR**		
	Rep A	**Rep B**	**Comment**
$CaCl_2$ phased assayed directly after application	65	69	LSC of aqueous phase resulted in poor efficiency
after centrifugation:			
$CaCl_2$ phase	10	8	LSC of aqueous phase resulted in poor efficiency
$CaCl_2$ after DCM extraction	nd	nd	
DCM before concentration	124	114	
DCM after concentration	125	123	No loss on concentration.
vessel acetone rinse	nd	nd	No adsorption observed.
vessel surfactant rinse	nd	nd	No adsorption observed.
after filtration:			
$CaCl_2$ phase	6	7	High losses may be due to adsorption on glassware and/or cellulose nitrate filter.
$CaCl_2$ after DCM extraction	nd	nd	
DCM before concentration	12	18	
DCM after concentration	9	21	
vessel acetone rinse	nd	nd	
vessel surfactant rinse	nd	nd	

Table 7.2.3.1/ 9 Container adsorption test results

Sample description	%AR		
	Rep A	**Rep B**	**Mean**
Chapel Hill Farm clay soil			
$CaCl_2$ after DCM extraction	nd	nd	nd
DCM extract of $CaCl_2$	2.7	2.4	2.5
vessel DCM rinse	5.7	6.7	6.2
Soil combustion	81.7	86.0	83.8
Mass Balance	90.1	95.1	92.6
Chelmorton silt loam			
$CaCl_2$ after DCM extraction	nd	nd	nd
DCM extract of $CaCl_2$	3.6	3.3	3.5
vessel DCM rinse	7.4	10.0	8.7
Soil combustion	80.0	87.8	83.9
Mass Balance	90.9	101.1	96.0
Kenslow Farm loam			
$CaCl_2$ after DCM extraction	nd	nd	nd
DCM extract of $CaCl_2$	2.1	1.7	1.9
vessel DCM rinse	13.6	9.1	11.4
Soil combustion	79.8	79.7	79.8
Mass Balance	95.5	90.6	93.0
Control (no soil)			
$CaCl_2$ after DCM extraction	nd	nd	nd
DCM extract of $CaCl_2$	15.2	10.9	13.1
vessel DCM rinse	76.4	91.3	83.9
Soil combustion	na	na	na
Mass Balance	96.6	102.2	96.9

Table 7.2.3.1/ 10 Adsorption equilibrium time

	Sample description	%AR		
		Rep A	Rep B	Mean
Chelmorton soil				
after 6 hours	DCM extract of $CaCl_2$	2.7	2.4	2.5
	vessel DCM rinse	5.7	6.7	6.2
	Soil combustion	81.7	86.0	83.8
	Mass Balance	90.1	95.1	92.6
after 24 hours	DCM extract of $CaCl_2$	3.6	3.3	3.5
	vessel DCM rinse	7.4	10.0	8.7
	Soil combustion	80.0	87.8	83.9
	Mass Balance	90.9	101.1	96.0
after 48 hours	DCM extract of $CaCl_2$	2.1	1.7	1.9
	vessel DCM rinse	13.6	9.1	11.4
	Soil combustion	79.8	79.7	79.8
	Mass Balance	95.5	90.6	93.0
Kenslow Farm Soil				
after 6 hours	DCM extract of $CaCl_2$	2.6	3.3	2.9
	vessel DCM rinse	8.5	9.1	8.8
	Soil combustion	84.5	83.0	83.7
	Mass Balance	95.5	95.4	95.4
after 24 hours	DCM extract of $CaCl_2$	2.3	1.4	1.9
	vessel DCM rinse	7.7	7.3	7.5
	Soil combustion	84.7	89.9	87.3
	Mass Balance	94.7	98.7	96.7
after 48 hours	DCM extract of $CaCl_2$	1.4	1.6	1.5
	vessel DCM rinse	7.4	8.5	7.9
	Soil combustion	91.9	92.0	92.0
	Mass Balance	100.7	102.1	101.4
Control Sample (no Soil)				
		6 hr	48 hr	
	DCM extract of $CaCl_2$	22.7	15.5	
	vessel DCM rinse	65.6	65.9	
	Soil combustion	na	na	
	Mass Balance	88.3	81.3	

Table 7.2.3.1/ 11 Desorption equilibrium time

	Sample description	%AR		
		Rep A	Rep B	Mean
Chelmorton soil				
after 24 hours	DCM extract of $CaCl_2$	1.7	1.8	1.7
	vessel DCM rinse	6.5	6.9	6.7
	Soil combustion	78.8	81.2	80.0
	Mass Balance	87.0	89.8	88.4
after 48 hours	DCM extract of $CaCl_2$	2.1	1.2	1.6
	vessel DCM rinse	7.9	7.0	7.5
	Soil combustion	77.3	77.4	77.3
	Mass Balance	87.2	85.6	86.4
after 96 hours	DCM extract of $CaCl_2$	2.1	1.5	1.8
	vessel DCM rinse	5.3	5.5	5.4
	Soil combustion	75.5	73.8	74.7
	Mass Balance	83.0	80.8	81.9
Kenslow Farm Soil				
after 24 hours	DCM extract of $CaCl_2$	1.6	1.1	1.3
	vessel DCM rinse	4.4	5.4	4.9
	Soil combustion	78.8	79.1	79.0
	Mass Balance	84.8	85.6	85.2
after 48 hours	DCM extract of $CaCl_2$	1.3	1.3	1.3
	vessel DCM rinse	6.3	5.9	6.1
	Soil combustion	80.7	75.8	78.3
	Mass Balance	88.3	83.0	85.7
after 96 hours	DCM extract of $CaCl_2$	1.1	1.3	1..2
	vessel DCM rinse	3.3	4.6	4.0
	Soil combustion	64.8	77.8	71.3
	Mass Balance	96.3	83.7	76.5
Control Sample (no Soil)				
after 48 hours	DCM extract of $CaCl_2$	11.1	5.0	8.0
	vessel DCM rinse	65.0	48.1	56.5
	Soil combustion			
	Mass Balance	76.1	53.0	64.6

Table 7.2.3.1/ 12 Adsorption results - Chelmorton soil

Conc. (µg/L)	Rep	$CaCl_2$ (%AR)	$CaCl_2$ (µg/mL)	Soil (%AR)	Soil (µg/g)	Container (%AR)	Total (%AR)	$K_{d,ads}$	K_{oc}
0.25	A	9.13	0.000024	85.7	0.0222	5.4	100.2	939	32370
	B	8.11	0.000021	83.4	0.0216	12.4	103.9	1028	35460
	Mean	8.62	0.000022	84.6	0.0219	8.9	102.1	984	33920
0.50	A	1.86	0.000010	75.9	0.0413	7.7	85.4	4081	140700
	B	3.11	0.000017	85.6	0.0465	8.3	96.9	2747	94720
	Mean	2.49	0.000014	80.7	0.0439	8.0	91.2	3414	117710
1.0	A	2.35	0.000026	83.8	0.0916	12.0	98.1	3565	122900
	B	4.21	0.000046	85.9	0.0939	12.9	103.0	2042	70410
	Mean	3.28	0.000036	84.9	0.0928	12.4	100.6	2804	96660
2.0	A	2.30	0.000047	90.6	0.1838	11.7	104.6	3939	135800
	B	2.20	0.000045	81.5	0.1654	11.9	95.6	3706	127800
	Mean	2.25	0.000046	86.1	0.1746	11.8	100.1	3823	131800
						overall mean and S.D.		2756 ±1282	95030 ±44220

Table 7.2.3.1/ 13 Desorption results - Chelmorton soil

Conc. (µg/L)	Rep	Adsorbed to soil		Desorbed from soil		Desorption Percentage	$K_{d,des}$
		µg/g	µg	µg/mL	µg		
0.25	A	0.0193	0.0483	0.000029	0.0073	13.13	662
	B	0.0206	0.0516	0.000010	0.0025	4.63	2060
	Mean	0.0200	0.0499	0.000020	0.0049	8.88	1361
0.50	A	0.0406	0.1005	0.000007	0.0017	1.66	5926
	B	0.0457	0.1142	0.000009	0.0021	1.83	5351
	Mean	0.0431	0.1079	0.000008	0.0019	1.75	5638
1.0	A	0.0891	0.2228	0.000025	0.0062	2.70	3600
	B	0.0914	0.2286	0.000025	0.0062	2.65	3678
	Mean	0.0903	0.2257	0.000025	0.0062	2.67	3639
2.0	A	0.1805	0.4511	0.000033	0.0083	1.81	5432
	B	0.1624	0.4060	0.000030	0.0075	1.80	5448
	Mean	0.1714	0.4286	0.000032	0.0079	1.80	5440
					overall mean and S.D.		4020 ±1884

Table 7.2.3.1/ 14 Adsorption results - Kenslow Farm soil

Conc. (µg/L)	**Rep**	**$CaCl_2$ (%AR)**	**$CaCl_2$ (µg/mL)**	**Soil (%AR)**	**Soil (µg/g)**	**Container (%AR)**	**Total (%AR)**	**$K_{d,ads}$**	**K_{oc}**
0.25	A	4.01	0.000010	84.9	0.0220	14.3	103.3	2120	54360
	B	7.24	0.000019	88.7	0.0230	8.4	104.3	1224	31400
	Mean	5.62	0.000015	86.8	0.0225	11.4	103.8	1672	42880
0.50	A	3.38	0.000020	84.3	0.0488	7.3	95.0	2492	63910
	B	3.23	0.000019	79.9	0.0463	9.3	92.5	2487	63540
	Mean	3.30	0.000019	82.1	0.0476	8.3	93.7	2485	63730
1.0	A	1.90	0.000021	88.3	0.0965	9.8	100.0	4639	118950
	B	3.19	0.000035	89.9	0.0983	10.5	103.6	2820	72300
	Mean	2.55	0.000028	89.1	0.0974	10.2	101.8	3730	95630
2.0	A	1.52	0.000032	86.8	0.1802	8.7	97.0	5714	146510
	B	1.35	0.000028	81.6	0.1692	7.7	90.6	6042	154930
	Mean	1.43	0.000030	84.2	0.1747	8.2	93.8	5878	150720
						overall mean and S.D.		3441 ±1782	88240 ±45700

Table 7.2.3.1/ 15 Desorption results - Kenslow Farm soil

Conc. (µg/L)	Rep	Adsorbed to soil		Desorbed from soil		Desorption Percentage	$K_{d,des}$
		µg/g	µg	µg/mL	µg		
0.25	A	0.0197	0.0493	0.000023	0.0058	10.51	852
	B	0.0230	0.0542	0.000013	0.0032	5.63	1677
	Mean	0.0207	0.0518	0.000018	0.0045	8.07	1265
0.50	A	0.0485	0.1213	0.000003	0.0007	0.58	17077
	B	0.0454	0.1135	0.000009	0.0023	1.95	5019
	Mean	0.0470	0.1174	0.000006	0.0015	1.27	11048
1.0	A	0.0948	0.2370	0.000017	0.0043	1.78	5513
	B	0.0955	0.2388	0.000028	0.0069	2.80	3470
	Mean	0.0952	0.2379	0.000022	0.0056	2.29	4492
2.0	A	0.1776	0.4439	0.000026	0.0065	1.44	6837
	B	0.1667	0.4168	0.000025	0.0062	1.47	6717
	Mean	0.1721	0.4304	0.000025	0.0063	1.46	6777
					overall mean and S.D.		5895 ±5023

Section A7.2.3.1 Adsorption and Mobility in soil

BPD Annex Point IIIA, XII.1.2 Adsorption and desorption studies (Flufenoxuron degradate)

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**3) Zirnstein M (2003)** Adsorption/Desorption - Study of BAS 307 I Metabolite (Reg. No. 4064702) on Five European Soils. XXXX. unpublished XXXX	
1.2.	**Data protection**	Yes	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Yes, OECD 106, U.S. EPA N 163-1	
2.2.	**GLP**	Yes (laboratory certified by Landesamt fuer Umweltschutz und Gewerbeaufsicht, Mainz, Germany)	
2.3.	**Deviations**	No	
		3. MATERIALS AND METHODS	
3.1.	**Test material**	[fluoroaniline-ring-U-^{14}C] -N-{4-[2-chloro-4-(trifluoromethyl)-phenoxy]-2-fluorphenyl}urea	
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	See below	
3.1.3.	Purity	> 98% radiopure, >99% chemically pure	

Section A7.2.3.1 Adsorption and Mobility in soil

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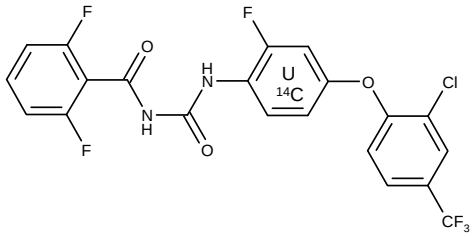
3.1.4.	Radiolabeling	
3.1.5.	Specific Activity	3.48 MBq/mg
3.1.6.	Further relevant properties	The water solubility of Reg. No. 4064702 (CL 932338) is 1.7 µg/L.
3.1.7.	Method of analysis	The concentrations of Reg. No. 4064702 were determined by liquid scintillation counting using a Packard TRI-CARB 2500TR. Ten mL aliquots of the decanted supernatants were added to 10 mL of Ultima Gold XR scintillation cocktail for counting. The stability of the test substance during the test was confirmed by HPLC analysis (see Table 7.2.3.1/ 16).
3.2.	**Degradation products**	The test substance is a degradation product of Flufenoxuron. No further degradation was observed during the study.
3.2.1.	Method of analysis for degradation products	Not applicable
3.3.	**Reference substance**	No
3.3.1.	Method of analysis for reference substance	Not applicable
3.4.	**Soil types**	The study was conducted with five European soils varying texture, organic carbon content, cation exchange capacity and pH. The properties of the soils are summarized in Table 7.2.3.1/ 17. Soils were sieved (2 mm) and air-dried to a constant weight. The actual moisture was determined by oven drying to be 2 to 9% and was taken into account in all calculations.
3.5.	**Testing procedure**	
3.5.1.	Test system	The tests were conducted in 150 mL glass centrifuge tubes.
3.5.2.	Test solution and Test conditions	A stock solution of 0.0462 mg of ^{14}C-4064702 in 7.70 mL of acetonitrile:water (1:1) was prepared and 1.0 mL diluted to 5000 mL with 0.01 M $CaCl_2$ solution to make a 1.1585 ng/mL solution (nominal 1.2 ng/mL). Aliquots of this solution were diluted with 0.01M $CaCl_2$ to make actual concentrations of 0.8247 ng/mL, 0.3846 ng/mL, and 0.2064

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		ng/mL. One hundred mL of each solution was equilibrated with 0.1 g of each soil (soil/solution ratio 1:100) in duplicate. Samples were shaken for 24 hours on a mechanical shaker at 19.4 ± 0.2ºC in the dark. The samples were centrifuged and the supernatant was decanted and assayed by LSC. Solution remaining in the soil was determined gravimetrically and taken into account in all calculations. Fresh $CaCl_2$ solution was added, shaken for 24 hours as above then centrifuged, decanted, and analyzed by LSC. Mass balance was determined only for the highest concentration samples. For mass balance determination, the soils remaining after the desorption step were extracted with methanol and then combusted and analyzed by LSC.	
3.6.	**Test performance**		
3.6.1.	Preliminary test	According to (a)"OECD 106": Yes Soil Ratio No test for soil/solution ratio was conducted. A ratio of 1:100 was chosen based on the low water solubility of Reg. No 4064702. Equilibrium time For the equilibrium time test, 4 replicates of each soil were prepared at the nominal 1.2 ng/mL concentration as above and shaken for 8, 16, 24, or 48 hours before centrifugation, and LSC assay of the supernatant.	X
3.6.2.	Screening test: Adsorption	According to (a) "OECD 106": Yes Soils (1.0g dry weight basis) were equilibrated with 0.01 M $CaCl_2$ solutions (100 mL) containing 0.2 to 1.2 ng/mL Reg. No. 4064702 by shaking for 48 hours.	
3.6.3.	Screening test: Desorption	According to (a) "OECD 106": Performed After removal of the adsorption solution, the solution remaining in the soil was determined gravimetrically and fresh solution was added, equilibrated, centrifuged, decanted and analyzed by LSC as for the adsorption step. For the highest concentration samples, the soil remaining after desorption was extracted with methanol and combusted to determine mass balance.	
		4. RESULTS	
4.1.	**Preliminary test**	The results of the equilibrium time test are given in Table 7.2.3.1/ 18 Equilibrium was essentially complete at 24 hours and this time was used in the adsorption and desorption tests.	
4.2.	**Screening test: Adsorption**	The results of the adsorption test are given in Table 7.2.3.1/ 19.	
4.3.	**Screening test: Desorption**	The results of the desorption test are given in Table 7.2.3.1/ 20. The results of the mass balance determination for the high concentration samples are shown in Table 7.2.3.1/ 21.	
Calculations			

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4.3.1.	K_d	The average distribution coefficients and standard deviations for the adsorption phase were 143 ± 8 for the Borgeby soil, 70 ± 5 for the Birnbaum soil, 206 ± 19 for the 2.2 soil, 154 ± 14 for the Sora soil, and 68 ± 4 for the Stetten soil.
4.3.2.	K_{OC}	The average distribution coefficients and standard deviations for the adsorption phase corrected for organic carbon content were 10210 ± 563 for the Borgeby soil, 8802 ± 623 for the Birnbaum soil, 7972 ± 722 for the 2.2 soil, 9032 ± 827 for the Sora soil, and 6789 ± 631 for the Stetten soil. The K_{OC} showed some pH trend with the highest values at pH 5.6 and the lowest at pH 7.5.
4.3.3.	K_F	The Freundlich coefficients varied from 37.52 for the Birnbaum soil to 118.5 for the Borgeby soil. Adsorption isotherms are shown in Figure 7.2.3.1/ 1 to Figure 7.2.3.1/ 8.
4.3.4.	1/n	The Freundlich exponents for the adsorption phase ranged from 0.895 to 0.978.
4.3.5.	K_{FOC}	The Freundlich adsorption coefficients corrected for organic carbon content varied from 3711 for the Sora soil to 8467 for the Borgeby soil.
4.3.6.	$K_{d,des}$	The average distribution coefficients and standard deviations for the desorption phase were 211 ± 13 for the Borgeby soil, 126 ± 12 for the Birnbaum soil, 332 ± 50 for the 2.2 soil, 248 ± 37 for the Sora soil, and 131 ± 21 for the Stetten soil.
4.3.7.	K_{Fdes}	The Freundlich coefficients for the desorption varied from 37.52 for the Birnbaum soil to 118.5 for the Borgeby soil. Desorption isotherms are shown in Figure 7.2.3.1/ 9 to Figure 7.2.3.1/ 13.
4.3.8.	$1/n_{des}$	The Freundlich exponents for the desorption phase ranged from 0.819 to 0.951.
4.3.9.	K_{FOCdes}	The Freundlich desorption coefficients corrected for organic carbon content varied from 2343 for the 2.2 soil to 9625 for the Borgeby soil.
Degradation product(s)		Not applicable

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1.	**Materials and methods**	The adsorption and desorption of Reg. No. 4064702, the "urea" metabolite of Flufenoxuron, was studied on five European soils according to OECD guideline 106 and U. S. EPA Guideline subdivision N 163-1. One gram aliquots of soil in glass centrifuge tubes were equilibrated with 0.01M $CaCl_2$ containing ca 0.2 to 1.2 ng/mL of ^{14}C labeled test substance by shaking for 24 hours in the dark at 19ºC. The samples were centrifuged and decanted and the supernatant analyzed by LSC. The solution remaining in the soil was determined gravimetrically and fresh $CaCl_2$ was added and equilibrated, centrifuged, decanted and analyzed as above. Soils from the highest concentration of test substance were further analyzed after desorption by methanol extraction and then combustion and LSC.
5.2.	**Results and**	The test substance was stable during the test and mass balances of 93.2

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	discussion	to 95.9% indicate no significant losses during the study. Within the five soils studied, a slight dependence of adsorption on soil pH was observed, with the most acid soil (Borgeby, pH = 5.6) showing the strongest adsorption (K_{OC} = 10371).		
5.2.1.	Adsorbed a.s. [%]	The percentage of applied radiocarbon in adsorbed to the soil in the equilibrium test was 38.5 to 58.8%. This value was not reported for all concentrations in the definitive test, but can be determined for the highest concentration from the percentage in the aqueous as 39.2 to 65.5%.		
5.2.2.	K_d	Soil	K_d (avg ± SD)	
		Borgeby	143 ± 8	
		Birnbaum	70 ± 5	
		2.2 F222002	206 ± 19	
		Sora	154 ± 14	
		Stetten	68 ± 4	
5.2.3.	K_{OC}	Soil	pH	K_{OC} (avg ± SD)
		Borgeby	5.6	10210 ± 563
		Birnbaum	6.1	8802 ± 623
		2.2 F222002	6.3	7972 ± 722
		Sora	6.5	9032 ± 827
		Stetten	7.5	6789 ± 631
5.2.4.	K_F	Soil	K_F	
		Borgeby	118.5	
		Birnbaum	37.52	
		2.2 F222002	101.7	
		Sora	63.09	
		Stetten	52.37	
5.2.5.	1/n	Soil	1/n	
		Borgeby	0.978	
		Birnbaum	0.922	
		2.2 F222002	0.918	
		Sora	0.895	
		Stetten	0.968	
5.2.6.	K_{FOC}	Soil	K_{FOC}	
		Borgeby	8467	
		Birnbaum	4690	
		2.2 F222002	3928	
		Sora	3711	
		Stetten	5237	

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5.2.7.	$K_{d,des}$	Soil	$K_{d,des}$ (avg ± SD)
		Borgeby	211 ± 13
		Birnbaum	126 ± 12
		2.2 F222002	332 ± 50
		Sora	248 ± 37
		Stetten	131 ± 21
5.2.8.	K_{Fdes}	Soil	K_{Fdes}
		Borgeby	134.8
		Birnbaum	42.71
		2.2 F222002	60.69
		Sora	129.3
		Stetten	33.19
5.2.9.	$1/n_{des}$	Soil	$1/n_{des}$
		Borgeby	0.951
		Birnbaum	0.882
		2.2 F222002	0.819
		Sora	0.935
		Stetten	0.853
5.2.10.	K_{FOCdes}	Soil	K_{FOCdes}
		Borgeby	9625
		Birnbaum	5339
		2.2 F222002	2343
		Sora	7604
		Stetten	3319
5.2.11.	Degradation products (% of a.s.)	No degradation occurred during the test.	
5.3.	**Conclusion**	The adsorption and desorption behavior of Flufenoxuron metabolite Reg. No. 4064702 was studied in five European soils. The study meets the criteria of OECD 106 and U.S. EPA Subdivision N 163-1. The adsorption of the test substance to the tested soils showed a slight dependence on pH with the most acid soil (Borgeby, pH = 5.6) showing the strongest adsorption (K_{OC} = 10371). Even in the soil with the lowest K_{OC}, (Stetten, K_{OC} = 6789). Reg.No.406302 is classified as non-mobile in the UK Soil Survey and Land Research Centre Pesticide Mobility Classification.	
5.3.1.	Reliability	1	
5.3.2.	Deficiencies	No	

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	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/03/2005
Materials and Methods	Applicant's version is acceptable with the following modifications: 3.6.1 Preliminary test – Equilibrium time: Add at the end of the paragraph: "[A blank run per soil was carried out to check the background radioactivity. Adsorption to glass walls: To show whether the test item was adsorbed to the surface of the centrifuge glass tube or not, 100 ml aliquots of the solutions at 1.1585 ng/ml, 0.8247 ng/ml, 0.3846 ng/ml, and 0.2064 mg/ml of the test item was shaken without soil for 24 h and radioassayed (control samples).]"
Results and discussion	Applicant's version is acceptable.
Conclusion	Applicant's version is acceptable.
Reliability	2 Deficiencies: the reliability of the analytical method was not provided with the results of the study.
Acceptability	Acceptable
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.2.3.1/ 16 HPLC conditions for purity and stability confirmation

Instrument	HPLC unit, Fa. Gynkotek Radio-HPLC detector, Fa. Berthold
Column	ThermoHypersil BetaMax Neutral (150 x 4.6 mm)
Mobile phase	acetonitrile:water 60/40 v/v
Flow rate	1.0 mL/min.
Reg. No. 4064702 retention time	6.3 min

Table 7.2.3.1/ 17 Classification and physico-chemical properties of soils used as adsorbents

Soil		**Organic C**	**pH**		**Particle size distribution (%)***			**CEC**
Origin	**Type***	**(%)**	**$CaCl_2$**	**H_2O**	**< 2 µm (clay)**	**2-63 µm (silt)**	**63-2000 µm (sand)**	**(mVal/100 g)**
Borgeby	Loamy sand	1.4	5.6	6.3	7	15	78	13
Birnbaum	Loamy sand	0.8	6.1		11	7	82	13
2.2 F222002	Silty sand	2.6	6.3	6.9	1.2	12.8	85.9	10.9
Sora Bevern H9	loam	1.7	6.5	7.1	16	42	42	18
Stetten	Loam	1.0	7.5	8.1	26	34	40	25

* according to UK / German scheme (DIN 4220)

Table 7.2.3.1/ 18 Adsorption equilibrium test results

Soil			% applied radiocarbon adsorbed on soil after shaking for			
No	**Origin**	**Type**	**8 h**	**16 h**	**24 h**	**48 h**
99/1330	Borgeby (Schweden) Flur Nr. 8327	Loamy sand	53.9	57.4	58.8	62.4
99/1403	Birnbaum (Henninger)	Loamy sand	33.8	38.6	41.0	42.9
02/736/02	2.2 F222002	Loamy sand	57.7	66.8	64.8	68.5
98/1301	Sora Bevern H9	Loam	47.2	--[1]	58.0	61.1
98/1288	Stetten Flur Nr. 1774	Loam	35.4	32.8	38.5	39.6

[1] lost in lab accident

Table 7.2.3.1/ 19 Adsorption results

Soil	Concentration of 406702			Adsorption				
	C_o ng/mL	C_{soil} µg/g	C_{aq} µg/mL	K_d	K_{OC}	K_F	1/n	K_{FOC}
Borgeby (Schweden) Flur Nr. 8327	1.159	0.06850	0.00049	139.8	9985	118.5	0.978	8467
		0.07079	0.00047	150.6	10758			
	0.825	0.04847	0.00035	138.5	9892			
		0.04759	0.00036	132.2	9443			
	0.385	0.02345	0.00016	146.6	10469			
		0.02316	0.00016	144.7	10337			
	0.206	0.01245	0.00008	155.6	11114			
		0.01220	0.00009	135.5	9681			
Birnbaum (Henninger)	1.159	0.06850	0.00070	68.28	8535	37.52	0.922	4690
		0.07079	0.00070	68.72	8590			
	0.825	0.04847	0.00051	64.49	8061			
		0.04759	0.00051	62.98	7873			
	0.385	0.02345	0.00022	73.67	9209			
		0.02316	0.00022	75.50	9437			
	0.206	0.01245	0.00012	74.87	9359			
		0.01220	0.00012	74.85	9356			
2.2 F222002	1.159	0.06850	0.00042	191.7	7402	101.7	0.916	3928
		0.07079	0.00040	206.2	7960			
	0.825	0.04847	0.00030	189.2	7304			
		0.04759	0.00031	180.9	6984			
	0.385	0.02345	0.00013	216.8	8371			
		0.02316	0.00012	238.8	9220			
	0.206	0.01245	0.00007	215.7	8327			
		0.01220	0.00007	212.7	8212			
Sora Bevern H9	1.159	0.06850	0.00049	149.8	8814	63.09	0.895	3711
		0.07079	0.00051	140.4	8257			
	0.825	0.04847	0.00037	135.7	7980			
		0.04759	0.00036	140.0	8238			
	0.385	0.02345	0.00016	156.7	9216			
		0.02316	0.00015	168.5	9912			
	0.206	0.01245	0.00008	170.0	9998			
		0.01220	0.00008	167.3	9842			
Stetten Flur Nr 1774	1.159	0.06850	0.00071	66.99	6699	52.37	0.968	5237
		0.07079	0.00070	68.12	6812			
	0.825	0.04847	0.00051	64.02	6402			
		0.04759	0.00051	63.95	6395			
	0.385	0.02345	0.00023	72.67	7267			
		0.02316	0.00023	70.28	7028			
	0.206	0.01245	0.00013	64.63	6463			
		0.01220	0.00012	72.45	7245			

Table 7.2.3.1/ 20 Desorption results

Soil	concentration of 406702			Adsorption			
	C_o ng/mL	C_{soil} µg/g	C_{aq} µg/mL	$K_{d,des}$	$K_{F,des}$	$1/n_{des}$	$K_{FOC,des}$
Borgeby (Schweden) Flur Nr. 8327	1.159	0.04587	0.00023	199.4	134.8	0.951	9625
		0.04919	0.00024	204.9			
	0.825	0.03342	0.00016	208.9			
		0.03228	0.00016	201.7			
	0.385	0.01659	0.00007	237.0			
		0.01608	0.00008	201.0			
	0.206	0.00893	0.00004	223.2			
		0.00846	0.00004	211.6			
Birnbaum (Henninger)	1.159	0.02679	0.00023	116.5	42.71	0.882	5339
		0.02694	0.00023	117.1			
	0.825	0.01851	0.00016	115.7			
		0.01783	0.00015	118.9			
	0.385	0.00964	0.00008	120.5			
		0.00985	0.00007	140.7			
	0.206	0.00561	0.00004	140.2			
		0.00568	0.00004	142.0			
2.2 F222002	1.159	0.05856	0.00022	266.2	60.69	0.819	2343
		0.06130	0.00021	291.9			
	0.825	0.04193	0.00014	299.5			
		0.04115	0.00014	294.0			
	0.385	0.02158	0.00006	359.7			
		0.02204	0.00006	367.4			
	0.206	0.01179	0.00003	393.1			
		0.01160	0.00003	386.8			
Sora Bevern H9	1.159	0.05038	0.00022	229.0	129.3	0.935	7604
		0.04849	0.00022	220.4			
	0.825	0.03406	0.00015	227.1			
		0.03420	0.00015	228.0			
	0.385	0.01765	0.00007	252.1			
		0.01777	0.00007	253.9			
	0.206	0.01000	0.00003	333.3			
		0.00965	0.00004	241.2			
Stetten Flur Nr 1774	1.159	0.02548	0.00022	115.8	33.19	0.853	3319
		0.02582	0.00022	117.4			
	0.825	0.01807	0.00015	120.5			
		0.01794	0.00015	119.6			
	0.385	0.00987	0.00007	141.0			
		0.00923	0.00007	131.9			
	0.206	0.00489	0.00004	122.2			
		0.00538	0.00003	179.2			

Table 7.2.3.1/ 21 Mass balance for adsorption and desorption of Reg. No. 4064702

Soil	Initial Amount		In Aqueous at Equilibrium		Desorbed from soil		Extraction		Combustion		Mean Mass Balance
	µg	%	µg	%	µg	%	µg	%	µg	%	%
Borgeby	0.116	100	0.049	42.1	0.022	19.1	0.037	31.9	0.002	1.57	95.2
	0.116	100	0.047	40.2	0.021	18.3	0.041	35.7	0.002	1.54	
Birnbaum	0.116	100	0.070	60.1	0.020	17.5	0.020	17.3	0.001	1.14	95.9
	0.116	100	0.069	59.8	0.020	17.7	0.020	17.1	0.001	1.12	
2.2	0.116	100	0.042	36.0	0.020	17.5	0.044	38.2	0.002	1.94	93.2
	0.116	100	0.040	34.5	0.020	16.8	0.045	39.2	0.003	2.33	
Sora	0.116	100	0.049	42.1	0.021	18.2	0.036	31.0	0.003	2.35	93.7
	0.116	100	0.050	43.8	0.021	18.2	0.034	29.6	0.003	2.26	
Stetten	0.116	100	0.070	60.8	0.021	18.2	0.017	14.3	0.002	1.60	94.7
	0.116	100	0.070	60.7	0.021	18.0	0.016	14.2	0.002	1.62	

Figure 7.2.3.1/ 4 Adsorption isotherm for Reg. No. 4064702 on Borgeby soil

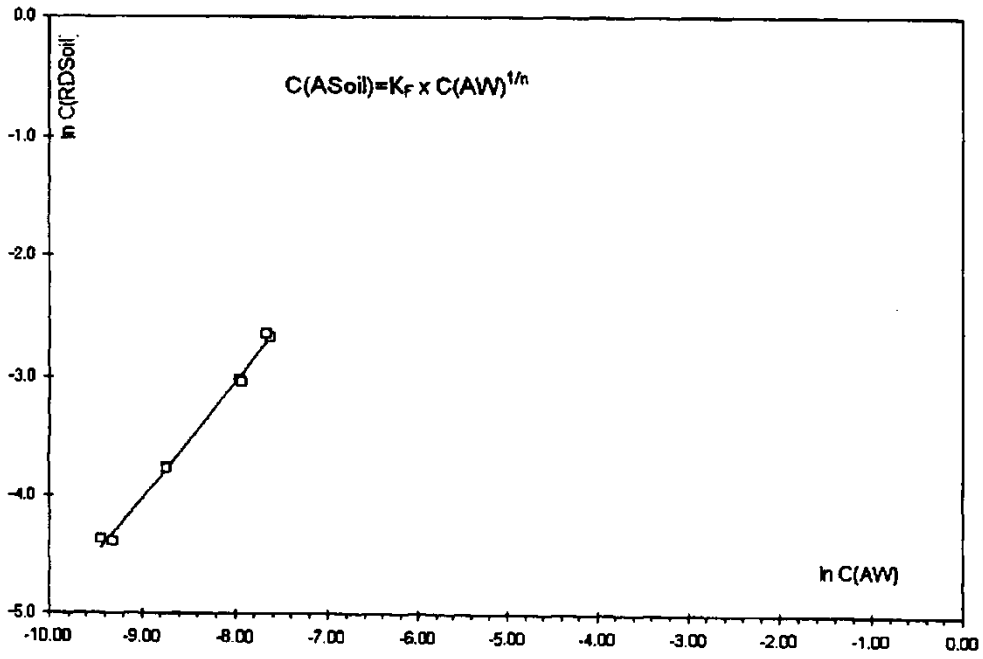


Figure 7.2.3.1/ 5 Adsorption isotherm for Reg. No. 4064702 on Birnbaum soil

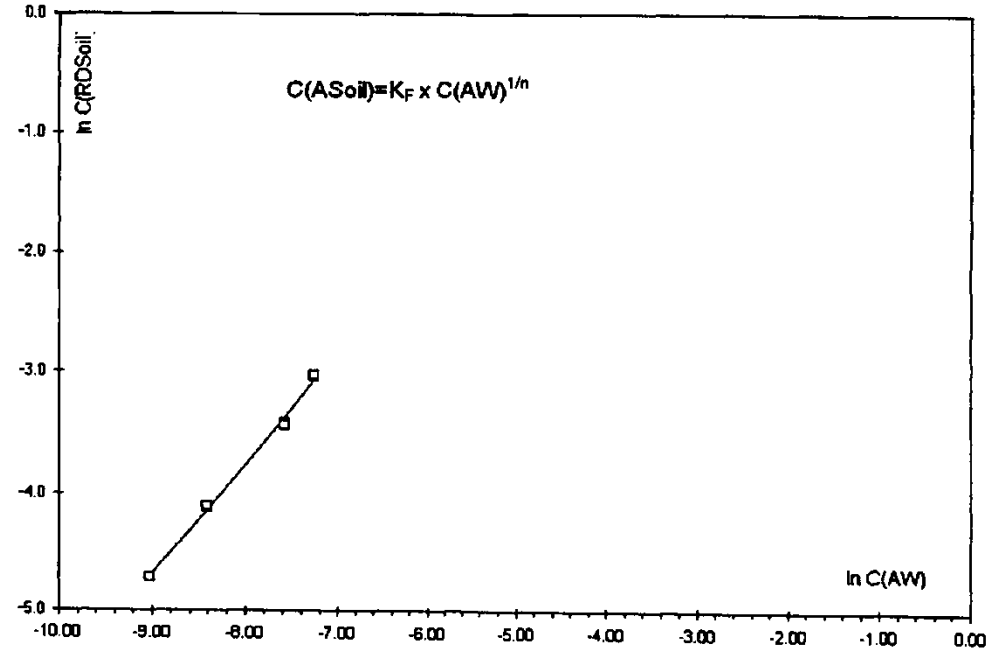


Figure 7.2.3.1/ 6 Adsorption isotherm for Reg. No. 4064702 on 2.2 soil

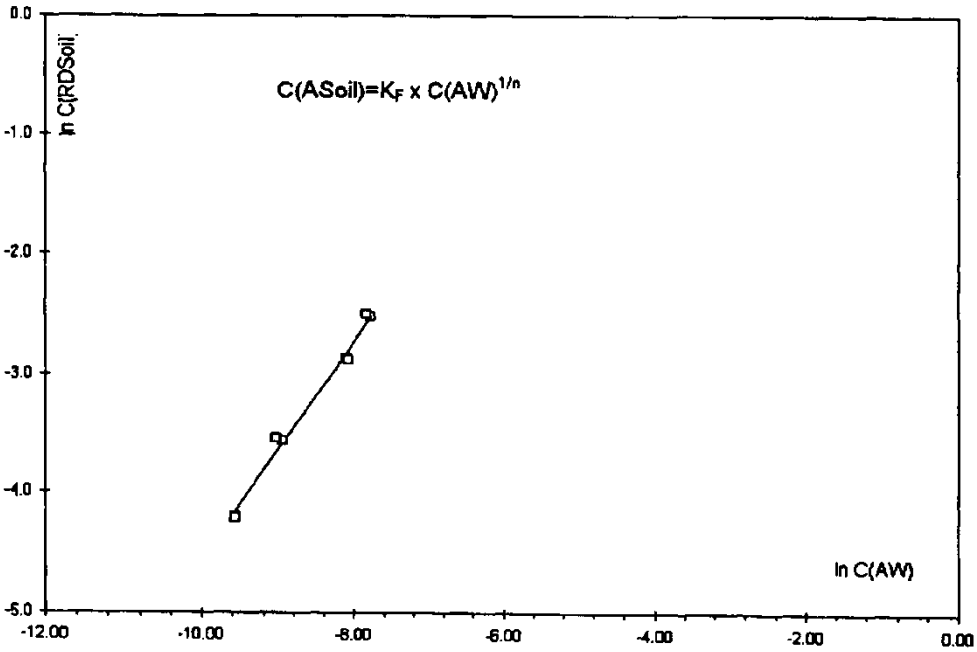


Figure 7.2.3.1/ 7 Adsorption isotherm for Reg. No. 4064702 on Sora soil

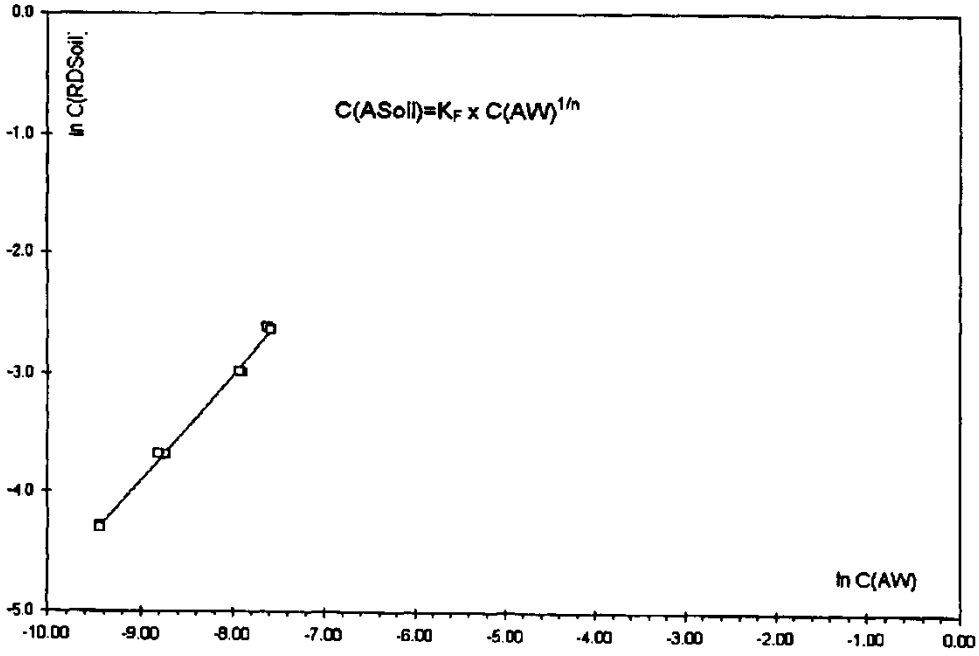


Figure 7.2.3.1/ 8 Adsorption isotherm for Reg. No. 4064702 on Stetten soil

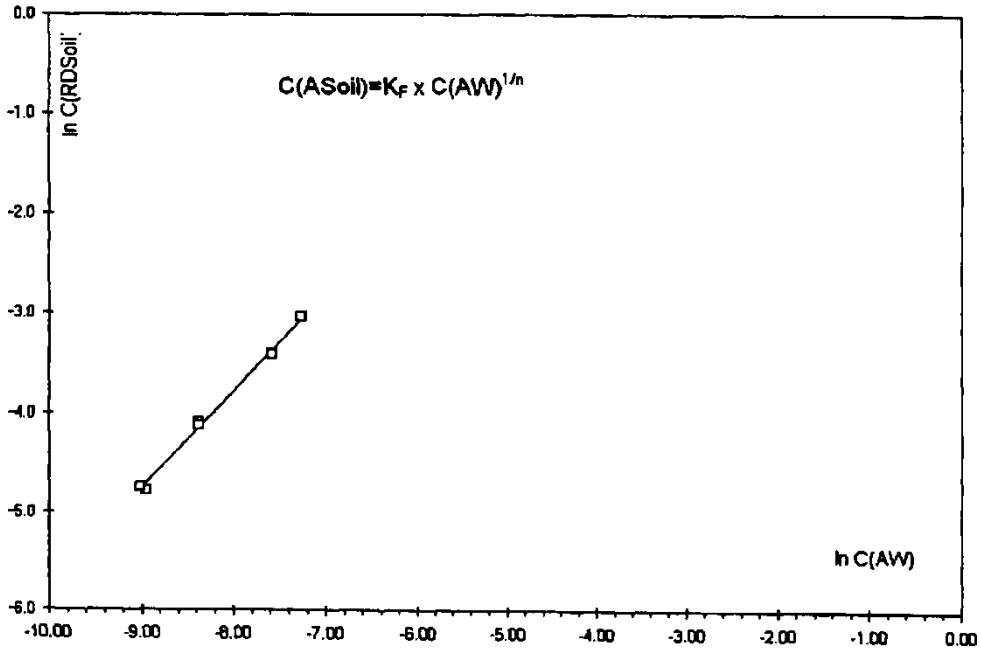


Figure 7.2.3.1/ 9 Desorption isotherm for Reg. No. 4064702 on Borgeby soil

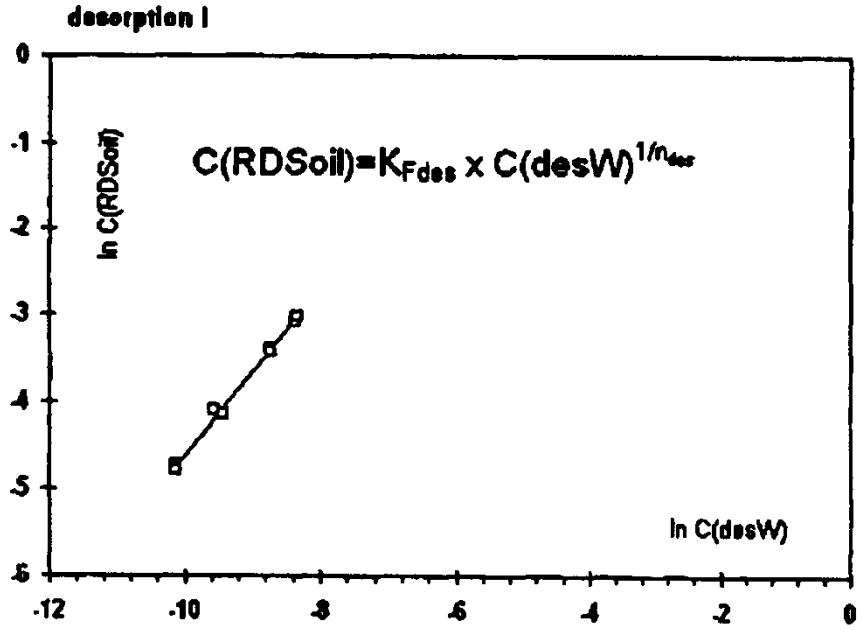


Figure 7.2.3.1/ 10 Desorption isotherm for Reg. No. 4064702 on Birnbaum soil

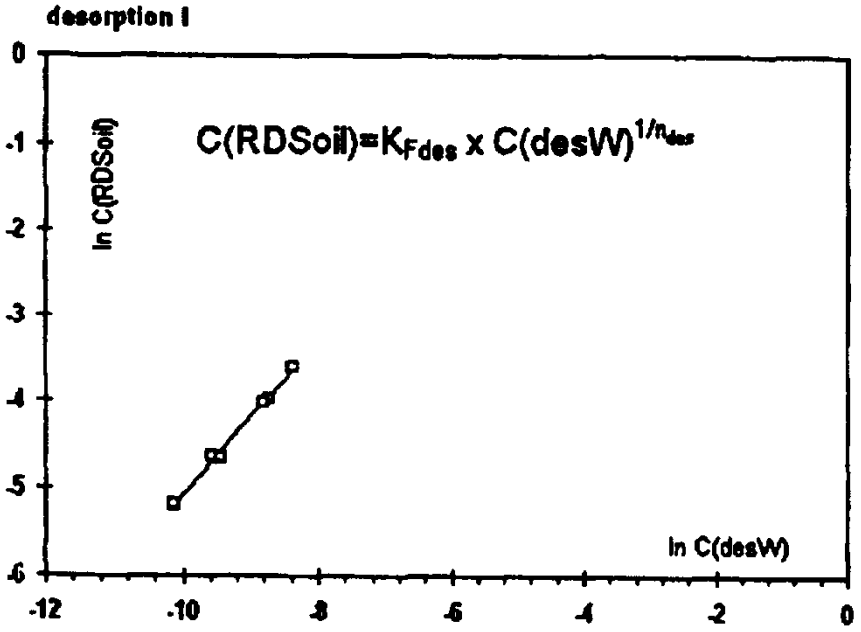


Figure 7.2.3.1/ 11 Desorption isotherm for Reg. No. 4064702 on 2.2 soil

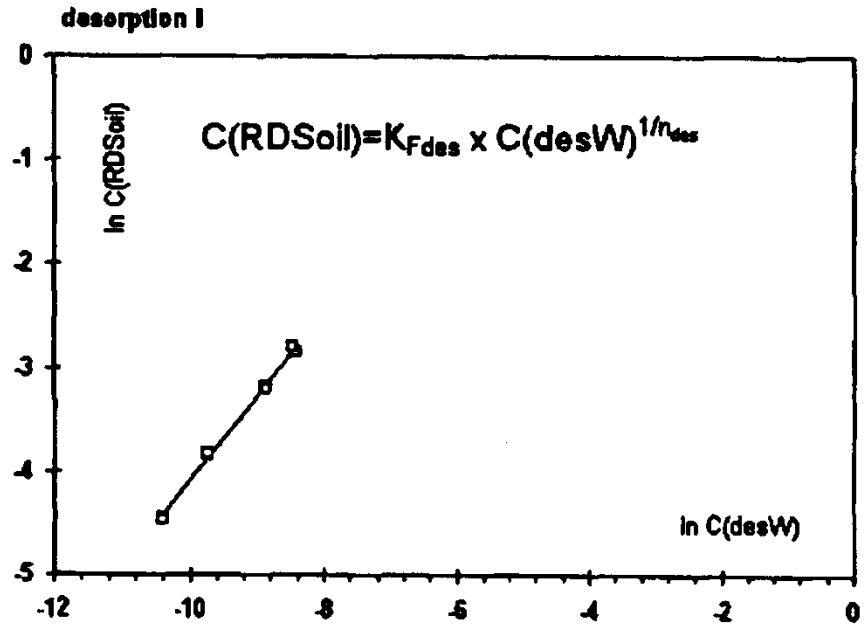


Figure 7.2.3.1/ 12 Desorption isotherm for Reg. No. 4064702 on Sora soil

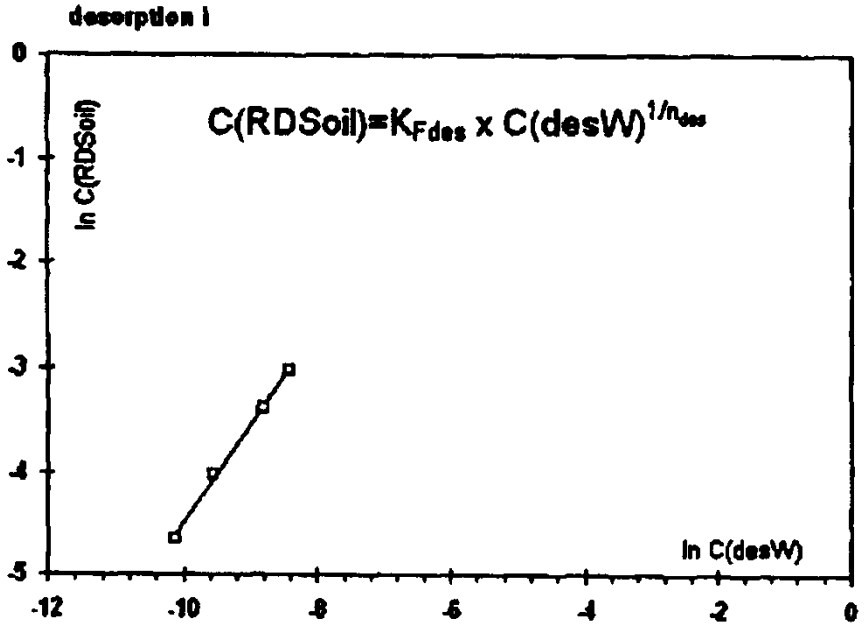
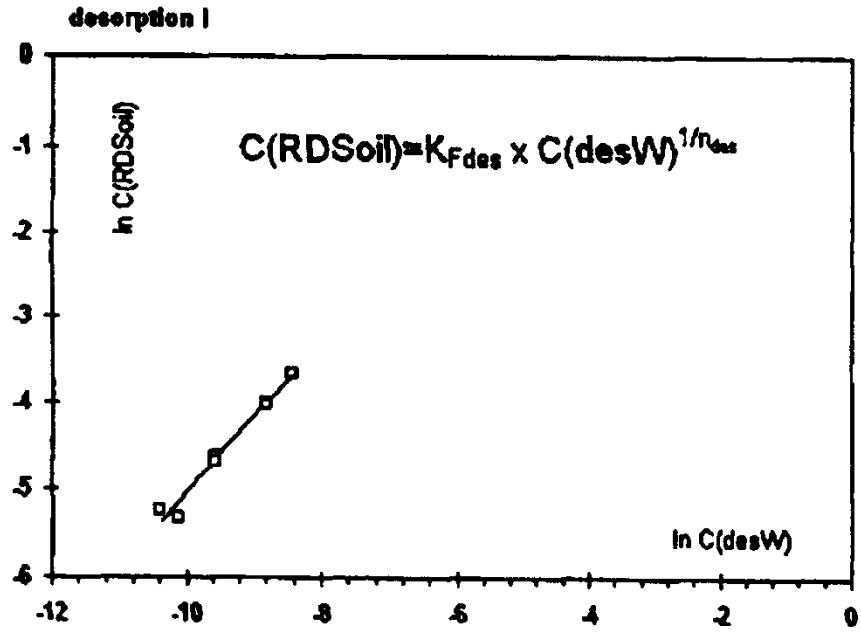


Figure 7.2.3.1/ 13 Desorption isotherm for Reg. No. 4064702 on Stetten soil



Section A7.2.3.2 **Adsorption and Mobility in soil**

BPD Annex Point IIIA, XII.1.3. 7.2.3.2 Mobility

	JUSTIFICATION FOR NON-SUBMISSION OF DATA	**Official use only**
Other existing data [X]	**Technically not feasible [ ] Scientifically unjustified [X]**	
Limited exposure [ ]	**Other justification [ ]**	
Detailed justification:	**Since the soil absorption (IIIA 7.2.3) is very strong for Flufenoxuron (Koc> 8800) and for its "urea" metabolite (Reg.No. 4064702, CL932338) (Koc > 3780), any risk of leaching and subsequent ground contamination can be excluded.**	
Undertaking of intended data submission [ ]		

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/02/2005
Evaluation of applicant's justification	Applicant's version is acceptable.
Conclusion	Applicant's version is acceptable.
Remarks	None.
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A7.3.1	**Fate and Behaviour in air**
BPD Annex Point IIIA, VII.5	7.3.1 Phototransformation in air (Atkinson)

Official use only

1. REFERENCE

1.1.	**Reference**	**1) Hassink J. (2003)** Photochemical oxidative degradation of Flufenoxuron (BAS 307 I) (QSAR estimates). XXXX. unpublished XXXX
1.2.	**Data protection**	Yes
1.2.1.	Data owner	BASF
1.2.2.	Companies with letter of access	XXXX
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I

2. GUIDELINES AND QUALITY ASSURANCE

2.1.	**Guideline study**	Yes, Commission Directive 94/37/EC of July 22, 1994
2.2.	**GLP**	Not applicable
2.3	**Deviations**	No

3. MATERIALS AND METHODS

3.1.	**Test material**	No actual materials used as Flufenoxuron was simulated.
3.2.	**Testing procedure**	
3.2.1.	Test system	The rate constant for reactions of Flufenoxuron with OH radicals in the atmosphere was calculated using the AOPWIN Program (Atmospheric Oxidation Program for Microsoft Windows 3.1, Version 1.88, Syracuse Research Corp. 1988-97) based on Atkinson's increment method (Atkinson, R. (1987) A Structure-Activity Relationship for the Estimation of Rate Constants for the Gas-Phase Reactions of OH Radicals with Organic Compounds, Int.J.Chem.Kin. 19, 799). At first, the rate constant k of the active substance was estimated based on the chemical structure. Using the weighted global average OH radical concentration in the troposphere (8×10^5 cm^{-3}), the degradation of the active substance follows pseudo-first order kinetics with the rate constant $k' = k \cdot$ [OH radicals]: $$-d[\text{BAS 307 I}]/dt = k' \cdot [\text{BAS 307 I}]$$ The half-life of this process can then be calculated by the following equation:

Section A7.3.1 **Fate and Behaviour in air**

BPD Annex Point IIIA, VII.5 7.3.1 Phototransformation in air (Atkinson)

$t_{1/2}$ = ln2/k' = ln2/k · [OH radicals].

AOPWIN does not calculate degradation processes resulting from ozone attack to aromatic rings and reasonable approximation of the substituted aromatic rings by groups with known increments is not possible. Therefore, although O_3 is likely to react with Flufenoxuron by attack of the aromatic ring no degradation estimation can be given.

4. RESULTS

4.1. **k** 14.2568 x 10^{-12} cm^3 $molecule^{-1}$ s^{-1}.

4.2. **$T_{1/2, OH}$** 0.7 days

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1. **Materials and methods**

The rate constant for reactions of Flufenoxuron with OH radicals in the atmosphere was calculated was estimated based on the chemical structure using the AOPWIN Program based on Atkinson's increment method.

Using the weighted global average OH radical concentration in the troposphere, the half-life of this process was then calculated.

5.2. **Results and discussion**

AOPWIN does not calculate degradation processes resulting from ozone attack to aromatic rings and reasonable approximation of the substituted aromatic rings by groups with known increments is not possible. Therefore, although O_3 is likely to react with Flufenoxuron by attack of the aromatic ring no degradation estimation can be given.

5.3.1. k 14.2568 x 10^{-12} cm^3 $molecule^{-1}$ s^{-1}.

5.3.2. $T_{1/2, OH}$ 0.7 days

5.3. **Conclusion**

Flufenoxuron has a very low volatilization potential (vapor pressure 6.52 x 10^{-12} kPa at 20 °C) (details in section 3). Based on Atkinson calculation, Flufenoxuron would be rapidly degraded by photochemical processes when reaching the troposphere (DT_{50} < 17 h). Therefore, it can be concluded that there is no risk of short or long-range transport of Flufenoxuron via air.

5.3.1. Reliability 1

5.3.2. Deficiencies No

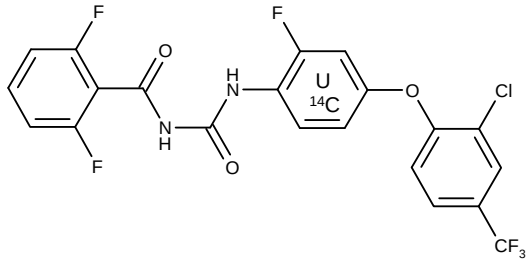
Section A7.3.1	**Fate and Behaviour in air**
BPD Annex Point IIIA, VII.5	7.3.1 Phototransformation in air (Atkinson)

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/02/2005
Materials and Methods	Applicant's version is acceptable. Remarks: - AOPWIN Program version 1.88 was used. Calculations in the updated version v 1.91 lead to the same results. - The weighted global average OH radical concentration in the troposphere of 8.10^5 cm^{-3} (24-hr day) was used, based on the publication of Prinn *et al.* (1992). US-EPA recommends the use of $1.5.10^6$ cm^{-3} (12-h day) and the TGD recommends the use of a 24-hr day with $0.5.10^6$ cm^{-3}. The choice to use published values is not clearly explained in the study report. However, the value chosen is acceptable.
Results and discussion	Applicant's version is acceptable with the following amendments: - 4.2 T1/2, OH: specified: "*0.7 days* [(24-hr day, 8.10^5 OH cm^{-3}).]" *According to the TGD, assuming a 24hrs - day and an OH concentration of 5.0 x 10^5 cm^{-1} this gives a half-life of 1.12 days or 27 hours.*
Conclusion	Applicant's version is acceptable.
Reliability	1
Acceptability	acceptable
Remarks	
	COMMENTS FROM ...
Date	Give date of comments submitted
Materials and Methods	Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion. Discuss if deviating from view of rapporteur member state
Results and discussion	Discuss if deviating from view of rapporteur member state
Conclusion	Discuss if deviating from view of rapporteur member state
Reliability	Discuss if deviating from view of rapporteur member state
Acceptability	Discuss if deviating from view of rapporteur member state
Remarks	

Section A7.3.2	**Fate and Behaviour in air**
BPD Annex Point IIIA, XII.3	7.3.2 Further studies

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**1) Hassink J. (2003)** Volatilisation of BAS 307I after Application of BAS 307 10 I on Soil and on Plant Surfaces. XXXX. unpublished XXXX	
1.2.	**Data protection**	Yes	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	No, No guidelines available	
2.2.	**GLP**	Yes (laboratory certified by Landesamt fuer Umweltschutz und Gewerbeaufsicht, Mainz, Germany)	
2.3.	**Deviations**	No	
		3. MATERIALS AND METHODS	
3.1.	**Test material**	Flufenoxuron, [fluoroaniline ring-U-^{14}C]- Flufenoxuron, and a blank formulation were used as test materials	
3.1.1.	Lot/Batch number	XXXX	X
3.1.2.	Specification	See below	
3.1.3.	Purity	Flufenoxuron - 99.3% [fluoroaniline ring-U-^{14}C]- Flufenoxuron - >99% radiopure	

Section A7.3.1	**Fate and Behaviour in air**
BPD Annex Point IIIA, VII.5	7.3.1 Volatilisation from soil and plant

3.1.4.	Radiolabeling	
3.1.5.	Specific Activity	3.89 MBq/mg
3.1.6.	Further relevant properties	The vapor pressure of Flufenoxuron is 6.52 x 10^{-12} kPa at 20ºC.
3.1.7.	Method of analysis	All analyses were by LSC.
3.2.	**Degradation products**	Degradation products tested: No
3.2.1.	Method of analysis for degradation products	Not applicable
3.3.	**Reference substance**	No
3.3.1.	Method of analysis for reference substance	Not applicable
3.4.	**Soil/Plant type**	See Table 7.3.1/ 1 for soil characteristics. The plant was a Bush bean in the growth stage before the first blossom.
3.5.	**Testing procedure**	
3.5.1.	Test system	Soil and plant were treated in a special glass container. The formulation was applied via a nozzle (FullCone TG 0.5, 1.2 bar) to a small dish filled with soil (first experiment), and to a dish with a plant (bush bean, soil covered; second experiment). After application, the treated soil or plant was removed from the application chamber and transferred as fast as possible into the circulation chamber. The circulation chamber consisted of a 3 l flat flange beaker with a lid. A fan, mounted in the center of the lid, produced an air flow rate of 1 m/s, which was directed perpendicular to the test system. Fresh air was sucked through the circulation chamber exchanging the atmosphere in the apparatus at a rate of about 200 l/h and an air temperature of about 21 °C. The radioactive volatiles were trapped by a cryotrap, charcoal

Section A7.3.1	**Fate and Behaviour in air**
BPD Annex Point IIIA, VII.5	7.3.1 Volatilisation from soil and plant

		absorbers, and NaOH traps.	
3.5.2.	Test solution and Test conditions	5 mg of the unlabeled test substance was dissolved in 5 mL of acetonitrile (ca. 1mg/mL). Two solutions of labeled material were prepared by dissolving 2 mg in 2 mL acetone and determined to be 1.190 mg/mL and 1.574 mg/mL. For soil, about 1.8 mg of unlabeled, 370 µL of radiolabeled Flufenoxuron (1.190 mg/mL), and 14.6 mg of blank formulation were brought to 20 mL with water. For water, about 1.7 mg unlabeled, 270 µL radiolabeled Flufenoxuron (1.574 mg/ml), and 14.6 mg of blank formulation were brought to 20 mL with water. The traps were sampled 1, 3, 6, and 24 h after application (one trap per sampling time). At the end of the experiment, the remaining radioactivity in soil and plant was determined by extraction with acetone followed by combustion and LSC measurements. Application losses were determined by rinsing the glass container and all equipment with acetonitrile.	X
		4. RESULTS	
4.1.	**Plant test**	The results of the plant test are given in Table 7.3.1/ 2. A total of about 2% of the applied dose was volatilized in 24 hours. A graphical representation of the time course of the volatilization is shown in Figure 7.3.1/ 1.	
4.2.	**Soil test**	The results of the soil test are given in Table 7.3.1/ 3. A total of less than 1% of the applied dose was recovered in the traps after 24 hours. The majority of the radiocarbon recovered in the traps was in the NaOH traps, indicating that it was mineralized Flufenoxuron. A graphical representation of the time course of the volatilization is shown in Figure 7.3.1/ 2.	
		5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1.	**Materials and methods**	In this non-guideline study, the volatilization of Flufenoxuron from soil and plant surfaces, after application at rates corresponding to agricultural uses, was investigated by trapping the volatilized [^{14}C]-Flufenoxuron on charcoal followed by combustion and LSC.	
5.2.	**Results and discussion**	The total recovery of radioactivity was about 96% for the plant and about 91% for the soil experiment. The volatilization rates were about 2% from the plant surface and <1% from the soil surface. For the soil, the majority of the radiocarbon recovered in the traps was in the NaOH traps, indicating that it was mineralized Flufenoxuron.	
5.3.	**Conclusion**	Volatilization of Flufenoxuron from plant or soil surfaces can be	

Section A7.3.1	**Fate and Behaviour in air**
BPD Annex Point IIIA, VII.5	7.3.1 Volatilisation from soil and plant

		considered as negligible.
5.3.1.	Reliability	1
5.3.2.	Deficiencies	No

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/02/2005
Materials and Methods	Applicant's version is acceptable with the following amendments: 3.1.1 Lot/Batch number: according to the study report correct number is "XXXX". 3.5.2 Test solution and Test condiitons: change the third paragraph to " *For* [plant]*, about 1.7 mg unlabeled, 270 µL radiolabeled* […]*."*
Results and discussion	Applicant's version is acceptable.
Conclusion	Applicant's version is acceptable.
Reliability	2
Acceptability	acceptable Non-guideline study.
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.3.1/ 1 Classification and physico-chemical properties of the soil

Soil type	LUFA 2.1
Soil origin	LUFA Speyer
Classification (DIN 4220)	Sand
Sand [%]	88.8%
Silt [%]	10.3%
Clay [%]	0.9%
Classification (USDA)	Sand
Sand [%]	88.9%
Silt [%]	8.5%
Clay [%]	2.5%
Organic carbon [%]	1.7%
pH ($CaCl_2$)	6.3
Cation exchange capacity (MEQ/100 g)	6.6

Table 7.3.1/ 2 Results of the plant experiment:

	% TAR
Condensate	
1hr	0.01
2 hr	0.02
6 hr	0.01
24 hr	0.02
Charcoal	
1hr	0.04
2 hr	0.02
6 hr	0.01
24 hr	0.02
NaOH	
1hr	0.01
2 hr	0.00
6 hr	0.01
24 hr	0.00
Chamber Wash	
1	0.46
2	0.26
Fan Wash	0.33
Soil Extract[1]	0.57
Soil Residue[1]	0.29
Plant Extract	92.70
Plant Residue	1.28

[1]Included in volatilized total, as soil was covered during application

Table 7.3.1/ 3 Results of the soil experiment:

	% TAR
Condensate	
1hr	0.01
2 hr	0.01
6 hr	0.01
24 hr	0.16
Charcoal	
1hr	0.00
2 hr	0.00
6 hr	0.00
24 hr	0.01
NaOH	
1hr	0.10
2 hr	0.11
6 hr	0.15
24 hr	0.21
Chamber Wash	
1	0.13
2	0.07
Fan Wash	0.30
Soil Extract	88.60
Soil Residue	1.45

Figure 7.3.1/ 1 Kinetics of volatilization from plant surfaces

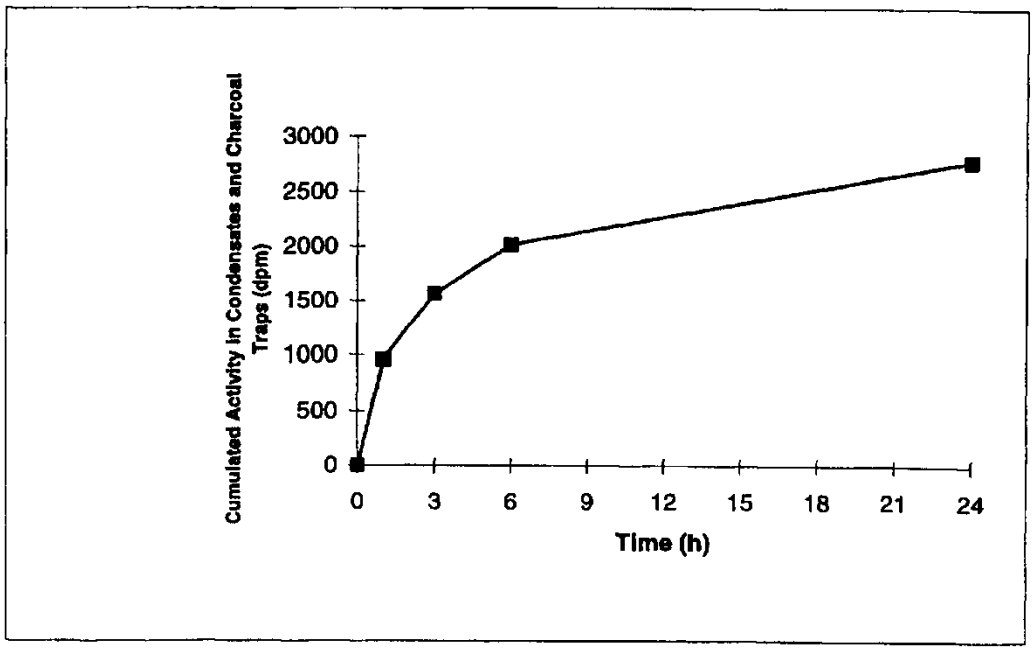
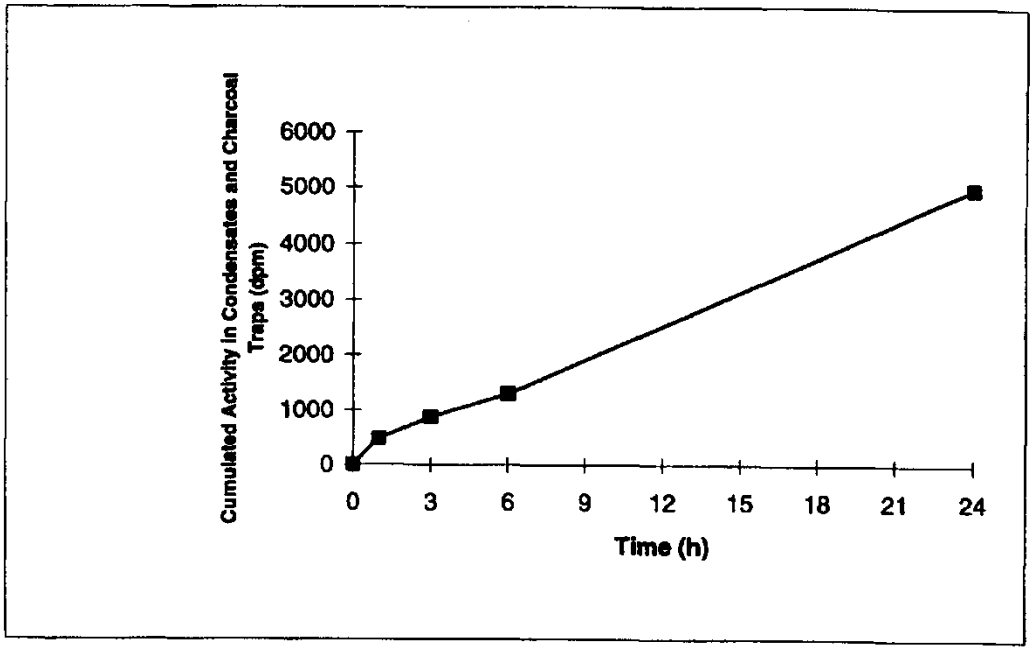


Figure 7.3.1/ 2 Kinetics of volatilization from soil surfaces



Section A7.4.1.1	**Acute toxicity to fish**
BPD Annex Point IIA, VII.7.1	7.4.1.1 Acute fish (parent)

0.0 Justification of the key study

Seven studies are submitted for this endpoint (8 references) :

Four of them are dedicated to the active substance Flufenoxuron, while four other studies were conducted with Flufenoxuron metabolites :

- References 1/2/3 : Flufenoxuron (RI[1] = 1/1/3)
- References 4-5: Reg. No. 4108386; (RI = 2)
- Reference 6: Reg. No. 4064703; (RI = 2)
- Reference 7: Reg. No. 4064702; (RI = 2)
- Reference 8: Reg. No. 102719. (RI = 2)

Reference 1 (XXXX) and **Reference 2** (XXXX) are flow-through studies where LC_{50} were found to be higher than the highest concentration tested (> 4.9 µg/L and > 5.19 µg/L, respectively; close to the solubility limit). Only one concentration and one replicate were included in the test conditions for Reference 1 against 5 concentrations and 2 replicates in reference 2.

No analytical control of the concentrations was performed in **reference 3** (XXXX).

References 4 (XXXX) and **6** (XXXX) correspond to semi-static system where results are based on mean-measured concentrations. **References 7** (XXXX) and **8** (XXXX) correspond to static systems where measured concentrations are representative of nominal values and were LC_{50} calculations are based on nominal values. LC_{50} are 570 µg/L (reference 7, XXXX) and >100 mg/L (reference 8, XXXX). Nevertheless, only one replicate was tested for each treatment. Given that deficiency, reliability index is 2 for these four studies.

The notifier did not propose a key study for this endpoint.

For the above reasons, RMS proposes to retained the following key studies :

- **Reference 2 for flufenoxuron** **LC_{50} > 5.19 µg/L**
- References 4-5: Reg. No. 4108386 **LC_{50} : 2096 µg/L**
- Reference 6: Reg. No. 4064703; **LC_{50} : 462 µg/L**
- Reference 7: Reg. No. 4064702; **LC_{50} : 570 µg/L**
- Reference 8: Reg. No. 102719. **LC_{50} > 100 mg/L**

[1] RI : Reliability Index

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**1) XXXX** WL115110: Acute toxicity to Salmo gairdneri, Daphnia magna and Selenastrum capricornutum XXXX unpublished XXXX	
1.2.	**Data protection**	No	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	No data protection claimed	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	No reported, method description given in the report	
2.2.	**GLP**	No, at the time the study was conducted GLP was not compulsory. However the study was conducted according to the principle of Good Laboratory Practices	
2.3.	**Deviations**	Not applicable	
		3. MATERIALS AND METHODS	
3.1.	**Test material**		X
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	As given in section 2	
3.1.3.	Purity	96.6% (1986), 93.6% (1987)	
3.1.4.	Composition of Product	Not applicable	
3.1.5.	Further relevant properties	Water solubility (IIIA 3.5): pH 7: 136 µg/l pH 4: 186 µg/l pH 9: 369 µg/l	X
3.1.6.	Method of analysis	HPLC-UV detection	
3.2.	**Preparation of TS solution for poorly soluble or volatile test**	None	

Section A7.4.1.1	**Acute toxicity to fish**	
BPD Annex Point IIA, VII.7.1	7.4.1.1 Acute fish (parent)	
	substances	
3.3.	**Reference substance**	No
3.3.1.	Method of analysis for reference substance	Not applicable
3.4.	**Testing procedure**	
3.4.1.	Dilution water	Control, 4.0 µg a.s./L (nominal).
3.4.2.	Test organisms	Rainbow trout (*Oncorhynchus mykiss* WALBAUM 1792, formerly *Salmo gairdnerie* Richardson), fingerlings, mean body length 3.9 (3.4 - 4.2) cm, mean body weight 0.46 (0.31 - 0.57) g; source: XXXX.
3.4.3.	Test system	Flow through system (96 hours), 30 fish per treatment (1 replicate).
3.4.4.	Test conditions	Temperature: 13 °C - 17 °C, pH 7.5 - 7.8, oxygen content: 9.2 mg/L - 10.0 mg/L.
3.4.5.	Duration of the test	96 h
3.4.6.	Test parameter	$LC_{50,}$ sublethal effects
3.4.7.	Sampling	At test initiation and termination
3.4.8.	Monitoring of TS concentration	See 3.4.7
3.4.9.	Statistics	Descriptive statistics
	4. RESULTS	
Limit Test		Performed
4.1.1.	Concentration	4.0 µg a.s./L (nominal)
4.1.2.	Number/ percentage of animals showing adverse effects	See Table 7.4.1.1/101.
4.1.3.	Nature of adverse effects	See Table 7.4.1.1/101.
Results test substance		
4.1.4.	Initial	The analytical results for the test item were within a range of X

Section A7.4.1.1	**Acute toxicity to fish**	
BPD Annex Point IIA, VII.7.1	7.4.1.1 Acute fish (parent)	
	concentrations of test substance	87.5% to 145.0% of the nominal concentrations throughout the test. Hence the results are based on mean measured concentrations.
4.1.5.	Actual concentrations of test substance	See 4.1.4 X
4.1.6.	Effect data (Mortality)	See Table 7.4.1.1/101.
4.1.7.	Concentration / response curve	Not applicable as on test concentration
4.1.8.	Other effects	See Table 7.4.1.1/101.
Results of controls		
4.1.9.	Number/ percentage of animals showing adverse effects	See Table 7.4.1.1/101.
4.1.10.	Nature of adverse effects	See Table 7.4.1.1/101.
Test with reference substance		Not performed
	5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1.	**Materials and methods**	Fish was exposed for 96-h to a test substance as describe under 3.1. The test procedure is detailed under 3.4.
5.2.	**Results and discussion**	Biological results: Flufenoxuron caused no mortality in the test item concentration and the control. Based on the measured concentrations a LC_{50} (96 h) of > 4.9 µg a.s./L was derived. No test item related effects were observed in the fish. The results are summarized in Table 7.4.1.1/101.
5.2.1.	LC_0	Not defined in the study
5.2.2.	LC_{50}	(96 h) of > 4.9 µg a.s./L
5.2.3.	LC_{100}	Not applicable
5.3.	**Conclusion**	In a flow-through acute toxicity study with Flufenoxuron, the LC_{50} on the rainbow trout was > 4.9 µg a.s./L (measured).
5.3.1.	Other Conclusions	None
5.3.2.	Reliability	1

Section A7.4.1.1	**Acute toxicity to fish**
BPD Annex Point IIA, VII.7.1	7.4.1.1 Acute fish (parent)
5.3.3. Deficiencies	No

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/03/2005
Materials and Methods	Applicant's version is acceptable with the following amendments: 3.1: Test material : Flufenoxuron (WL115110) 3.1.5: Further relevant properties: correct values are: pH 7: 1.36 µg/L pH 4: 1.86 µg/L pH 9: 3.69 µg/L
Results and discussion	Applicant's version is acceptable with the following amendments : 4.1.4 Initial concentrations of test substance The analytical results for the test item were within a range of *83%* to *138%* of the nominal concentrations throughout the test *and* the results are based on mean measured concentrations. 4.1.5 Actual concentrations of test substance Mean measured concentration on the whole study is 4.9 +/- 0.9 µg/L
Conclusion	Applicant's version is acceptable.
Reliability	Reliability index is 1.
Acceptability	See above.
Remarks	Despite the low LC_{50} value obtained (compared to Reference 2), this test can not be retained as key study as only one concentration and one replicate were tested, while another study (Reference 2) was realised with five concentrations and two replicates per treatment.

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.4.1.1/101 Acute toxicity (96 h) of Flufenoxuron on rainbow trout (*Oncorhynchus mykiss*)

Concentration [µg a.s./L] nominal	**Control**	**4.0**
Concentration [µg a.s./L] mean measured	**Control**	**4.9**
Mortality [%]	0	0
Symptoms	none	none
Endpoints [µg a.s./L mean measured]		
LC_{50}	> 4.9	

Table 7.4.1.1.1/102 Validity criteria for acute fish test according to OECD Guideline 203

	Fulfilled	**Not fulfilled**
Mortality of control animals <10%	**Yes**	
Concentration of dissolved oxygen in all test vessels > 60% saturation	**Yes**	
Concentration of test substance ≥80% of initial concentration during test	**Yes**	
Criteria for poorly soluble test substances	**Yes**	

Section A7.4.1.1	**Acute toxicity to fish**
BPD Annex Point IIA, VII.7.1	7.4.1.1 Acute fish (parent)

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**2) XXXX** Acute toxicity of Flufenoxuron (AC 811678) technical to zebra fish (Brachydanio rerio) under flow-through test conditions XXXX unpublished XXXX	
1.2.	**Data protection**	Yes	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I.	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	EEC 91/414, EEC 96/12, EPA 40 CFR 158, EPA 72-1(c)	X
2.2.	**GLP**	Yes (laboratory certified by Department of Health of the Government of the United Kingdom, United Kingdom)	
2.3.	**Deviations**	No	
		3. MATERIALS AND METHODS	
3.1.	**Test material**		X
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	As given in section 2	
3.1.3.	Purity	94.9%	
3.1.4.	Composition of Product	Not applicable	
3.1.5.	Further relevant properties	Water solubility (IIIA 3.5): pH 7: 136 µg/l pH 4: 186 µg/l pH 9: 369 µg/l	X

Section A7.4.1.1	**Acute toxicity to fish**
BPD Annex Point IIA, VII.7.1	7.4.1.1 Acute fish (parent)

3.1.6.	Method of analysis	HPLC-UV detection	
3.2.	**Preparation of TS solution for poorly soluble or volatile test substances**	None	
3.3.	**Reference substance**	No	
3.3.1.	Method of analysis for reference substance	Not applicable	
3.4.	**Testing procedure**		
3.4.1.	Dilution water	Control, vehicle (acetone) control, 0.31, 0.63, 1.25, 2.5, and 5.0 µg a.s./L (nominal)	
3.4.2.	Test organisms	Zebra fish (*Brachydanio rerio*), mean standard length 27.1 ± 1.47 mm, mean wet weight 0.3048 g; source: XXXX	
3.4.3.	Test system	Static system (96 hours); 10 fish per treatment (2 replicates)	
3.4.4.	Test conditions	Temperature: 21 °C, pH 8.09 - 8.24, oxygen content: 8.73 mg/L - 9.38 mg/L	X
3.4.5.	Duration of the test	96 h	
3.4.6.	Test parameter	$LC_{50,}$ sublethal effects	
3.4.7.	Sampling	Test initiation and at the end	
3.4.8.	Monitoring of TS concentration	See 3.4.7	
3.4.9.	Statistics	Descriptive statistics, ANOVA followed by Dunnett-test (α = 0.05) for mortality data	
		4. RESULTS	
Limit Test		Not performed	
4.1.1.	Concentration	Not applicable	
4.1.2.	Number/ percentage of animals showing adverse effects	Not applicable	

Section A7.4.1.1	**Acute toxicity to fish**
BPD Annex Point IIA, VII.7.1	7.4.1.1 Acute fish (parent)

4.1.3.	Nature of adverse effects	Not applicable
Results test substance		
4.1.4.	Initial concentrations of test substance	At test initiation, the analytical results for the test item were within a range of 79.0% to 108.0% of the nominal concentrations. 101% - 163% at the end of the test. The results are based on the measured concentrations.
4.1.5.	Actual concentrations of test substance	See 4.1.4
4.1.6.	Effect data (Mortality)	See Table 7.4.1.1/103
4.1.7.	Concentration / response curve	Not relevant, see Table 7.4.1.1/103
4.1.8.	Other effects	See 5.2
Results of controls		
4.1.9.	Number/ percentage of animals showing adverse effects	See Table 7.4.1.1/103
4.1.10.	Nature of adverse effects	See Table 7.4.1.1/103
Test with reference substance		Not performed

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1.	**Materials and methods**	Fish was exposed for 96-h to a test substance as describe under 3.1. The test procedure is detailed under 3.4.
5.2.	**Results and discussion**	Analytical measurements: At test initiation, the analytical results for the test item were within a range of 79.0% to 108.0% of the nominal concentrations and 101% - 163% at the end of the test. The results are based on the measured concentrations. Biological results: Flufenoxuron caused no mortality in the test item concentrations. Based on the measured concentrations a LC_{50} of > 5.19 µg a.s./L was observed. No test item related effects

Section A7.4.1.1	**Acute toxicity to fish**
BPD Annex Point IIA, VII.7.1	7.4.1.1 Acute fish (parent)

		were observed in fish. The results are summarized in Table 7.4.1.1/103.	
5.2.1.	LC_0	Not reported	
5.2.2.	LC_{50}	LC_{50} of > 5.19 µg a.s./L	
5.2.3.	LC_{100}	Not reported	
5.3.	**Conclusion**	In a static acute toxicity study with Flufenoxuron, the LC_{50} on the zebra fish was > 5.19 µg a.s./L, the NOEC was 5.19 µg a.s./L (based on measured concentrations).	X
5.3.1.	Other Conclusions	None	
5.3.2.	Reliability	1	
5.3.3.	Deficiencies	No	

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	03/15/2005

Section A7.4.1.1	**Acute toxicity to fish**
BPD Annex Point IIA, VII.7.1	7.4.1.1 Acute fish (parent)

Materials and Methods	Applicant's version is acceptable with the following amendments: 2.1 Guideline study : EEC 91/414, EEC 96/12, EPA 40 CFR 158, EPA 72-1(c) *(Newly OPPTS 850.1075), OECD 203* 3.1 Test material : Flufenoxuron 3.1.5: Further relevant properties: correct values are: pH 7: 1.36 µg/L pH 4: 1.86 µg/L pH 9: 3.69 µg/L 3.4.4 Test conditions : *Controls and vehicle controls :* Temperature 21 -*22°C*, pH 8.09 - 8.24, oxygen content: 8.73 mg/L - 9.38 mg/L *Treatments : Temperature 21-22°C, pH 8.17 - 8.26, oxygen content: 8.54 - 9.43 mg/L*
Results and discussion	Applicant's version is acceptable.
Conclusion	Applicant's version is acceptable with the following amendments : 5.3 Conclusion : In a ***flow-through*** acute toxicity study with Flufenoxuron, the LC_{50} on the zebra fish was > 5.19 µg a.s./L, the NOEC was 5.19 µg a.s./L (based on measured concentrations).
Reliability	Reliability index is 1 (study has retained as key study).
Acceptability	Acceptable
Remarks	Despite the lower LC_{50} value obtained in reference 1, this test is retained as **key study** as five concentrations and two replicates per treatment were tested, while Reference 1 was realised with only one concentration and one replicate.

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.4.1.1/103 Acute toxicity (96 h) of Flufenoxuron on zebra fish (*Brachydanio rerio*)

Concentration [µg a.s./L] nominal	**Control**	**Vehicle control**	**0.31**	**0.63**	**1.25**	**2.5**	**5.0**
Concentration [µg a.s./L] measured	**Control**	**Vehicle control**	**0.358**	**0.674**	**1.27**	**2.58**	**5.19**
Mortality [%]	0	0	0	0	0	0	0
Symptoms	none	none	none	none	none	none	none
Endpoints [µg a.s./L measured]							
LC_{50}	> 5.19						
NOEC	5.19						

Table 7.4.1.1.1/104 Validity criteria for acute fish test according to OECD Guideline 203

	Fulfilled	**Not fulfilled**
Mortality of control animals <10%	**Yes**	
Concentration of dissolved oxygen in all test vessels > 60% saturation	**Yes**	
Concentration of test substance ≥80% of initial concentration during test	**Yes**	

Criteria for poorly soluble test substances	**Yes**	

Acute toxicity to fish

Section A7.4.1.1 7.4.1.1 Acute fish (parent)

BPD Annex Point IIA, VII.7.1

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**3) XXXX** Acute toxicity of SKI-8503 to Cyprinus carpio XXXX unpublished XXXX	
1.2.	**Data protection**	No	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	No data protection claimed	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	No, description of the method included in the report, in general compliance with JMAFF guideline.	
2.2.	**GLP**	No	
2.3.	**Deviations**	No	
		3. MATERIALS AND METHODS	
3.1.	**Test material**		X
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	As given in section 2	
3.1.3.	Purity	98%	
3.1.4.	Composition of Product	Not applicable	
3.1.5.	Further relevant properties	Water solubility (IIIA 3.5): pH 7: 136 µg/l pH 4: 186 µg/l pH 9: 369 µg/l	X
3.1.6.	Method of analysis	None	

Section A7.4.1.1		**Acute toxicity to fish**
BPD Annex Point IIA, VII.7.1		7.4.1.1 Acute fish (parent)
3.2.	**Preparation of TS solution for poorly soluble or volatile test substances**	None
3.3.	**Reference substance**	No
3.3.1.	Method of analysis for reference substance	Not applicable
3.4.	**Testing procedure**	
3.4.1.	Dilution water	Control, 500, 1000, 2000, 5000 and 10000 µg a.s./L (nominal)
3.4.2.	Test organisms	Common carp (*Cyprinus carpio*), length 5.0 ± 0.2 cm, body weight 3.1 ± 0.3 g; source: Shimizu Goldfish Co. Ltd., Japan
3.4.3.	Test system	Static system (96 hours), 10 fish per treatment (1 replicate), (loading 0.6 g fish/L).
3.4.4.	Test conditions	Temperature: 25 °C ± 1 °C, pH 6.7 - 7.2, oxygen content: 6.0 mg/L - 7.8 mg/L, photoperiod: 13 hours light : 11 hours dark
3.4.5.	Duration of the test	96 h
3.4.6.	Test parameter	$LC_{50,}$ sublethal effects
3.4.7.	Sampling	Not applicable as no analysis
3.4.8.	Monitoring of TS concentration	See 3.4.7
3.4.9.	Statistics	Descriptive statistics, Doudoroff method for determination of the LC_x values
		4. RESULTS
Limit Test		Not performed
4.1.1.	Concentration	Not applicable
4.1.2.	Number/ percentage of animals showing adverse effects	Not applicable
4.1.3.	Nature of adverse	Not applicable

Section A7.4.1.1	**Acute toxicity to fish**
BPD Annex Point IIA, VII.7.1	7.4.1.1 Acute fish (parent)

	effects	
Results test substance		
4.1.4.	Initial concentrations of test substance	Not applicable as no analysis performed
4.1.5.	Actual concentrations of test substance	Not applicable as no analysis performed
4.1.6.	Effect data (Mortality)	See 5.2
4.1.7.	Concentration / response curve	See 5.2
4.1.8.	Other effects	See 5.2
Results of controls		
4.1.9.	Number/ percentage of animals showing adverse effects	See Table 7.4.1.1/105.
4.1.10.	Nature of adverse effects	See Table 7.4.1.1/105.
Test with reference substance		Not performed

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1.	**Materials and methods**	Fish was exposed for 96-h to a test substance as describe under 3.1. The test procedure is detailed under 3.4.
5.2.	**Results and discussion**	Biological results: Flufenoxuron caused no mortality in the test item concentrations and the control. Based on the nominal concentrations a LC_{50} (96 h) of > 10000 µg a.s./L was derived. No test item related effects were observed. The results are summarized in Table 7.4.1.1/105.
5.2.1.	LC_0	Not reported
5.2.2.	LC_{50}	> 10000 µg a.s./L
5.2.3.	LC_{100}	Not reported

Section A7.4.1.1	**Acute toxicity to fish**
BPD Annex Point IIA, VII.7.1	7.4.1.1 Acute fish (parent)

5.3.	**Conclusion**	In a static acute toxicity study with Flufenoxuron, the LC_{50} on the common carp was > 10000 µg a.s./L (nominal).	
5.3.1.	Other Conclusions	None	
5.3.2.	Reliability	2	X
5.3.3.	Deficiencies	No	X

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	03/16/2005
Materials and Methods	Applicant's summary is acceptable with the following amendments: 3.1 Test material : Flufenoxuron 3.1.5 Further relevant properties: correct values are: pH 7: 1.36 µg/L pH 4: 1.86 µg/L pH 9: 3.69 µg/L
Results and discussion	Applicant's summary is acceptable.
Conclusion	Applicant's summary is acceptable with the following amendments : 5.3.4. Deficiencies : *Yes* Test substance was not analysed. Given that, there is no evidence that concentration of the substance being tested has been satisfactorily maintained in the water throughout the exposure period.
Reliability	Given deficiencies above, this study can not be considered as reliable. Therefore, whole study summary was not read in detail. Reliability index is 3.
Acceptability	See above
Remarks	No other

Section A7.4.1.1	**Acute toxicity to fish**
BPD Annex Point IIA, VII.7.1	7.4.1.1 Acute fish (parent)

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.4.1.1/105 Acute toxicity (96 h) of Flufenoxuron on common carp (*Cyprinus carpio*)

Concentration [µg a.s./L] nominal	**Control**	**500**	**1000**	**2000**	**5000**	**10000**
Mortality [%]	0	0	0	0	0	0
Symptoms	none	none	none	none	none	none
Endpoints [µg a.s./L nominal]						
LC_{50}	> 10000					

Table 7.4.1.1.1/106 Validity criteria for acute fish test according to OECD Guideline 203

	Fulfilled	**Not fulfilled**
Mortality of control animals <10%	**Yes**	
Concentration of dissolved oxygen in all test vessels > 60% saturation	**Yes**	
Concentration of test substance ≥80% of initial concentration during test	**No analysis**	

Criteria for poorly soluble test substances	**Yes**	

Section A7.4.1.1	**Acute toxicity to fish**
BPD Annex Point IIA, VII.7.1	7.4.1.1 Acute fish (parent)

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**4) XXXX** 4-Amino-3-Fluorophenol: Acute toxicity to Daphnia magna and Salmo gairdneri XXXX unpublished XXXX **5) XXXX** 4-Amino-3-Fluorophenol : Acute toxicity to Daphnia magna and Salmo gairdneri XXXX unpublished XXXX	
1.2.	**Data protection**	No	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	No data protection claimed	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Official Journal of the European Communities No. L251 Part C: Methods for the determination of Ecotoxicity. C2 Acute toxicity for Daphnia	X
2.2.	**GLP**	Yes (laboratory certified by Department of Health of the Government of the United Kingdom, United Kingdom)	
2.3.	**Deviations**	No	X
		3. MATERIALS AND METHODS	
3.1.	**Test material**		X
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	See Business Confidential Information folder	
3.1.3.	Purity	86%	

Section A7.4.1.1	**Acute toxicity to fish**
BPD Annex Point IIA, VII.7.1	7.4.1.1 Acute fish (parent)

3.1.4.	Composition of Product	Not applicable	
3.1.5.	Further relevant properties	None	
3.1.6.	Method of analysis	None	
3.2.	**Preparation of TS solution for poorly soluble or volatile test substances**	None	
3.3.	**Reference substance**	No	
3.3.1.	Method of analysis for reference substance	Not applicable	
3.4.	**Testing procedure**		
3.4.1.	Dilution water	Control, 350, 600, 1000, 2000, 3500, 6000 and 10000 µg a.s./L (nominal)	
3.4.2.	Test organisms	Rainbow trout (*Oncorhynchus mykiss* WALBAUM 1792, former *Salmo gairdneri*), mean body length 5.1 (4.4 - 5.6) cm, mean body weight 1.3 (0.72 - 1.8) g	
3.4.3.	Test system	Semi-static renewal system (96 hours, renewal of test solutions at 12 h intervals); 10 fish per treatment	
3.4.4.	Test conditions	Temperature: 25 °C ± 1 °C, pH 6.7 - 7.2, oxygen content: 6.0 mg/L - 7.8 mg/L, photoperiod: 13 hours light: 11 hours dark	X
3.4.5.	Duration of the test	96 h	
3.4.6.	Test parameter	$LC_{50,}$ sublethal effects	
3.4.7.	Sampling	See 4.1.4	
3.4.8.	Monitoring of TS concentration	HPLC-UV detections	
3.4.9.	Statistics	Descriptive statistics, log-log analysis for determination of the LC_{50} (siehe XXXX).	X

Section A7.4.1.1	**Acute toxicity to fish**
BPD Annex Point IIA, VII.7.1	7.4.1.1 Acute fish (parent)

4. RESULTS

Limit Test		Not performed	
4.1.1.	Concentration	Not applicable	
4.1.2.	Number/ percentage of animals showing adverse effects	Not applicable	
4.1.3.	Nature of adverse effects	Not applicable	
Results test substance			
4.1.4.	Initial concentrations of test substance	The test item was lost rapidly from aerated water, test solutions were therefore changed at 12 h intervals to maintain the nominal test item concentrations and dissolved oxygen concentrations. At test initiation, the analytical results for the freshly prepared test solutions were 100% - 130% of the nominal concentrations. The test item concentrations in the freshly prepared solutions were averaged 107% of the nominal over the study.	
4.1.5.	Actual concentrations of test substance	At test termination the concentrations of the old solutions were between 18% and 83%. The results based on the nominal concentrations.	X
4.1.6.	Effect data (Mortality)	See Table 7.4.1.1/107.	
4.1.7.	Concentration / response curve	See Table 7.4.1.1/107.	
4.1.8.	Other effects	None	
Results of controls			
4.1.9.	Number/ percentage of animals showing adverse effects	See Table 7.4.1.1/107.	
4.1.10.	Nature of adverse effects	See Table 7.4.1.1/107.	
Test with reference substance		Not performed	

Section A7.4.1.1	**Acute toxicity to fish**
BPD Annex Point IIA, VII.7.1	7.4.1.1 Acute fish (parent)

		5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1.	**Materials and methods**	Fish was exposed for 96-h to a test substance as describe under 3.1. The test procedure is detailed under 3.4.	
5.2.	**Results and discussion**	Biological results: 4-Amino-3-Fluorophenol caused no mortality in the control and the two lowest test item concentrations (350 and 600 µg a.s./L). Mortality rates in the 1000, 2000, 3500, 6000 and 10000 µg a.s./L test item concentrations were 10%, 10%, 90%, 100% and 100%, respectively. Based on the mean measured concentrations an LC_{50} of 2096 µg a.s./L was calculated (siehe auch XXXX). No toxic signs were observed up to 1000 µg a.s./L. The results are summarized in Table 7.4.1.1/107.	
5.2.1.	LC_0	Not applicable	
5.2.2.	LC_{50}	2096 µg a.s./L	
5.2.3.	LC_{100}	Not applicable	
5.3.	**Conclusion**	In a semi-static acute toxicity study with 4-Amino-3-Fluorophenol the LC_{50} on the rainbow trout was 2096 µg a.s./L.	
5.3.1.	Other Conclusions	None	
5.3.2.	Reliability	1	X
5.3.3.	Deficiencies	No	

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	03/16/2005
Materials and Methods	Applicant's summary is acceptable with the following amendments : 2.1 Guideline study : Official Journal of the European Communities No. L251 Part C: Methods for the determination of Ecotoxicity. *C1* Acute toxicity for *Fish* 2.3 Deviations: Yes Only one replicate tested 3.1 Test material : 4-amino-fluorophenol (Reg. No. 4108386) 3.4.4 Test conditions : Controls : Temperature: *13.9 - 15.1*°C, pH *7.3 - 7.9*, oxygen content:

	9.2 mg/L – 10.2 mg/L, photoperiod: *16 hours light: 8 hours dark* Top concentration : Temperature: *13.9 - 15.1*°C, pH *7.6 - 7.9*, oxygen content: *9.0 mg/L – 10.2* mg/L, photoperiod: *16 hours light: 8 hours dark* 4.1.5 Actual concentrations of test substance : *At test termination the concentrations of the old solutions were between 18% and 83%. The results* **are** *based on the* ~~*nominal*~~ **mean-measured** *concentrations.* **The calculations are presented in XXXX (Annex 2 of IIIA 7.6).**
Results and discussion	Applicant's summary is acceptable
Conclusion	Applicant's summary is acceptable.
Reliability	Reliability index is 2.
Acceptability	See above.
Remarks	Additional data in Table 7.4.1.1/7 and 8 were added in bold and underlined.

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.4.1.1/107 Acute toxicity (96 h) of 4-Amino-3-Fluorophenol on rainbow trout (*Oncorhynchus mykiss)*

Nominal Concentrations [µg a.s./L]	**Control**	**350**	**600**	**1000**	**2000**	**3500**	**6000**	**10000**
Mean-measured Concentrations [µg a.s./L]	**Control**	**250**	**370**	**690**	**1580**	**2920**	**5050**	**11050**
Mortality [%]	0	0	0	10	10	90	100	100
Symptoms [1)]	none	none	none	none	S	S	--	--
Endpoints [µg a.s./L – mean-measured value]								
LC_{50}	2096 (95% limits: 1681 - 2614)							

1) Symptoms: S = swimming abnormally (on side or back)

Table 7.4.1.1.1/108 Validity criteria for acute fish test according to OECD Guideline 203

	Fulfilled	**Not fulfilled**
Mortality of control animals <10%	**Yes**	
Concentration of dissolved oxygen in all test vessels > 60% saturation	**Yes**	
Concentration of test substance ≥80% of initial concentration during test	~~**No analysis**~~	**Results are based on mean-measured concentrations**
Criteria for poorly soluble test substances	**Yes**	

Section A7.4.1.1	**Acute toxicity to fish**
BPD Annex Point IIA, VII.7.1	7.4.1.1 Acute fish (parent)

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**6) XXXX** WL125892: Acute toxicity to Salmo gairdneri and Daphnia magna XXXX unpublished XXXX	
1.2.	**Data protection**	No	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	No data protection claimed	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Official Journal of the European Communities No. L251 Part C: Methods for the determination of Ecotoxicity. C2 Acute toxicity for Daphnia	X
2.2.	**GLP**	Yes (laboratory certified by Department of Health of the Government of the United Kingdom, United Kingdom)	
2.3.	**Deviations**	No	X
		3. MATERIALS AND METHODS	
3.1.	**Test material**		X
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	See Business Confidential Information folder	
3.1.3.	Purity	97.3%	
3.1.4.	Composition of Product	Not applicable	
3.1.5.	Further relevant properties	None	
3.1.6.	Method of analysis	None	
3.2.	**Preparation of**	None	

Section A7.4.1.1	**Acute toxicity to fish**
BPD Annex Point IIA, VII.7.1	7.4.1.1 Acute fish (parent)

	TS solution for poorly soluble or volatile test substances		
3.3.	**Reference substance**	No	
3.3.1.	Method of analysis for reference substance	Not applicable	
3.4.	**Testing procedure**		
3.4.1.	Dilution water	Control, 60, 100, 200, 350, 600, 1000 and 2000 µg a.s./L (nominal).	
3.4.2.	Test organisms	Rainbow trout (*Oncorhynchus mykiss* WALBAUM 1792, former *Salmo gairdneri*), fingerlings, mean length 6.2 (5.5 - 7.4) cm, mean body weight 2.6 (1.9 - 3.7) g; source: Itchin Valley Trout Farm, Hampshire, UK	
3.4.3.	Test system	Semi-static system (96 h, renewal of test solutions at 12 h intervals); 7 test item concentrations and control (Analar acetone), 10 fish per treatment (1 replicate). To minimize loss of the test item, the aquaria were filled and the water aerated for 12 hours before the test item was added. The test solutions were not aerated during the exposure period. Before each renewal of the test solutions the fish were observed and the number exhibiting toxic symptoms was recorded.	
3.4.4.	Test conditions	Temperature: 14.9 °C - 15.4 °C, pH 7.4 - 7.9, oxygen content: 9.2 mg/L - 10.4 mg/L, photoperiod: 16 hours light: 8 hours dark; no feeding.	X
3.4.5.	Duration of the test	96 h	
3.4.6.	Test parameter	$LC_{50,}$ sublethal effects	
3.4.7.	Sampling	See 4.1.4	
3.4.8.	Monitoring of TS concentration	HPLC-UV detections	
3.4.9.	Statistics	Descriptive statistics, probit analysis for determination of the LC_{50} (see also XXXX).	X

Section A7.4.1.1	**Acute toxicity to fish**
BPD Annex Point IIA, VII.7.1	7.4.1.1 Acute fish (parent)

4. RESULTS

Limit Test		Not performed	
4.1.1.	Concentration	Not applicable	
4.1.2.	Number/ percentage of animals showing adverse effects	Not applicable	
4.1.3.	Nature of adverse effects	Not applicable	
Results test substance			
4.1.4.	Initial concentrations of test substance	Analytical measurements: Concentrations of the test item were determined before and after each change of solution. At test initiation, the analytical results for the freshly prepared test solutions were 90% - 110% of the nominal concentrations, results for the old solutions were 65% - 95%. At test termination the concentrations of the fresh solutions were between 97% and 120%, the old solutions showed results between 95% and 102% of the nominal values. The test item concentrations in the freshly prepared solutions were averaged 107% of the nominal over the study. The results are based on the nominal concentrations.	X
4.1.5.	Actual concentrations of test substance	See 4.1.4	
4.1.6.	Effect data (Mortality)	See Table 7.4.1.1/109.	
4.1.7.	Concentration / response curve	See Table 7.4.1.1/109.	
4.1.8.	Other effects	None	
Results of controls			
4.1.9.	Number/ percentage of animals showing adverse effects	See Table 7.4.1.1/109.	
4.1.10.	Nature of adverse effects	See Table 7.4.1.1/109.	
Test with reference substance		Not performed	

Section A7.4.1.1	**Acute toxicity to fish**
BPD Annex Point IIA, VII.7.1	7.4.1.1 Acute fish (parent)

		5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1.	**Materials and methods**	Fish was exposed for 96-h to a test substance as describe under 3.1. The test procedure is detailed under 3.4.	
5.2.	**Results and discussion**	Biological results: WL125892 caused no mortality up to 200 µg a.s./L test item concentration. Mortality rates in the 350, 600, 1000 and 2000 µg a.s./L test item concentrations were 10%, 90%, 100% and 100%, respectively. Based on the mean measured concentrations a LC_{50} of 462 µg a.s./L was determined (siehe auch XXXX). Toxic signs like abnormal swimming behaviour were observed in the 200 µg a.s./L test item concentration, immobilization was detected in the 350 and 600 µg a.s./L test item concentration. The results are summarized in Table 7.4.1.1/109.	
5.2.1.	LC_0	Not applicable	
5.2.2.	LC_{50}	462 µg a.s./L (mean measured).	
5.2.3.	LC_{100}	Not applicable	
5.3.	**Conclusion**	Reg. No. 4064703 (WL125892) was tested in a semi-static acute toxicity study on rainbow trout. The LC_{50} was 462 µg a.s./L (mean measured).	
5.3.1.	Other Conclusions	None	
5.3.2.	Reliability	1	X
5.3.3.	Deficiencies	No	

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	03/16/2005
Materials and Methods	Applicant's summary is acceptable with the following amendments : 2.1 Guideline study : Official Journal of the European Communities No. L251 Part C: Methods for the determination of Ecotoxicity. *C1* Acute toxicity for *Fish* 4.14 Initial concentrations of test substance: Analytical measurements: Concentrations of the test item were determined before and after each change of solution. The test item concentrations were averaged 102% of the nominal over the study in the freshly prepared solutions, while they were averaged 95% of the nominal over the study in old solutions. However, at test initiation, the analytical results for the old solutions were 65% - 95%. Therefore, results are based on the nominal concentrations but on mean-measured ones. The calculations are presented in DocID 2006/1004526 (Annex 2 of IIIA 7.6). 3.1 Test Material: Reg. No. 4064703 3.4.4 Test conditions: Controls: Temperature: *14.9 - 15.4*°C, pH *7.6 - 7.8*, oxygen content: *9.2 mg/L – 10.2* mg/L, photoperiod: 16 hours light: 8 hours dark Top concentration: Temperature: *14.9 - 15.4*°C, pH *7.5 - 7.8*, oxygen content: *9.2 mg/L – 10.2* mg/L, photoperiod: 16 hours light: 8 hours dark
Results and discussion	Applicant's summary is acceptable.
Conclusion	Applicant's version with following amendments: 5.3.4. Deficiencies : *Yes* Only one replicate tested.
Reliability	See deficiencies above. Reliability index is 2.
Acceptability	See above.
Remarks	Additional data in Table 7.4.1.1/9 were added in bold and underlined.

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.4.1.1/109 Acute toxicity (96 h) of WL125892 on rainbow trout (*Oncorhynchus mykiss)*

Nominal Concentration [µg a.s./L]	**Control**	**60**	**100**	**200**	**350**	**600**	**1000**	**2000**
Mean-measured Concentration [µg a.s./L]	**Control**	**60**	**110**	**200**	**350**	**610**	**950**	**1770**
Mortality [%]	0	0	0	0	10	90	100	100
Symptoms [1)]	none	none	none	S	I	I	--	--
Endpoints [µg a.s./L mean-measured concentration]								
LC_{50}	462 (95% limits: 393 - 543)							

1) Symptoms: S = swimming abnormally (on side or back), I = immobilized, but still alive

Table 7.4.1.1.1/110 Validity criteria for acute fish test according to OECD Guideline 203

	Fulfilled	**Not fulfilled**
Mortality of control animals <10%	**Yes**	
Concentration of dissolved oxygen in all test vessels > 60% saturation	**Yes**	
Concentration of test substance ≥80% of initial concentration during test	**Yes**	

Criteria for poorly soluble test substances	**Yes**	

Section A7.4.1.1	**Acute toxicity to fish**
BPD Annex Point IIA, VII.7.1	7.4.1.1 Acute fish (metabolite of BAS 307 I)

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**7) XXXX** Reg.No. 406 4702 (metabolite of BAS 307 I) - Acute toxicity study on the rainbow trout (Oncorhynchus mykiss) in a static system over 96 hours XXXX. unpublished XXXX	
1.2.	**Data protection**	Yes	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	EPA 72-1; EEC 92/69 A V C 1; OECD 203; EPA-SEP 540/9-85-006	
2.2.	**GLP**	Yes (laboratory certified by Landesanstalt fuer Pflanzenbau und Pflanzenschutz Rheinland-Pfalz, Mainz)	
2.3.	**Deviations**	No	
		3. MATERIALS AND METHODS	
3.1.	**Test material**		X
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	See chemical glossary	
3.1.3.	Purity	95%.	
3.1.4.	Composition of Product	Not applicable	
3.1.5.	Further relevant properties	None	
3.1.6.	Method of analysis	HPLC-UV detection (details given in report)	

Section A7.4.1.1	**Acute toxicity to fish**
BPD Annex Point IIA, VII.7.1	7.4.1.1 Acute fish (metabolite of BAS 307 I)

3.2.	**Preparation of TS solution for poorly soluble or volatile test substances**	Not applicable	
3.3.	**Reference substance**	No	
3.3.1.	Method of analysis for reference substance	Not applicable	
3.4.	**Testing procedure**		
3.4.1.	Dilution water	Control, 200, 400, 800, 1590 and 3170 µg a.s./L (nominal).	
3.4.2.	Test organisms	Rainbow trout (*Oncorhynchus mykiss* WALBAUM 1792), 4 months old, body length 6.3 (5.4 - 7.1) cm, body weight 2.14 (1.24 - 3.46) g; source: Forellenzucht Trostadt GbR, Germany.	
3.4.3.	Test system	Static system (96 h); 10 fish per treatment (1 replicate) (loading 0.4 g fish/L).	
3.4.4.	Test conditions	Temperature: 12 °C - 13 °C, pH 8.0 - 8.5, oxygen content: 6.2 mg/L - 10.3 mg/L, total hardness 2.5 mmol/L), photoperiod: 16 hours light : 8 hours dark, light intensity: 82 lux - 280 lux.	
3.4.5.	Duration of the test	96 h	
3.4.6.	Test parameter	$LC_{50,}$ sublethal effects	
3.4.7.	Sampling	See 4.1.4	X
3.4.8.	Monitoring of TS concentration	Not applicable	
3.4.9.	Statistics	Descriptive statistics, probit analysis for determination of the LC_x.	

4. RESULTS

Limit Test		Not performed	
4.1.1.	Concentration	Not applicable	

Section A7.4.1.1	**Acute toxicity to fish**
BPD Annex Point IIA, VII.7.1	7.4.1.1 Acute fish (metabolite of BAS 307 I)

4.1.2.	Number/ percentage of animals showing adverse effects	Not applicable	
4.1.3.	Nature of adverse effects	Not applicable	
Results test substance			
4.1.4.	Initial concentrations of test substance	Analytical measurements: At test initiation, the analytical results of the test item were in a range of 90.8% - 114.5%, at test termination the analytical results were 79.5% - 112.3% of the nominal concentrations. The results based on the nominal concentrations.	X
4.1.5.	Actual concentrations of test substance	Test parameter expressed as nominal concentrations	
4.1.6.	Effect data (Mortality)	See in Table 7.4.1.1/111	
4.1.7.	Concentration / response curve	See in Table 7.4.1.1/111	
4.1.8.	Other effects	None	
Results of controls			
4.1.9.	Number/ percentage of animals showing adverse effects	See in Table 7.4.1.1/111	
4.1.10.	Nature of adverse effects	See in Table 7.4.1.1/111	
Test with reference substance		Not performed	

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1.	**Materials and methods**	Fish was exposed for 96-h to a test substance as describe under 3.1. The test procedure is detailed under 3.4.	
5.2.	**Results and discussion**	Analytical measurements: At test initiation, the analytical results of the test item were in a range of 90.8% - 114.5%, at test termination the analytical results were 79.5% - 112.3% of the nominal concentrations. The results based on the nominal	X

Section A7.4.1.1	**Acute toxicity to fish**
BPD Annex Point IIA, VII.7.1	7.4.1.1 Acute fish (metabolite of BAS 307 I)

		concentrations. Biological results: Reg. No. 4064702 caused no mortality up to 400 µg/L test item concentration. Mortality rates in the 800, 1590 and 3170 µg/L test item concentrations were 100%, respectively. Based on the nominal concentrations a LC_{50} of 570 µg/L was observed, based on the analytically detected concentrations, the LC_{50} was 520 µg/L. In the 400 µg/L test item concentration fish showed apathy. The NOEC was determined to be 200 µg/L based on nominal concentrations and 230 µg/L based on measured concentrations. The results are summarized in Table 7.4.1.1/111	
5.2.1.	LC_0	Not determined	
5.2.2.	LC_{50}	570 µg a.s./L (nominal).	X
5.2.3.	LC_{100}	Not determined	
5.3.	**Conclusion**	Reg. No. 4064702 was tested in a static acute toxicity study on rainbow trout. The LC_{50} was 570 µg/L. The NOEC was determined to be 200 µg/L (based on nominal concentrations).	
5.3.1.	Other Conclusions	None	
5.3.2.	Reliability	1	X
5.3.3.	Deficiencies	No	

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	03/16/2005
Materials and Methods	Applicant's summary is acceptable with following amendment: 3.1 Test material : Reg. No. 4064702 3.4.7 Sampling : *At test initiation and test termination* 4.1.4 Initial concentration of test substance Analytical measurements: At test initiation, the analytical results of the test item were in a range of 90.8% - 114.5%, at test termination the analytical results were 79.5% - 112.3% of the nominal concentrations. *The results are based on the nominal concentrations and on analytically determined concentrations.*
Results and discussion	Applicant's summary is acceptable with following amendment: 5.2 Results and Discussion : Analytical measurements: At test initiation, the analytical results of the test item were in a range of 90.8% - 114.5%, at test termination the analytical results were 79.5% - 112.3% of the nominal concentrations *The results are based on the nominal concentrations and on analytically determined concentrations.* 5.2.2 LC_{50} : 570 µg a.s./L (nominal) LC_{50} : 520 µg a.s./L (mean-measured)
Conclusion	Applicant's version is acceptable.
Reliability	Reliability index is 2.
Acceptability	Acceptable
Remarks	Only one replicate tested.
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.4.1.1/111 Acute toxicity (96 h) of Reg. No. 406 4702 on rainbow trout (*Oncorhynchus mykiss)*

Concentration [µg/L nominal]	**Control**	**200**	**400**	**800**	**1590**	**3170**
Mortality [%]	0	0	0	100	100	100
Symptoms [1)]	none	none	A	--	--	--
Endpoints [µg/L nominal]						
LC_{50}	570					
NOEC	200					

1) Symptoms: A = apathy

Table 7.4.1.1.1/112 Validity criteria for acute fish test according to OECD Guideline 203

	Fulfilled	**Not fulfilled**
Mortality of control animals <10%	**Yes**	
Concentration of dissolved oxygen in all test vessels > 60% saturation	**Yes**	
Concentration of test substance ≥80% of initial concentration during test	**Yes**	

Criteria for poorly soluble test substances	**Yes**	

Section A7.4.1.1	**Acute toxicity to fish**
BPD Annex Point IIA, VII.7.1	7.4.1.1 Acute fish (metabolite of BAS 307 I)

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**8) XXXX** Reg.No. 102719 (metabolite of BAS 307 I) - Acute toxicity study on the rainbow trout (Oncorhynchus mykiss) in a static system over 96 hours XXXX. unpublished XXXX	
1.2.	**Data protection**	Yes	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I.	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	EPA 72-1, EEC 92/69 A V C 1, OECD 203, EPA-SEP 540/9-85-006	
2.2.	**GLP**	Yes (laboratory certified by Landesanstalt fuer Pflanzenbau und Pflanzenschutz Rheinland-Pfalz, Mainz)	
2.3.	**Deviations**	No	
		3. MATERIALS AND METHODS	
3.1.	**Test material**		X
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	See chemical glossary	
3.1.3.	Purity	100%	
3.1.4.	Composition of Product	Not applicable	
3.1.5.	Further relevant properties	None	
3.1.6.	Method of	HPLC-UV detection	

Section A7.4.1.1	**Acute toxicity to fish**
BPD Annex Point IIA, VII.7.1	7.4.1.1 Acute fish (metabolite of BAS 307 I)

	analysis	
3.2.	**Preparation of TS solution for poorly soluble or volatile test substances**	None
3.3.	**Reference substance**	No
3.3.1.	Method of analysis for reference substance	Not applicable
3.4.	**Testing procedure**	
3.4.1.	Dilution water	Control, 100 mg/L (nominal).
3.4.2.	Test organisms	Rainbow trout (Oncorhynchus mykiss WALBAUM 1792), 4 months old, body length 5.6 (5.0 - 6.1) cm, body weight 1.48 (1.02 - 1.79) g; source: Forellenzucht Trostadt GbR, Germany
3.4.3.	Test system	Static system (96 h); 10 fish per treatment (1 replicate) (loading 0.5 g fish/L).
3.4.4.	Test conditions	Temperature: 12 °C - 13 °C, pH 8.1 - 8.4, oxygen content: 7.4 mg/L - 10.2 mg/L, total hardness 2.5 mmol/L, photoperiod: 16 hours light : 8 hours dark, light intensity: 82 lux - 280 lux
3.4.5.	Duration of the test	96 h
3.4.6.	Test parameter	$LC_{50,}$ sublethal effects
3.4.7.	Sampling	At test initiation and termination
3.4.8.	Monitoring of TS concentration	No, see 3.4.6.
3.4.9.	Statistics	Descriptive statistics

4. RESULTS

Limit Test		Not Performed
4.1.1.	Concentration	Not applicable
4.1.2.	Number/ percentage of	Not applicable

Section A7.4.1.1	**Acute toxicity to fish**
BPD Annex Point IIA, VII.7.1	7.4.1.1 Acute fish (metabolite of BAS 307 I)

	animals showing adverse effects	
4.1.3.	Nature of adverse effects	Not applicable
Results test substance		
4.1.4.	Initial concentrations of test substance	Analytical measurements: At test initiation, the analytical results of the test item were in a range of 97.4% - 100.3%, at test termination the analytical results were 94.6% - 98.4% of the nominal concentrations. The results are based on the nominal concentrations
4.1.5.	Actual concentrations of test substance	**See 4.1.4.**
4.1.6.	Effect data (Mortality)	See Table 7.4.1.1/113.
4.1.7.	Concentration / response curve	See Table 7.4.1.1/113.
4.1.8.	Other effects	See 5.2
Results of controls		
4.1.9.	Number/ percentage of animals showing adverse effects	See Table 7.4.1.1/113.
4.1.10.	Nature of adverse effects	See Table 7.4.1.1/113.
Test with reference substance		Not performed

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1.	**Materials and methods**	Fish was exposed for 96-h to a test substance as describe under 3.1. The test procedure is detailed under 3.4.
5.2.	**Results and discussion**	Biological results: Reg. No. 102719 caused no mortality in any test item concentration. Based on the nominal concentrations a LC_{50} of > 100 mg/L was observed, based on the analytically detected concentrations the LC_{50} was > 97.4 mg/L. Toxic signs were not observed. The NOEC was determined to be 100 mg/L based on nominal concentrations and 97.4 mg/L based on

Section A7.4.1.1	**Acute toxicity to fish**
BPD Annex Point IIA, VII.7.1	7.4.1.1 Acute fish (metabolite of BAS 307 I)

		analytically detected concentrations. The results are summarized in Table 7.4.1.1/113.	
5.2.1.	LC_0	Not reported	
5.2.2.	LC_{50}	> 100 mg a.s./L	
5.2.3.	LC_{100}	Not reported	
5.3.	**Conclusion**	Reg. No. 102719 was tested in a static acute toxicity study on the rainbow trout. The LC_{50} was > 100 mg/L, the NOEC was 100 mg/L (based on nominal concentrations)	
5.3.1.	Other Conclusions	None	
5.3.2.	Reliability	1	X
5.3.3.	Deficiencies	No	

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	03/17/2005
Materials and Methods	Applicant's summary is acceptable. 3.1 Test material: Reg. No. 102 719 (2,6-Difluorobenzamide)
Results and discussion	Applicant's summary is acceptable.
Conclusion	Applicant's version is acceptable.
Reliability	Reliability index is 2.
Acceptability	Acceptable.
Remarks	Only one replicate tested.

Section A7.4.1.1	**Acute toxicity to fish**
BPD Annex Point IIA, VII.7.1	7.4.1.1 Acute fish (metabolite of BAS 307 I)

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.4.1.1/113 Acute toxicity (96 h) of Reg. No. 102719 on rainbow trout (*Oncorhynchus mykiss)*

Concentration [mg/L nominal]	**Control 1**	**Control 2**	**100**	**100**	**100**
Mortality [%]	0	0	0	0	0
Symptoms	none	none	none	none	none
Endpoints [µg/L nominal]					
LC_{50}	> 100				
NOEC	100				

Table 7.4.1.1.1/114 Validity criteria for acute fish test according to OECD Guideline 203

	Fulfilled	**Not fulfilled**
Mortality of control animals <10%	**Yes**	
Concentration of dissolved oxygen in all test vessels > 60% saturation	**Yes**	
Concentration of test substance ≥80% of initial concentration during test	**Yes**	

Criteria for poorly soluble test substances	**Yes**	

Section A7.4.1.2 Acute toxicity to invertebrates

BPD Annex Point IIA, VII.7.2 7.4.1.2 Acute toxicity to *Daphnia magna*

0.0 Justification of the key study

Daphnia magna

The endpoint studied in tests on *Daphnia magna* is immobilization of the organisms. Nine studies are submitted for this endpoint (10 references).

Three of them are dedicated to the active substance **Flufenoxuron** (BAS 307 I) :

- Reference 1 – XXXX (Funk, 2003)
  Reliability Index : 1
- Reference 2 – XXXX (Croucher, 1987)
  Reliability Index : 2
- Reference 3 – XXXX (Shumei, 1987)
  Reliability Index : 3

In the study of Croucher (1987), mean-measured values are available only for 4 concentrations. Other concentrations were recalculated into mean-measured concentrations based on average recovery of the measured groups (73.6%). For this reason, the reliability index of the study is 2.

Shumei (1987) did not measure the concentrations of flufenoxuron during the test. Given that information, reliability index is 3 for this study.

Funk (2003) realised a static acute test on *Daphnia magna*, were measured concentrations are representative of nominal values. No deviation is observed to OECD 202 Guideline. The reported CE_{50} is 42,9 ng/L.

Six other studies were conducted with **Flufenoxuron metabolites**

- Reference 5 – XXXX (Girling, 1987) & 6 (Ede, 1988) :
  4. 4-Amino-3-fluorophenol
  5. Reliability Index : 1
- Reference 7 – XXXX (Girling, 1988) :
  - Reg. 4064703 = 4-[2-chloro-4-(trifluoromethyl)phenoxy]-2-fluroaniline hydrochloride
  - Reliability Index : 2
- Reference 8 – XXXX (Jatzek, 2003) :
  - Reg. 4064702 = N-[4-[2-chloro-4-(trifluoromethhyl) phenoxy]-2-fluoro phenyl urea
  - **Reliability Index : 1**
- Reference 9 – XXXX (Jatzek, 2003) :
  - Reg. 102719 = 2,6-fluorobenzamide

Section A7.4.1.2	**Acute toxicity to invertebrates**
BPD Annex Point IIA, VII.7.2	7.4.1.2 Acute toxicity to *Daphnia magna*

- **Reliability Index : 1**

- Reference 10 – XXXX (Jatzek, 2003) :
  - Reg. 241208 = 4-[2-chloro-4-(trifluoromethyl)phenoxy]-2-flurobenzenamine
  - **Reliability Index : 1**
- Reference 11 – XXXX (Jatzek, 2003) :
  - Reg. 206925 = 2,6-difluorobenzoic acid
  - **Reliability Index : 1**

Other crustaceans

Reference 4 – FXXXXX (Pearson & Girling, 1989) is dedicated to the effect of Flufenoxuron on the mortality of four other aquatic invertebrates : *Gammarus pulex*, *Lymnaea stagnalis*, *Tubifex tubifex* and *Chironomus lugubris*. Only one concentration was tested in this study. Reliability Index is 3.

The notifier did not propose a key study for immobilization endpoint for *Daphnia magna*.

For reasons cited above, RMS proposes to retain as key studies for the immobilization of *Daphnia magna* :

- for Flufenoxuron :
  - Ref. 1– XXXX (Funk, 2003) : EC_{50} = 42.9 ng/L
- For metabolite 4-amino-3-fluorophenol :
  - Ref. 5-6 – XXXX (Girling, 1987) : EC_{50} = 3.361 mg/L
- For metabolite Reg. 4064703 :
  - Ref. 7– XXXX (Girling, 1988) : EC_{50} = 5.45 µg/L
- for the four other metabolites, bioassays reported by Jatzek (2003) :
  - Reg. 4064702 – Ref.8 – XXXX : EC_{50} = 1.03 mg/L
  - Reg. 102719 – Ref.9 – XXXX : EC_{50} >100 mg/L
  - Reg. 241208 – Ref.10 – XXXX : EC_{50} = 0.654 mg/L
  - Reg. 206925 – Ref.11 – XXXX : EC_{50} >100 mg/L

Section A7.4.1.2 Acute toxicity to invertebrates

BPD Annex Point IIA, VII.7.2 7.4.1.2 Acute toxicity to Daphnia magna

Official use only

1. REFERENCE

1.1.	**Reference**	**1) Funk M. 2003** Effect of radiolabelled Flufenoxuron on the immobility of Daphnia magna STRAUS in a 48 hours static, acute toxicity test XXXX. unpublished XXXX
1.2.	**Data protection**	Yes
1.2.1.	Data owner	BASF
1.2.2.	Companies with letter of access	XXXX
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I.

2. GUIDELINES AND QUALITY ASSURANCE

2.1.	**Guideline study**	OECD 202; EEC Directive 79/831 Annex V, Part C 2; EPA 72-2; OPPTS 850.1010 (draft April 1996)
2.2.	**GLP**	Yes (laboratory certified by Landesamt fuer Umweltschutz und Gewerbeaufsicht, Mainz, Germany)
2.3.	**Deviations**	No

3. MATERIALS AND METHODS

3.1.	**Test material**	^{14}C-Flufenoxuron
3.1.1.	Lot/Batch number	XXXX
3.1.2.	Specification	See below
3.1.3.	Purity	Purity: > 99%; specific activity: 7.61 mBq/mg
3.1.4.	Composition of Product	Not relevant
3.1.5.	Further relevant properties	None
3.1.6.	Method of	LSC

Section A7.4.1.2	**Acute toxicity to invertebrates**
BPD Annex Point IIA, VII.7.2	7.4.1.2 Acute toxicity to Daphnia magna

	analysis	
3.2.	**Preparation of TS solution for poorly soluble or volatile test substances**	None
3.3.	**Reference substance**	None
3.3.1.	Method of analysis for reference substance	Not applicable
3.4.	**Testing procedure**	
3.4.1.	Dilution water	Control, solvent control, 10, 18, 32, 56, 100 and 180 ng a.s./L (nominal)
3.4.2.	Test organisms	Water flea (*Daphnia magna* STRAUS), neonates collected from inhouse culture, with age at test initiation less than 24 hours
3.4.3.	Test system	Static test (48 hours), 6 test concentrations plus control and solvent (control, 4 replicates with 5 daphnids in each; assessment of immobility (and other effects) after 24 and 48 hours
3.4.4.	Test conditions	Spring water, pH 7.81 - 8.09, oxygen content: 8.08 mg/L - 8.89 mg/L, no feeding, temperature: 20.1 °C - 20.5 °C, under darkness
3.4.5.	Duration of the test	48 hours
3.4.6.	Test parameter	EC_{50}, based on immobility of daphnids.
3.4.7.	Sampling	Study initiation and termination
3.4.8.	Monitoring of TS concentration	See 3.4.7
3.4.9.	Statistics	Descriptive statistics, probit analysis for determination of EC_{50}

4. RESULTS

Limit Test		Not performed
4.1.1.	Concentration	Not applicable
4.1.2.	Number/ percentage of animals showing	Not applicable

Section A7.4.1.2	**Acute toxicity to invertebrates**
BPD Annex Point IIA, VII.7.2	7.4.1.2 Acute toxicity to Daphnia magna

	adverse effects	
4.1.3.	Nature of adverse effects	Not applicable
Results test substance		
4.1.4.	Initial concentrations of test substance	The analytically detected concentrations for Flufenoxuron ranged from 105.7% to % 148.4% (except for the lowest concentration: 95.9% - 296.3%) of nominal values at the beginning of the test. At study termination, the results were in a range of 104.3% to 138.9%. Therefore, the results are based on the nominal concentrations.
4.1.5.	Actual concentrations of test substance	See 4.1.4
4.1.6.	Effect data (Immobilisation)	See Table **7.4.1.2/115**
4.1.7.	Concentration / response curve	See Table **7.4.1.2/115**
4.1.8.	Other effects	See none
Results of controls		See Table **7.4.1.2/115**.
Test with reference substance		Not applicable
4.1.9.	Concentrations	See Table **7.4.1.2/115**.
4.1.10.	Results	See Table **7.4.1.2/115**.

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1.	**Materials and methods**	*Daphnia magna* was exposed for 48-h to a test substance as describe under 3.1. The test procedure is detailed under 3.4.
5.2.	**Results and discussion**	Biological results: Flufenoxuron had no effects on *Daphnia magna* immobility at 10 ng a.s./L (48 h). At study termination, immobility in the 18, 32, 56, 100 and 180 ng/L treatment groups was 15%, 40%, 65% 85% and 95%, respectively. The NOEC was determined to be 10 ng a.s./L. The results are summarized in Table 7.4.1.2/115.
5.2.1.	EC_0	Not determined

Section A7.4.1.2	**Acute toxicity to invertebrates**
BPD Annex Point IIA, VII.7.2	7.4.1.2 Acute toxicity to Daphnia magna

5.2.2.	EC_{50}	42.9 ng a.s./L
5.2.3.	EC_{100}	Not determined
5.3.	**Conclusion**	In a 48 hours static acute toxicity study with Daphnia magna, the EC_{50} of Flufenoxuron was determined to be 42.9 ng a.s./L. The NOEC was 10 ng a.s./L.
5.3.1.	Reliability	1
5.3.2.	Deficiencies	No

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	02/11/2005
Materials and Methods	Applicant version is acceptable.
Results and discussion	Applicant version is acceptable.
Conclusion	Applicant version is acceptable.
Reliability	Reliability index is 1 (study has retained as key study).
Acceptability	Acceptable.
Remarks	Only remark could be : composition of M4 medium is not identical as recommended in OCDE Guideline (OCDE 202).

Section A7.4.1.2 Acute toxicity to invertebrates

BPD Annex Point IIA, VII.7.2 7.4.1.2 Acute toxicity to Daphnia magna

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.4.1.2/115 Effect (48 h) of Flufenoxuron on *Daphnia magna* immobility

Concentration (nominal) [ng a.s./L]	**Control**	**Solvent control**	**10**	**18**	**32**	**56**	**100**	**180**
Immobile (24 h) [%]	0	0	0	0	0	5	15	25
Immobile (48 h) [%]	0	0	0	15	40	65	85	95
	Endpoints [ng a.s./L]							
EC_{50} (48 h)	42.9							
NOEC (48 h)	10							

Table 7.4.1.2/116 Validity criteria for acute daphnia immobilisation test according to OECD `Guideline 202

	Fulfilled	**Not fulfilled**
Immobilisation of control animals <10%	**Yes**	
Control animals not staying at the surface	**Yes**	
Concentration of dissolved oxygen in all test vessels >3 mg/l	**Yes**	
Concentration of test substance ≥80% of initial concentration during test	**Yes**	

Criteria for poorly soluble test substances	**Yes**	

Section A7.4.1.2 Acute toxicity to invertebrates

BPD Annex Point IIA, VII.7.2 7.4.1.2 Acute toxicity to Daphnia magna

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**2) Croucher E. 1987** WL115110: Acute toxicity to Salmo gairdneri, Daphnia magna and Selenastrum capricornutum XXXX unpublished XXXX)	
1.2.	**Data protection**	No	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	No data protection claimed	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Not reported, method description given in the report	
2.2.	**GLP**	No, at the time the study was conducted GLP was not compulsory. However the study was conducted according to the principle of Good Laboratory Practices	
2.3.	**Deviations**	Not applicable	
		3. MATERIALS AND METHODS	
3.1.	**Test material**		X
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	As given in section 2	
3.1.3.	Purity	96.6% (1986), 93.6% (1987)	
3.1.4.	Composition of Product	Not applicable	
3.1.5.	Further relevant properties	Water solubility (IIIA 3.5): pH 7: 136 µg/l pH 4: 186 µg/l pH 9: 369 µg/l	X
3.1.6.	Method of analysis	HPLC-UV detection	
3.2.	**Preparation of TS solution for**	None	

	poorly soluble or volatile test substances	
3.3.	**Reference substance**	No
3.3.1.	Method of analysis for reference substance	Not applicable
3.4.	**Testing procedure**	
3.4.1.	Dilution water	Test 1: control, 0.026, 0.05, 0.1, 0.26, 0.5, 1.0 and 2.6 µg a.s./L (nominal). Test 2: control, 0.00475, 0.01, 0.02, 0.0475, 0.1, 0.2, 0.475, 1.0, 2.0 and 4.75 µg a.s./L (nominal).
3.4.2.	Test organisms	Water flea (*Daphnia magna* STRAUS), neonates with age at test initiation less than 24 hours, source: Institut National de Recherche Chimique Applique, France
3.4.3.	Test system	Static test (48 hours). Test 1: 7 concentrations plus control, 3 replicates with 10 daphnids in each; assessment of immobility after 24 and 48 hours. Test 2: 10 concentrations plus control, 3 replicates with 10 daphnids in each; assessment of immobility after 24 and 48 hours
3.4.4.	Test conditions	**Reconstituted fresh water,** **Test 1: pH 7.9 - 8.1, oxygen content: 9.0 mg/L - 9.4 mg/L, temperature: 18 C - 22 °C** **Test 2: pH 8.0 - 8.1, oxygen content: 9.0 mg/L - 9.2 mg/L, temperature: 18 C - 22 °C;** no feeding, photoperiod: 16 hours light : 8 hours dark
3.4.5.	Duration of the test	48 h
3.4.6.	Test parameter	EC_{50}, based on immobility of daphnids.
3.4.7.	Sampling	See 4.1.4
3.4.8.	Monitoring of TS concentration	See 4.1.4
3.4.9.	Statistics	Descriptive statistics. Log-loganalysis for determination of EC_{50}(siehe auch XXXX) .

4. RESULTS

Limit Test		Not performed
4.1.1.	Concentration	Not applicable
4.1.2.	Number/	Not applicable

	percentage of animals showing adverse effects		
4.1.3.	Nature of adverse effects	Not applicable	
Results test substance			
4.1.4.	Initial concentrations of test substance	The analyzed concentrations for the test item in the first test ranged from 83% to 88% of nominal values at the beginning of the test. After 48 h of exposure, the results were in a range of 29% to 96% of nominal values. The analyzed concentrations for the test item in the second test ranged from 65% to 109% of nominal values at the beginning of the test. After 48 h of exposure, the results were in a range of 31% to 95% of nominal values. Therefore the results are based on the nominal concentrations.	X
4.1.5.	Actual concentrations of test substance	See 4.1.4	
4.1.6.	Effect data (Mortality)	See Table 7.4.1.2/117	
4.1.7.	Concentration / response curve	See Table 7.4.1.2/117	
4.1.8.	Other effects	Describe any other observations differentiating organisms in tests and controls (e.g. loss of equilibrium, erratic swimming, hyperventilation, lethargy, changes in appearance)	
Results of controls			
4.1.9.	Number/ percentage of animals showing adverse effects	See Table 7.4.1.2/117	
4.1.10.	Nature of adverse effects	See Table 7.4.1.2/117	
Test with reference substance		Not performed	

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1.	**Materials and methods**	Daphnia magna was exposed for 48-h to a test substance as described under 3.1. The test procedure is detailed under 3.4.
5.2.	**Results and**	Biological results: Test 1: Flufenoxuron caused Daphnia immobility all test concentrations at study termination (48 h). Immobility in the 0.026,

	discussion	0.05, 0.1, 0.26, 0.5, 1.0 and 2.6 µg a.s./L treatment groups was 27%, 57%, 80%, 97%, 100%, 100% and 100%, respectively. Test 2: Flufenoxuron had no effects on Daphnia immobility up to a test concentration of 0.01 µg a.s./L. After 48 hours of exposure, immobility in the 0.02, 0.0475, 0.1, 0.2, 0.475, 1.0, 2.0 and 4.75 µg a.s./L treatment groups was 7%, 23%, 47%, 77%, 100%, 100%, 100% and 100%, respectively. The results are summarized in Table 7.4.1.2/117.	
5.2.1.	LC_0	Not reported	
5.2.2.	LC_{50}	0.083 µg a.s./L (mean measured)	
5.2.3.	LC_{100}	Not reported	
5.3.	**Conclusion**	In the first 48 hours static acute toxicity study with *Daphnia magna* the EC_{50} of Flufenoxuron was determined to be 0.04 µg a.s./L, in the second test, the EC_{50} was 0.083 µg a.s./L based on mean measured concentrations (siehe auch XXXX).	
5.3.1.	Other Conclusions	None	
5.3.2.	Reliability	1	X
5.3.3.	Deficiencies	No	X

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	02/09/2005
Materials and Methods	Applicant version is acceptable with the following amendments : 3.1 Test material : Flufenoxuron 3.1.5 : PH 7 : 1.36 µg/L pH 4 : 1.86 µg/L pH 9 : 3.69 µg/L
Results and discussion	Applicant's summary is acceptable with the following amendments : 4.14 Initial concentrations of test substance : *Therefore the results are based on the ~~nominal~~* **mean-measured** *concentrations.* **The calculations are presented in XXXX (Annex 2 of IIIA 7.6)**
Conclusion	Agree with the applicant.

Reliability	Reliability index : 2. Deficiencies : yes Mean-measured values are available only for 4 concentrations. Other concentrations were recalculated into mean-measured concentrations based on average recovery of the measured groups (73.6%). The highest treatment group was excluded from statistical analysis, since Toxstat can handle maximal 10 treatment groups. Detailed calculation is provided in XXXX.
Acceptability	See above.
Remarks	Additional data are added in Table 7.4.1.2/3 and 4 in bold and underlined.

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.4.1.2/117 Effect (48 h) of Flufenoxuron on *Daphnia magna* immobility

Test 1								
Nominal Concentration [µg a.s./L]	**Control**	**0.026**	**0.05**	**0.1**	**0.26**	**0.5**	**1.0**	**2.6**
Immobile (24 h) [%]	0	0	0	7	30	23	50	67
Immobile (48 h) [%]	0	27	57	80	97	100	100	100
Endpoints [µg a.s./L nominal]								
EC_{50} (48 h)	0.04 (95% limits: 0.03 - 0.06)							

Test 2											
Nominal Concentration [µg a.s./L]	**Control**	**0.00475**	**0.01**	**0.02**	**0.0475**	**0.1**	**0.2**	**0.475**	**1.0**	**2.0**	**4.75**
Mean-measured Concentration [µg a.s./L]	**Control**	**0.0042**	**0.007**	**0.015**	**0.037**	**0.074**	**0.147**	**0.38**	**0.74**	**1.47**	**-**
Immobile (24 h) [%]	0	0	0	0	0	0	0	0	0	30	87
Immobile (48 h) [%]	0	0	0	7	23	47	77	100	100	100	100
	Endpoints [µg a.s./L mean-measured concentration]										
EC_{50} (48 h)	0.083 (95% limits: 0.068 - 0.102)										

Table 7.4.1.2/118 Validity criteria for acute daphnia immobilisation test according to OECD Guideline 202

	Fulfilled	**Not fulfilled**
Immobilisation of control animals <10%	**Yes**	
Control animals not staying at the surface	**Yes**	
Concentration of dissolved oxygen in all test vessels >3 mg/l	**Yes**	
Concentration of test substance ≥80% of initial concentration during test	~~**Yes**~~	**Results in test 2 are based on mean-measured concentrations**

Criteria for poorly soluble test substances ergänzen	**Yes**	

Section A7.4.1.2 Acute toxicity to invertebrates

BPD Annex Point IIA, II.7.2 7.4.1.2 Acute toxicity to Daphnia magna

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**3) Shumei W. 1987** Acute toxicity of SKI-8503 on Daphnia carinata XXXX unpublished XXXX)	
1.2.	**Data protection**	No	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	No data protection claimed	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	EPA-540/9-82-024	
2.2.	**GLP**	No, at the time the study was conducted GLP was not compulsory. However the study was conducted according to the principle of Good Laboratory Practices	
2.3.	**Deviations**	No	X
		3. MATERIALS AND METHODS	
3.1.	**Test material**		X
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	As given in section 2	
3.1.3.	Purity	98%	
3.1.4.	Composition of Product	Not applicable	
3.1.5.	Further relevant properties	Water solubility (IIIA 3.5): pH 7: 136 µg/l pH 4: 186 µg/l pH 9: 369 µg/l	X
3.1.6.	Method of analysis	No analysis	
3.2.	**Preparation of TS solution for**	None	

Section A7.4.1.2	**Acute toxicity to invertebrates**
BPD Annex Point IIA, II.7.2	7.4.1.2 Acute toxicity to Daphnia magna

	poorly soluble or volatile test substances	
3.3.	**Reference substance**	No
3.3.1.	Method of analysis for reference substance	Not applicable
3.4.	**Testing procedure**	
3.4.1.	Dilution water	Test 1: control, 500, 1000, 2000, 5000 and 10000 µg a.s./L (nominal). Test 2: control, 0.8, 1.0, 1.3, 1.7, 2.2, 3.0 and 5.0 µg a.s./L (nominal).
3.4.2.	Test organisms	Water flea (*Daphnia carinata*), adult females; source: in-house
3.4.3.	Test system	Static test (48 hours). Test 1: 5 concentrations plus control, 1 replicate with 20 daphnids in each; assessment of immobility after 1, 2, 3, 6, 24 and 48 hours. Test 2: 7 concentrations plus control, 1 replicate with 20 daphnids in each; assessment of immobility after 1, 2, 3, 6, 24 and 48 hours.
3.4.4.	Test conditions	pH 8.1 - 8.5, oxygen content: 8.6 mg/L - 9.1 mg/L, no feeding, temperature: 25 °C ± 1 °C, photoperiod: 13 hours light : 11 hours dark
3.4.5.	Duration of the test	48 h
3.4.6.	Test parameter	EC_{50}, based on immobility of daphnids.
3.4.7.	Sampling	Not applicable as no analysis performed
3.4.8.	Monitoring of TS concentration	Not applicable as no analysis performed
3.4.9.	Statistics	Descriptive statistics, Doudoroff method for determination of EC_{50}

4. RESULTS

Limit Test		Not performed
4.1.1.	Concentration	Not applicable
4.1.2.	Number/ percentage of animals showing adverse effects	Not applicable

Section A7.4.1.2	**Acute toxicity to invertebrates**
BPD Annex Point IIA, II.7.2	7.4.1.2 Acute toxicity to Daphnia magna

4.1.3.	Nature of adverse effects	Not applicable
Results test substance		
4.1.4.	Initial concentrations of test substance	Not applicable as no analysis performed
4.1.5.	Actual concentrations of test substance	See 4.1.4
4.1.6.	Effect data (Mortality)	See Table 7.4.1.2/119
4.1.7.	Concentration / response curve	See Table 7.4.1.2/119
4.1.8.	Other effects	None
Results of controls		
4.1.9.	Number/ percentage of animals showing adverse effects	See Table 7.4.1.2/119
4.1.10.	Nature of adverse effects	See Table 7.4.1.2/119

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1. Materials and methods

Daphnia magna was exposed for 48-h to a test substance as describe under 3.1. The test procedure is detailed under 3.4.

5.2. Results and discussion

Test 1: Flufenoxuron caused mortalities in any test item group. After 48 hours of exposure, immobility in the 500, 1000, 2000, 5000 and 10000 µg a.s./L treatment groups was 100%, respectively. The EC_{50} was determined to be < 500 µg a.s./L.

Test 2: Flufenoxuron caused mortalities in any test item group. After 48 hours of exposure, immobility in the 0.8, 1.0, 1.3, 1.7, 2.2, 3.0 and 5.0 µg g a.s./L treatment groups was 30%, 40%, 40%, 70%, 65%, 75% and 75%, respectively. The EC_{50} was determined to be 1.4 µg a.s./L. The results are summarized in Table 7.4.1.2/119.

Section A7.4.1.2	**Acute toxicity to invertebrates**
BPD Annex Point IIA, II.7.2	7.4.1.2 Acute toxicity to Daphnia magna

5.2.1.	LC_0	Not defined in the study	
5.2.2.	LC_{50}	1.4 µg a.s./L	
5.2.3.	LC_{100}	Not applicable	
5.3.	**Conclusion**	In the first 48 hours static acute toxicity study with Daphnia magna the EC_{50} of Flufenoxuron was 1.4 µg a.s./L.	
5.3.1.	Other Conclusions	None	
5.3.2.	Reliability	2	X
5.3.3.	Deficiencies	No	

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	02/11/2005
Materials and Methods	Applicant's summary is acceptable except for the following point : 2.3 Deviations : *Yes* Given that significant concentrations were not measured, the study can not been considered as reliable. 3.1 Test substance : Flufenoxuron 3.1.5 Further relevant properties : correct values are : *pH 7 : 1.36 µg/L* *pH 4 : 1.86 µg/L* *pH 9 : 3.69 µg/L*
Results and discussion	Applicant's summary is acceptable.
Conclusion	Applicant's summary is acceptable.
Reliability	See deviations above. Reliability index : 3.
Acceptability	See above.
Remarks	Errors in Table 7.4.1.2/6 were corrected in bold and underlined.
	COMMENTS FROM ...

Section A7.4.1.2	**Acute toxicity to invertebrates**
BPD Annex Point IIA, II.7.2	7.4.1.2 Acute toxicity to Daphnia magna

Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.4.1.2/119 Effect (48 h) of Flufenoxuron on *Daphnia magna* immobility

Test 1						
Concentration [µg a.s./L]	**Control**	**500**	**1000**	**2000**	**5000**	**10000**
Immobile (24 h) [%]	0	25	25	35	30	40
Immobile (48 h) [%]	0	100	100	100	100	100
	Endpoints [µg a.s./L]					
EC_{50} (48 h)	< 500					

Test 2								
Concentration [µg a.s./L]	**Control**	**0.8**	**1.0**	**1.3**	**1.7**	**2.2**	**3.0**	**5.0**
Immobile (24 h) [%]	0	0	0	0	5	5	15	15
Immobile (48 h) [%]	0	30	40	40	70	65	75	75
	Endpoints [µg a.s./L]							
EC_{50} (48 h)	1.4							

Table 7.4.1.2/120 Validity criteria for acute daphnia immobilistaion test according to OECD Guideline 202

	Fulfilled	**Not fulfilled**
Immobilisation of control animals <10%	**Yes**	
Control animals not staying at the surface	**Yes**	
Concentration of dissolved oxygen in all test vessels >3 mg/l	**Yes**	
Concentration of test substance ≥80% of initial concentration during test	~~**Yes**~~ **No measure**	

Criteria for poorly soluble test substances ergänzen	**Yes**	

Section A7.4.1.2 Acute toxicity to invertebrates

BPD Annex Point IIA, VII.7.2 7.4.1.2 Acute toxicity to Daphnia magna

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**4) Pearson N.,Girling A.E. 1989** Flufenoxuron (WL115110): Acute toxicity to Gammarus pulex, Lymnaea stagnalis, Tubifex tubifex and Chironomus lugubris XXXX unpublished XXXX	
1.2.	**Data protection**	No	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	No data protection claimed	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	EPA 540/9-82-024	
2.2.	**GLP**	Yes (laboratory certified by Department of Health of the Government of the United Kingdom, United Kingdom)	
2.3.	**Deviations**	No	X
		3. MATERIALS AND METHODS	
3.1.	**Test material**	As given in section 2	X
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	As given in section 2	
3.1.3.	Purity	97.4% ± 0.7%	
3.1.4.	Composition of Product	Not applicable	
3.1.5.	Further relevant properties	Water solubility (IIIA 3.5): pH 7: 136 µg/l pH 4: 186 µg/l pH 9: 369 µg/l	X
3.1.6.	Method of analysis	HPLC-UV detection	
3.2.	**Preparation of**	None	

Section A7.4.1.2	**Acute toxicity to invertebrates**
BPD Annex Point IIA, VII.7.2	7.4.1.2 Acute toxicity to Daphnia magna

	TS solution for poorly soluble or volatile test substances	
3.3.	**Reference substance**	No
3.3.1.	Method of analysis for reference substance	Not applicable
3.4.	**Testing procedure**	
3.4.1.	Dilution water	*G. pulex*, *L. stagnalis*: control, 3.8 µg a.s./L,*T. tubifex*: control, 1.0 µg a.s./L, *C. lugubris*: control, 1.1 µg a.s./L (mean of fresh solution concentration).
3.4.2.	Test organisms	Freshwater shrimp (*Gammarus pulex*), collected from stream at Hollingbourne, Kent; size: > 1 mm < 2 mm Great pond snail (*Lymnea stagnalis*), young snails, hatched in-house, age 3 - 10 days. Sludge worm (*Tubifex tubifex*), age: > 3 d; collected from the aquatic supplies department of Eden Park Garden Centre, Tunstall. Midge (*Chironomus lugubris*) larvae (first instars); hatched in-house, stock originally obtained from a laboratory culture of Sittingbourne Research Centre, Kent, UK, cultures maintained in-house.
3.4.3.	Test system	*G. pulex, L. stagnalis, T. tubifex*: semi-static system (96 h) with daily renewal of the test solutions. 10 test animals per vessel; 1 concentration plus control, each with 3 replicates, no feeding. Daily assessments for mortality. *C. lugubris*: semi-static system (48 h) with daily renewal of the test solutions. 10 larvae per vessel; 1 concentration plus control, each with 3 replicates, feeding with fish food. Daily assessments for mortality.
3.4.4.	Test conditions	*G. pulex, L. stagnalis*: temperature: 13.5 °C - 16.5 °C, pH 7.3 - 8.0, oxygen content: 8.4 mg/L - 10.3 mg/L *T. tubifex, C. lugubris*: temperature: 13.5 °C - 16.5 °C, pH 7.2 - 7.7, oxygen content: 9.0 mg/L - 10.2 mg/L
3.4.5.	Duration of the test	See 3.4.3
3.4.6.	Test parameter	EC_{50}.
3.4.7.	Sampling	Not applicable as no analysis performed

Section A7.4.1.2 **Acute toxicity to invertebrates**
BPD Annex Point IIA, VII.7.2 7.4.1.2 Acute toxicity to Daphnia magna

3.4.8.	Monitoring of TS concentration	Not applicable as no analysis performed
3.4.9.	Statistics	Descriptive statistics

4. RESULTS

Limit Test		Not performed
4.1.1.	Concentration	Not applicable
4.1.2.	Number/ percentage of animals showing adverse effects	Not applicable
4.1.3.	Nature of adverse effects	Not applicable
Results test substance		
4.1.4.	Initial concentrations of test substance	The analyzed concentrations for Flufenoxuron ranged from 74% to 158% for *G. pulex* and *L. stagnalis*, 70% - 140% for *T. tubifex* and 64% - 127% for *C. lugubris* of fresh solution concentration (before introducing the test animals). Used test solution showed test item concentrations ranging from 32% - 34% for *G. pulex*, 29% - 47% for *L. stagnalis*, 40% - 100% for *T. tubifex* and 36% - 91% for *C. lugubris*. Losses of the test item solutions during the 24 h periods between renewals were due to falling out and adsorbing to the glassware. Therefore the results are based on the measured concentrations
4.1.5.	Actual concentrations of test substance	See 4.1.4
4.1.6.	Effect data (Mortality)	See Table 7.4.1.2/121
4.1.7.	Concentration / response curve	See Table 7.4.1.2/121
4.1.8.	Other effects	None
Results of controls		
4.1.9.	Number/ percentage of animals showing adverse effects	See Table 7.4.1.2/121
4.1.10.	Nature of adverse	See Table 7.4.1.2/121

Section A7.4.1.2	**Acute toxicity to invertebrates**
BPD Annex Point IIA, VII.7.2	7.4.1.2 Acute toxicity to Daphnia magna

	effects		
Test with reference substance		Not performed	
		5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1.	**Materials and methods**	Aquatic invertebrates were exposed to a test substance as described under 3.1. The test procedure is detailed under 3.4.	
5.2.	**Results and discussion**	Biological results: Flufenoxuron caused no significant mortality on *G. pulex, L. stagnalis, T. tubifex* and *C. lugubris*. Mortalities of *L. stagnalis* and *T. tubifex* were observed only in the control groups ≤ 10%. Mortality of *C. lugubris* was detected in the control and test item groups, but was less than 10%. The results are summarized in Table 7.4.1.2/121.	
5.2.1.	LC_0	Not defined in the study	
5.2.2.	LC_{50}	See Table 7.4.1.2/121.	
5.2.3.	LC_{100}	Not applicable	
5.3.	**Conclusion**	The EC_{50} for *G. pulex, L. stagnalis, T. tubifex* and *C. lugubris* were determined to be > 1.2, > 1.2, > 0.4 and > 0.6 µ a.s./L (minimum concentration measured).	X
5.3.1.	Other Conclusions	None	
5.3.2.	Reliability	1	X
5.3.3.	Deficiencies	No	

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	09/05/2010

Section A7.4.1.2	**Acute toxicity to invertebrates**
BPD Annex Point IIA, VII.7.2	7.4.1.2 Acute toxicity to Daphnia magna

Materials and Methods	Applicant's summary is acceptable except for the following point : 2.3 Deviations : *Yes* Only one concentration was tested per test per organism. Moreover, no mortality was observed for *Gammarus pulex* test, not enough mortality was observed for *Chironomus lugubris* and significant mortality was observed in controls for *Tubifex tubifex* and *Lymnea stagnalis* tests. Hence, no lethal concentrations could be derived and they are expressed in terms of "superior to". Given that remarks, the results of this study can not be considered as reliable. 3.1 Test substance : Flufenoxuron 3.1.5 Further relevant properties: correct values are : *pH 7 : 1.36 µg/L* *pH 4 : 1.86 µg/L* *pH 9 : 3.69 µg/L*
Results and discussion	Applicant's summary is acceptable.
Conclusion	Applicant's summary is acceptable with following correction: 5.3 Conclusion : *The EC_{50} for* G. pulex, L. stagnalis, T. tubifex *and* C. lugubris *were determined to be > 1.2, > 1.2, > 0.4 and > 0.6* **µg** *a.s./L (minimum concentration measured).*
Reliability	See deviations above. Reliability index : 2 (stated at the technical meeting II-09) .
Acceptability	See above.
Remarks	Errors in Table 7.4.1.2/8 were corrected in bold and underlined.

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.4.1.2/121 Effects (96 h) of Flufenoxuron on *G. pulex, L. stagnalis, T. tubifex* and *C. lugubris*

Test species	Test item (nominal) [µg a.s./L]	Mean % mortality at test termination	
		Control	Test item
Gammarus pulex (96 h)	3.8	0	0
Lymnea stagnalis (96 h)	3.8	7	0
Tubifex tubifex (96 h)	1.0	10	0
Chironomus lugubris (48 h)	1.1	7	3
	Endpoint EC_{50} [µg a.s./L measured] 1)		
Gammarus pulex (96 h)	> 1.2		
Lymnea stagnalis (96 h)	> 1.2		
Tubifex tubifex (96 h)	> 0.4		
Chironomus lugubris (48 h)	> 0.6		

1) minimum concentration of Flufenoxuron measured in the test vessels

Table 7.4.1.2/122 Validity criteria for acute daphnia immobilisation test according to OECD Guideline 202

	Fulfilled	Not fulfilled
Immobilisation of control animals <10%	**Yes**	
Control animals not staying at the surface	**Yes**	
Concentration of dissolved oxygen in all test vessels >3 mg/l	**Yes**	
Concentration of test substance ≥80% of initial concentration during test	~~**Yes**~~	**Results are based on the mean-measured concentrations**

Criteria for poorly soluble test substances ergänzen	**Yes**	

Section A7.4.1.2 Acute toxicity to invertebrates

BPD Annex Point IIA, VII.7.2 7.4.1.2 Acute toxicity to Daphnia magna (Impurity Reg. No. 406703)

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**5) XXXX** 4-Amino-3-Fluorophenol: Acute toxicity to Daphnia magna and Salmo gairdneri XXXX unpublihed XXXX) **6) XXXX** 4-Amino-3-Fluorophenol : Acute toxicity to Daphnia magna and Salmo gairdneri XXXX unpublished XXXX	
1.2.	**Data protection**	No	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	No data protection claimed	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Official Journal of the European Communities No. L251 Part C: Methods for the determination of Ecotoxicity. C2 Acute toxicity for Daphnia	
2.2.	**GLP**	Yes (laboratory certified by Department of Health of the Government of the United Kingdom, United Kingdom)	
2.3.	**Deviations**	No	
		3. MATERIALS AND METHODS	
3.1.	**Test material**		X
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	As given in section 2	
3.1.3.	Purity	86% ± 2%.	

Section A7.4.1.2 Acute toxicity to invertebrates

BPD Annex Point IIA, VII.7.2 7.4.1.2 Acute toxicity to Daphnia magna (Impurity Reg. No. 406703)

3.1.4.	Composition of Product	Not applicable
3.1.5.	Further relevant properties	None
3.1.6.	Method of analysis	HPLC-UV detection
3.2.	**Preparation of TS solution for poorly soluble or volatile test substances**	None
3.3.	**Reference substance**	No
3.3.1.	Method of analysis for reference substance	Not applicable
3.4.	**Testing procedure**	
3.4.1.	Dilution water	Control, 600, 1000, 2000, 3000, 6000, 11000 and 20000 µg a.s./L (nominal).
3.4.2.	Test organisms	Water flea (*Daphnia magna* STRAUS), neonates with age at test initiation less than 24 hours, neonates from in-house culture, stock obtained from Institut National de Recherche Chimique Appliquée, France
3.4.3.	Test system	Static test (48 hours), test item was tested as freshly prepared and aged (48 h) solution; 7 test concentrations plus control, 2 replicates with 10 daphnids in each; assessment of immobility after 24 and 48 hours.
3.4.4.	Test conditions	Reconstituted fresh water, pH 7.7 - 8.1, oxygen content: 8.6 mg/L - 9.2 mg/L, no feeding, temperature: 20.6 °C - 21.4 °C, photoperiod: 16 hours light: 8 hours dark
3.4.5.	Duration of the test	48-h
3.4.6.	Test parameter	EC_{50}, based on immobility of daphnids
3.4.7.	Sampling	Test initiation and termination
3.4.8.	Monitoring of TS concentration	See 3.4.7

Section A7.4.1.2	**Acute toxicity to invertebrates**
BPD Annex Point IIA, VII.7.2	7.4.1.2 Acute toxicity to Daphnia magna (Impurity Reg. No. 406703)

3.4.9.	Statistics	Descriptive statistics, probit analysis for determination of EC_{50} (see also XXXX) .	
		4. RESULTS	
Limit Test		Not performed	
4.1.1.	Concentration	Not applicable	
4.1.2.	Number/ percentage of animals showing adverse effects	Not applicable	
4.1.3.	Nature of adverse effects	Not applicable	
Results test substance			
4.1.4.	Initial concentrations of test substance	The analyzed concentrations for freshly prepared solutions of 4-Amino-3-Fluorophenol ranged from 98% - 118% of nominal values at the beginning of the test and from < 0.3% to 0.7% at the end of the test. Analyzed concentrations for aged solutions ranged from < 0.3% to 0.7% at the start of the test and from < 0.2% - < 1.7% at end of the test. Therefore the results are based on the nominal concentrations	X
4.1.5.	Actual concentrations of test substance	See 4.1.4	
4.1.6.	Effect data (Mortality)	See Table 7.4.1.2/123	
4.1.7.	Concentration / response curve	See Table 7.4.1.2/123	
4.1.8.	Other effects	None	
Results of controls			
4.1.9.	Number/ percentage of animals showing adverse effects	See Table 7.4.1.2/123	
4.1.10.	Nature of adverse effects	See Table 7.4.1.2/123	
Test with reference		Not performed	

Section A7.4.1.2	**Acute toxicity to invertebrates**
BPD Annex Point IIA, VII.7.2	7.4.1.2 Acute toxicity to Daphnia magna (Impurity Reg. No. 406703)

substance

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1.	**Materials and methods**	*Daphnia magna* was exposed for 48-h to a test substance as described under 3.1. The test procedure is detailed under 3.4.
5.2.	**Results and discussion**	Biological results: Freshly prepared solutions of 4-Amino-3-Fluorophenol had no effects on Daphnia immobility up to a test item concentration of 2000 µg/L. After 48 hours of exposure, immobility in the 3000, 6000, 11000 and 20000 µg a.s./L treatment groups was 15%, 40%, 85% and 100%, respectively. Aged solutions of 4-Amino-3-Fluorophenol had no effects on Daphnia immobility up to a test item concentration of 3000 µg a.s./L. After 48 hours of exposure, immobility in the 6000, 11000 and 20000 µg a.s./L treatment groups was 15%, 60% and 95%, respectively. The results are summarized in Table 7.4.1.2/123.
5.2.1.	LC_0	Not defined in the study
5.2.2.	LC_{50}	3361 µg a.s./L (mean measured)
5.2.3.	LC_{100}	Not applicable
5.3.	**Conclusion**	In a 48 hours static acute toxicity study with *Daphnia magna* the EC_{50} of 4-Amino-3-Fluorophenol was determined to be 3361 µg a.s./L based on mean measured concentrations (see also XXXX) in freshly prepared solutions and 9700 µg a.s./L based on aged solutions of 4-Amino-3-Fluorophenol.
5.3.1.	Other Conclusions	None
5.3.2.	Reliability	1
5.3.3.	Deficiencies	No

Evaluation by Competent Authorities
Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
EVALUATION BY RAPPORTEUR MEMBER STATE

Section A7.4.1.2	**Acute toxicity to invertebrates**
BPD Annex Point IIA, VII.7.2	7.4.1.2 Acute toxicity to Daphnia magna (Impurity Reg. No. 406703)

Date	02/11/2005 and 03/11/2010
Materials and Methods	Applicant's summary is acceptable with the following amendment : 3.1 Test substance : 4-amino-3-fluorophenol (Reg. No. 4108386)
Results and discussion	Applicant's summary is acceptable. 4.1.4 Initial concentrations of test substance : *Therefore the results are based on the ~~nominal~~* **mean-measured** *concentrations.* **Calculations are provided in XXXX (Annex 2 of IIIA 7.6).**
Conclusion	Applicant's summary is acceptable NOEC : 1060 µg/L (measured concentration).
Reliability	Reliability index : 1.
Acceptability	Acceptable.
Remarks	Corrections in Tables 7.4.1.2/9 and 10 are added in bold and underlined.

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.4.1.2/123 Effect (48 h) of 4-Amino-3-Fluorophenol on *Daphnia magna* immobility

Concentration (nominal) [µg a.s./L]	**Control**	**600**	**1000**	**2000**	**3000**	**6000**	**11000**	**20000**
Concentration (mean-measured) [µg a.s./L]	**Control**	**310**	**490**	**1060**	**1500**	**3110**	**6520**	**11570**
Immobile (24 h) [%] [1)]	0	0	0	0	0	5	50	100
Immobile (48 h) [%] [1)]	0	0	0	0	15	40	85	100
Immobile (24 h) [%] [2)]	0	0	0	0	0	0	30	65
Immobile (48 h) [%] [2)]	0	0	0	0	0	15	60	95
	Endpoints [µg a.s./L]							
EC_{50} (48 h) [1)]	3361 (95% limits: 2742 - 4121)							
EC_{50} (48 h) [2)]	9700 (95% limits: 8100 - 12000)							

1) Based on mean measured concentrations. Daphnids exposed to freshly prepared test item solutions, immobile and dead daphnids, mean of two replicates

2) Daphnids exposed to test item solutions aged for 48 h, immobile and dead daphnids, mean of two replicates

Table 7.4.1.2/124 Validity criteria for acute daphnia immobilisation test according to OECD Guideline 202

	Fulfilled	**Not fulfilled**
Immobilisation of control animals <10%	**Yes**	
Control animals not staying at the surface	**Yes**	
Concentration of dissolved oxygen in all test vessels >3 mg/l	**Yes**	
Concentration of test substance ≥80% of initial concentration during test	~~**Yes**~~	**Results are based on mean-measured concentrations**

Criteria for poorly soluble test substances ergänzen	**Yes**	

Section A7.4.1.2 Acute toxicity to invertebrates

BPD Annex Point IIA, VII.7.2 7.4.1.2 Acute toxicity to *Daphnia magna* (Impurity Reg. No. 406703)

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**7) XXXX** WL125892: Acute toxicity to Salmo gairdneri and Daphnia magna XXXX unpublished XXXX	
1.2.	**Data protection**	No	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	No data protection claimed	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Official Journal of the European Communities No. L251 Part C: Methods for the determination of Ecotoxicity. C2 Acute toxicity for Daphnia, EEC 79/831 A V C	
2.2.	**GLP**	Yes (laboratory certified by Department of Health of the Government of the United Kingdom, United Kingdom)	
2.3.	**Deviations**	No	X
		3. MATERIALS AND METHODS	
3.1.	**Test material**		X
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	See Business Confidential Information folder	
3.1.3.	Purity	86% ± 2%.	
3.1.4.	Composition of Product	Not applicable	
3.1.5.	Further relevant properties	None	

Section A7.4.1.2	**Acute toxicity to invertebrates**
BPD Annex Point IIA, VII.7.2	7.4.1.2 Acute toxicity to *Daphnia magna* (Impurity Reg. No. 406703)

3.1.6.	Method of analysis	HPLC-UV detection
3.2.	**Preparation of TS solution for poorly soluble or volatile test substances**	None
3.3.	**Reference substance**	No
3.3.1.	Method of analysis for reference substance	Not applicable
3.4.	**Testing procedure**	
3.4.1.	Dilution water	Control, 0.01, 0.03, 0.1, 0.3, 1, 3, 10, 30, 100, 290, 500, 930, 1700 and 3000 µg a.s./L (nominal).
3.4.2.	Test organisms	Water flea (*Daphnia magna* STRAUS), neonates with age at test initiation less than 24 hours, neonates from in-house culture, stock obtained from Institut National de Recherche Chimique Appliquée, France
3.4.3.	Test system	Static test (48 hours), 14 test concentrations plus control, 2 replicates with 10 daphnids in each; assessment of immobility after 24 and 48 hours
3.4.4.	Test conditions	Reconstituted fresh water, pH 7.8 - 8.0, oxygen content: 9.0 mg/L - 9.2 mg/L, feeding with green algae, temperature: 21.5 C - 21.9 °C, photoperiod: 16 hours light : 8 hours dark
3.4.5.	Duration of the test	48-h
3.4.6.	Test parameter	EC_{50}, based on immobility of daphnids
3.4.7.	Sampling	Test initiation and termination
3.4.8.	Monitoring of TS concentration	See 3.4.7
3.4.9.	Statistics	Descriptive statistics, probit analysis for determination of EC_{50} (see also XXXX).

Section A7.4.1.2	**Acute toxicity to invertebrates**
BPD Annex Point IIA, VII.7.2	7.4.1.2 Acute toxicity to *Daphnia magna* (Impurity Reg. No. 406703)

4. RESULTS

Limit Test		Not performed	
4.1.1.	Concentration	Not applicable	
4.1.2.	Number/ percentage of animals showing adverse effects	Not applicable	
4.1.3.	Nature of adverse effects	Not applicable	
Results test substance			
4.1.4.	Initial concentrations of test substance	**The analytically detected concentrations for Reg. No. 4064703 ranged from 86% to 100% of nominal values at the beginning of the test. After 48 h of exposure, test item concentrations ranged from 67% to 100% of the nominal. Therefore the results are based on the nominal concentrations.**	X
4.1.5.	Actual concentrations of test substance	See 4.1.4	
4.1.6.	Effect data (Mortality)	See Table 7.4.1.2/125	
4.1.7.	Concentration / response curve	See Table 7.4.1.2/125	
4.1.8.	Other effects	None	
Results of controls			
4.1.9.	Number/ percentage of animals showing adverse effects	See Table 7.4.1.2/125	
4.1.10.	Nature of adverse effects	See Table 7.4.1.2/125	
Test with reference substance		Not performed	

Section A7.4.1.2	**Acute toxicity to invertebrates**
BPD Annex Point IIA, VII.7.2	7.4.1.2 Acute toxicity to *Daphnia magna* (Impurity Reg. No. 406703)

		5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1.	**Materials and methods**	*Daphnia magna* was exposed for 48-h to a test substance as described under 3.1. The test procedure is detailed under 3.4.	
5.2.	**Results and discussion**	Biological results: Reg. No. 4064703 had no effects on Daphnia immobility up to a test item concentration of 0.3 µg a.s./L. After 48 hours of exposure, immobility in the 1, 3, 10, 30, 100, 290, 500, 930, 1700 and 3000 µg a.s./L treatment groups was 15%, 40%, 70%, 75%, 95%, 100%, 100%, 100%, 100% and 100%, respectively. The results are summarized in Table 7.4.1.2/125.	
5.2.1.	LC_0	Not defined in the study	
5.2.2.	LC_{50}	5.45 µg a.s./L (mean measured)	
5.2.3.	LC_{100}	Not applicable	
5.3.	**Conclusion**	In a 48 hours static acute toxicity study with *Daphnia magna*, the EC_{50} of Reg. No. 4064703 was determined to be 5.45 µg a.s./L (mean measured) (see also XXXX).	
5.3.1.	Other Conclusions	None	
5.3.2.	Reliability	1	X
5.3.3.	Deficiencies	No	

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	02/10/2005

Section A7.4.1.2	**Acute toxicity to invertebrates**
BPD Annex Point IIA, VII.7.2	7.4.1.2 Acute toxicity to *Daphnia magna* (Impurity Reg. No. 406703)

Materials and Methods	Applicant's summary is acceptable with the following amendment : 2.3 Deviations : Yes Mean-measured values are available only for the 8 highest concentrations, due to analytical limitations (values below LoQ). Lower concentrations were recalculated into mean-measured concentrations based on an average recovery of the measured groups of about 90%. The 4 highest treatment groups and the lowest treatment group were excluded from statistical analysis, since Toxstat can handle maximal 10 treatment groups. Detailed calculation provided in XXXX (Annex 2 of IIIA 7.6). 3.1 Test substance : Reg. No. 4064703
Results and discussion	Applicant's summary is acceptable. 4.1.4 Initial concentrations of test substance : *Therefore the results are based on the ~~nominal~~* **mean-measured** *concentrations.* **Calculations are provided in XXXX (Annex 2 of IIIA 7.6).**
Conclusion	Applicant's summary is acceptable.
Reliability	See deviations above. Reliability index : 2.
Acceptability	Acceptable
Remarks	Corrections in Tables 7.4.1.2/11 and 12 are added in bold and underlined.

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.4.1.2/125 Effect (48 h) of Reg. No. 4064703 on *Daphnia magna* immobility

Nominal concentrations [µg a.s./L]	**Control**	**0.01**	**0.03**	**0.1**	**0.3**	**1**	**3**	**10**	**30**	**100**	**290**	**500**	**930**	**1700**	**3000**
Mean-measured concentrations **[µg a.s./L]**	**Control**	-	**0.03**	**0.09**	**0.27**	**0.9**	**2.7**	**10**	**25**	**95**	**250**	-	-	-	-
Immobile (24 h) [%]	0	0	0	0	0	0	0	0	0	0	15	50	90	100	100
Immobile (48 h) [%]	0	0	0	0	0	15	40	70	75	95	100	100	100	100	100
	Endpoints [µg a.s./L ~~nominal~~ mean-measured]														
EC_{50} (48 h)	5.45 (95% limits: 3.50 - 8.48)														

Table 7.4.1.2/126 Validity criteria for acute daphnia immobilisation test according to OECD Guideline 202

	Fulfilled	**Not fulfilled**
Immobilisation of control animals <10%	**Yes**	
Control animals not staying at the surface	**Yes**	
Concentration of dissolved oxygen in all test vessels >3 mg/l	**Yes**	
Concentration of test substance ≥80% of initial concentration during test	**~~Yes~~**	**Results are based on mean-measured concentrations**

Criteria for poorly soluble test substances ergänzen	**Yes**	

Section A7.4.1.2 Acute toxicity to invertebrates

BPD Annex Point IIA, VII.7.2

7.4.1.2 Acute toxicity to *Daphnia magna* (Flufenoxuron degradate Reg. No. 406702)

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**8) Jatzek H.-J. 2003** Reg.No. 406 4702 (metabolite of Flufenoxuron) - Determination of the acute effect on the swimming ability of the water flea Daphnia magna STRAUS XXXX. unpublished XXXX	
1.2.	**Data protection**	Yes	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I.	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	EEC 92/32 A V C 2, OECD 202, EPA 850.1010	
2.2.	**GLP**	Yes (laboratory certified by Landesanstalt fuer Pflanzenbau und Pflanzenschutz Rheinland-Pfalz, Mainz)	
2.3.	**Deviations**	No	
		3. MATERIALS AND METHODS	
3.1.	**Test material**		X
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	See chemical glossary	
3.1.3.	Purity	95%.	
3.1.4.	Composition of Product	Not applicable	
3.1.5.	Further relevant properties	None	
3.1.6.	Method of analysis	HPLC-UV detection	
3.2.	**Preparation of**	None	

Section A7.4.1.2 Acute toxicity to invertebrates

BPD Annex Point IIA, VII.7.2 7.4.1.2 Acute toxicity to *Daphnia magna* (Flufenoxuron degradate Reg. No. 406702)

	TS solution for poorly soluble or volatile test substances	
3.3.	**Reference substance**	No
3.3.1.	Method of analysis for reference substance	Not applicable
3.4.	**Testing procedure**	
3.4.1.	Dilution water	Control, solvent control, 63, 125, 250, 500 1000 and 2000 µg/L (nominal).
3.4.2.	Test organisms	Water flea (*Daphnia magna* STRAUS), neonates 2 - 24 hours old at test initiation, neonates from in-house culture, stock obtained from Institut National de Recherche Chimique Appliquée, France
3.4.3.	Test system	Static test (48 hours), 6 test concentrations plus control and solvent control (acetone water mixture), 4 replicates with 5 daphnids in each; assessment of immobility after 24 and 48 h.
3.4.4.	Test conditions	Synthetic fresh water "M4"; pH 7.8 - 8.2; oxygen content 8.8 mg/L - 9.1 mg/L at test initiation, 8.7 mg/L - 9.2 mg/L at test termination; glass vessels, test volume 50 mL; no feeding; temperature 20.0 °C - 20.6 °C; artificial illumination, photoperiod: 16 hours light : 8 hours dark
3.4.5.	Duration of the test	48-h
3.4.6.	Test parameter	EC_{50}, based on immobility of daphnids
3.4.7.	Sampling	Test initiation and termination
3.4.8.	Monitoring of TS concentration	See 3.4.7
3.4.9.	Statistics	Descriptive statistics, probit analysis for determination of EC_{50}.

Section A7.4.1.2	**Acute toxicity to invertebrates**
BPD Annex Point IIA, VII.7.2	7.4.1.2 Acute toxicity to *Daphnia magna* (Flufenoxuron degradate Reg. No. 406702)

4. RESULTS

Limit Test		Not performed
4.1.1.	Concentration	Not applicable
4.1.2.	Number/ percentage of animals showing adverse effects	Not applicable
4.1.3.	Nature of adverse effects	Not applicable
Results test substance		
4.1.4.	Initial concentrations of test substance	The measured values ranged from 81.4% to 104% of nominal at the beginning of the test and from 83.8% to 103% at the end of the test. Therefore the results are based on nominal concentrations
4.1.5.	Actual concentrations of test substance	See 4.1.4
4.1.6.	Effect data (Mortality)	See Table 7.4.1.2/127.
4.1.7.	Concentration / response curve	See Table 7.4.1.2/127.
4.1.8.	Other effects	None
Results of controls		
4.1.9.	Number/ percentage of animals showing adverse effects	See Table 7.4.1.2/127.
4.1.10.	Nature of adverse effects	See Table 7.4.1.2/127.
Test with reference substance		Not performed

Section A7.4.1.2	**Acute toxicity to invertebrates**
BPD Annex Point IIA, VII.7.2	7.4.1.2 Acute toxicity to *Daphnia magna* (Flufenoxuron degradate Reg. No. 406702)

5.

6. APPLICANT'S SUMMARY AND CONCLUSION

6.1.	**Materials and methods**	*Daphnia magna* was exposed for 48-h to a test substance as described under 3.1. The test procedure is detailed under 3.4.
6.2.	**Results and discussion**	Biological results: No immobility of the daphnids was observed in the 125 and 250 µg a.s./L test item concentration at study termination. Immobility in the control, solvent control, 63, 500, 1000 and 2000 µg a.s./L test item concentrations was 5%, 0%, 5%, 5%, 35% and 100%, respectively. The results are summarized in Table 7.4.1.2/127.
6.2.1.	LC_0	Not defined in the study.
6.2.2.	LC_{50}	1030 µg a.s./L
6.2.3.	LC_{100}	Not applicable
6.3.	**Conclusion**	In a 48 hours static acute toxicity study *with Daphnia magna*, the EC_{50} of Reg. No. 406 4702 was determined to be 1030 µg/L (nominal).
6.3.1.	Other Conclusions	None
6.3.2.	Reliability	1
6.3.3.	Deficiencies	No

Section A7.4.1.2 Acute toxicity to invertebrates

BPD Annex Point IIA, VII.7.2

7.4.1.2 Acute toxicity to *Daphnia magna* (Flufenoxuron degradate Reg. No. 406702)

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	02/14/2005
Materials and Methods	Applicant's version is acceptable with the following amendment : 3.1 Test substance : Urea metabolite (Reg. No. 4064702)
Results and discussion	Applicant's version is acceptable.
Conclusion	Applicant's version is acceptable.
Reliability	Applicant's reliability indicator is acceptable. Reliability index is : 1.
Acceptability	Acceptable.
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.4.1.2/127 Effects (48 h) of Reg. No. 406 4702 on *Daphnia magna* immobility

Concentration (nominal) [µg/L]	**Control**	**Solvent control**	**63**	**125**	**250**	**500**	**1000**	**2000**
Immobile (24 h) [%]	0	0	0	0	0	0	0	75
Immobile (48 h) [%]	5	0	5	0	0	5	35	100
Endpoints [µg/L]								
EC_{50} (48 h)	1030							
EC_0 (48 h)	500							

Table 7.4.1.2/128 Validity criteria for acute daphnia immobilisation test according to OECD Guideline 202

	Fulfilled	**Not fulfilled**
Immobilisation of control animals <10%	Yes	
Control animals not staying at the surface	Yes	
Concentration of dissolved oxygen in all test vessels >3 mg/l	Yes	
Concentration of test substance ≥80% of initial concentration during test	Yes	

Criteria for poorly soluble test substances ergänzen	Yes	

Section A7.4.1.2 Acute toxicity to invertebrates

BPD Annex Point IIA, VII.7.2

7.4.1.2 Acute toxicity to *Daphnia magna* (Flufenoxuron degradate Reg. No. 102719)

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**9) Jatzek H.-J. 2003** Reg.No. 102 719 (metabolite of Flufenoxuron) - Determination of the acute effect on the swimming ability of the water flea Daphnia magna STRAUS XXXX. unpublished XXXX	
1.2.	**Data protection**	Yes	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I.	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	EEC 92/32 A V C 2, OECD 202, EPA 850.1010	
2.2.	**GLP**	Yes (laboratory certified by Landesanstalt fuer Pflanzenbau und Pflanzenschutz Rheinland-Pfalz, Mainz)	
2.3.	**Deviations**	No	
		3. MATERIALS AND METHODS	
3.1.	**Test material**		X
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	See chemical glossary	
3.1.3.	Purity	100%.	
3.1.4.	Composition of Product	Not applicable	
3.1.5.	Further relevant properties	None	
3.1.6.	Method of analysis	HPLC-UV detection	
3.2.	**Preparation of**	None	

Section A7.4.1.2	**Acute toxicity to invertebrates**
BPD Annex Point IIA, VII.7.2	7.4.1.2 Acute toxicity to *Daphnia magna* (Flufenoxuron degradate Reg. No. 102719)

	TS solution for poorly soluble or volatile test substances		
3.3.	**Reference substance**	No	
3.3.1.	Method of analysis for reference substance	Not applicable	
3.4.	**Testing procedure**		
3.4.1.	Dilution water	Control, 12500, 25000, 50000, 100000 µg/L (nominal).	
3.4.2.	Test organisms	Water flea (*Daphnia magna* STRAUS), neonates 2 - 24 hours old at test initiation, neonates from in-house culture, stock obtained from Institut National de Recherche Chimique Appliquée, France	
3.4.3.	Test system	Static test (48 hours), 6 test concentrations plus control and solvent control (acetone water mixture), 4 replicates with 5 daphnids in each; assessment of immobility after 24 and 48 h.	X
3.4.4.	Test conditions	Synthetic fresh water "M4"; pH 7.8 - 8.2; oxygen content 8.8 mg/L - 9.1 mg/L at test initiation, 8.7 mg/L - 9.2 mg/L at test termination; glass vessels, test volume 50 mL; no feeding; temperature 20.0 °C - 20.6 °C; artificial illumination, photoperiod: 16 hours light: 8 hours dark	X
3.4.5.	Duration of the test	48-h	
3.4.6.	Test parameter	EC_{50}, based on immobility of daphnids	
3.4.7.	Sampling	Test initiation and termination	
3.4.8.	Monitoring of TS concentration	See 3.4.7	
3.4.9.	Statistics	Descriptive statistics	
		4. RESULTS	
Limit Test		Not performed	

Section A7.4.1.2	**Acute toxicity to invertebrates**
BPD Annex Point IIA, VII.7.2	7.4.1.2 Acute toxicity to *Daphnia magna* (Flufenoxuron degradate Reg. No. 102719)

4.1.1.	Concentration	Not applicable
4.1.2.	Number/ percentage of animals showing adverse effects	Not applicable
4.1.3.	Nature of adverse effects	Not applicable
Results test substance		
4.1.4.	Initial concentrations of test substance	The measured values ranged from 96.4% to 100% of nominal at the beginning of the test and from 102% to 105% at the end of the test. Therefore the biological results are based on nominal concentrations.
4.1.5.	Actual concentrations of test substance	See 4.1.4
4.1.6.	Effect data (Mortality)	See Table 7.4.1.2/129
4.1.7.	Concentration / response curve	See Table 7.4.1.2/129
4.1.8.	Other effects	None
Results of controls		
4.1.9.	Number/ percentage of animals showing adverse effects	See Table 7.4.1.2/129.
4.1.10.	Nature of adverse effects	See Table 7.4.1.2/129.
Test with reference substance		Not performed

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1.	**Materials and methods**	*Daphnia magna* was exposed for 48-h to a test substance as described under 3.1. The test procedure is detailed under 3.4.
5.2.	**Results and discussion**	Biological results: No immobility of the daphnids was observed up to 25000 µg/L at study termination. Immobility in the 50000 and 100000

Section A7.4.1.2	**Acute toxicity to invertebrates**
BPD Annex Point IIA, VII.7.2	7.4.1.2 Acute toxicity to *Daphnia magna* (Flufenoxuron degradate Reg. No. 102719)

		µg/L test item concentrations were 5% and 10% after 48 h, respectively [see Table 7.4.1.2/129].
5.2.1.	LC_0	25000 µg/L
5.2.2.	LC_{50}	> 100000 µg/L
5.2.3.	LC_{100}	Not applicable
5.3.	**Conclusion**	In a 48 hours static acute toxicity study with *Daphnia magna*, the EC_{50} of Reg. No. 102 719 was determined to be > 100000 µg/L, the EC_0 was 25000 µg/L.
5.3.1.	Other Conclusions	None
5.3.2.	Reliability	1
5.3.3.	Deficiencies	No

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	02/14/2005
Materials and Methods	Applicant's version is acceptable with the following amendments in : - 3.1 Test material : 2,6-Difluorobenzamide (Reg. No. 102719) - "3.4.3. Test system" : Static test (48 hours), *4 test concentrations plus control*, 4 replicates with 5 daphnids in each; assessment of immobility after 24 and 48 h. - "3.4.4. Test conditions" : Synthetic fresh water "M4"; pH *8.0* - 8.2; oxygen content 8.8 mg/L - *9.0 mg/L* at test initiation, *9.1 mg/L* at test termination; glass vessels, test volume 50 mL; no feeding; temperature *19.6 °C - 20.3 °C*; artificial illumination, photoperiod: 16 hours light: 8 hours dark.
Results and discussion	Applicant's version is acceptable.
Conclusion	Applicant's version is acceptable.

Section A7.4.1.2	**Acute toxicity to invertebrates**
BPD Annex Point IIA, VII.7.2	7.4.1.2 Acute toxicity to *Daphnia magna* (Flufenoxuron degradate Reg. No. 102719)

Reliability	Applicant's reliability indicator is acceptable. Reliability index is : 1.
Acceptability	Acceptable.
Remarks	The following amendments should be done in "1.1. References " : **9) Jatzek H.-J. 2003** Reg.No. 102 719 (metabolite of *BAS 307 I*) - Determination of the acute effect on the swimming ability of the water flea Daphnia magna STRAUS
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.4.1.2/129 **Effects (48 h) of Reg. No. 102 719 on *Daphnia magna* immobility**

Concentration [µg/L] nominal	**Control**	**12500**	**25000**	**50000**	**100000**
Immobile (24 hours) [%]	0	0	0	5	5
Immobile (48 hours) [%]	0	0	0	5	10
Endpoints [µg/L]					
EC_{50} (48 h)	> 100000				
EC_0 (48 h)	25000				

Table 7.4.1.2/130 Validity criteria for acute daphnia immobilisation test according to OECD Guideline 202

	Fulfilled	**Not fulfilled**
Immobilisation of control animals <10%	**Yes**	
Control animals not staying at the surface	**Yes**	
Concentration of dissolved oxygen in all test vessels >3 mg/l	**Yes**	
Concentration of test substance ≥80% of initial concentration during test	**Yes**	

Criteria for poorly soluble test substances ergänzen	**Yes**	

Section A7.4.1.2 Acute toxicity to invertebrates

BPD Annex Point IIA, VII.7.2

7.4.1.2 Acute toxicity to *Daphnia magna* (Flufenoxuron degradate Reg. No. 241208)

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**10) Jatzek H.-J. 2003** Reg.No. 241 208 (metabolite of Flufenoxuron) - Determination of the acute effect on the swimming ability of the water flea Daphnia magna STRAUS XXXX. unpublished XXXX	X
1.2.	**Data protection**	Yes	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I.	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	EEC 92/32 A V C 2, OECD 202, EPA 850.1010	
2.2.	**GLP**	Yes (laboratory certified by Landesanstalt fuer Pflanzenbau und Pflanzenschutz Rheinland-Pfalz, Mainz)	
2.3.	**Deviations**	No	
		3. MATERIALS AND METHODS	
3.1.	**Test material**		X
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	See chemical glossary	
3.1.3.	Purity	99%.	
3.1.4.	Composition of Product	Not applicable	
3.1.5.	Further relevant properties	None	
3.1.6.	Method of analysis	HPLC-UV detection	
3.2.	**Preparation of**	None	

Section A7.4.1.2	**Acute toxicity to invertebrates**
BPD Annex Point IIA, VII.7.2	7.4.1.2 Acute toxicity to *Daphnia magna* (Flufenoxuron degradate Reg. No. 241208)

	TS solution for poorly soluble or volatile test substances		
3.3.	**Reference substance**	No	
3.3.1.	Method of analysis for reference substance	Not applicable	
3.4.	**Testing procedure**		
3.4.1.	Dilution water	Control, solvent control, 125, 250, 500 and 1000 µg/L (nominal)	
3.4.2.	Test organisms	Water flea (*Daphnia magna* STRAUS), neonates 2 - 24 hours old at test initiation, neonates from in-house culture, stock obtained from Institut National de Recherche Chimique Appliquée, France	
3.4.3.	Test system	Static test (48 hours), 6 test concentrations plus control and solvent control (acetone water mixture), 4 replicates with 5 daphnids in each; assessment of immobility after 24 and 48 h.	X
3.4.4.	Test conditions	Synthetic fresh water "M4"; pH 7.8 - 8.2; oxygen content 8.8 mg/L - 9.1 mg/L at test initiation, 8.7 mg/L - 9.2 mg/L at test termination; glass vessels, test volume 50 mL; no feeding; temperature 20.0 °C - 20.6 °C; artificial illumination, photoperiod: 16 hours light : 8 hours dark	X
3.4.5.	Duration of the test	48-h	
3.4.6.	Test parameter	EC_{50}, based on immobility of daphnids	
3.4.7.	Sampling	Test initiation and termination	
3.4.8.	Monitoring of TS concentration	See 3.4.7	
3.4.9.	Statistics	Descriptive statistics, probit analysis for determination of the EC_x.	

4. RESULTS

Limit Test		Not performed
4.1.1.	Concentration	Not applicable

Section A7.4.1.2	**Acute toxicity to invertebrates**
BPD Annex Point IIA, VII.7.2	7.4.1.2 Acute toxicity to *Daphnia magna* (Flufenoxuron degradate Reg. No. 241208)

4.1.2.	Number/ percentage of animals showing adverse effects	Not applicable
4.1.3.	Nature of adverse effects	Not applicable
Results test substance		
4.1.4.	Initial concentrations of test substance	Analytical measurements: the measured values ranged from 103% to 106% of nominal at the beginning of the test and from 98.1% to 103% at the end of the test. Therefore the biological results are based on nominal concentrations
4.1.5.	Actual concentrations of test substance	See 4.1.4
4.1.6.	Effect data (Mortality)	See Table 7.4.1.2/131
4.1.7.	Concentration / response curve	See Table 7.4.1.2/131
4.1.8.	Other effects	None
Results of controls		
4.1.9.	Number/ percentage of animals showing adverse effects	See Table 7.4.1.2/131
4.1.10.	Nature of adverse effects	See Table 7.4.1.2/131
Test with reference substance		Not performed

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1.	**Materials and methods**	*Daphnia magna* was exposed for 48-h to a test substance as described under 3.1. The test procedure is detailed under 3.4.
5.2.	**Results and discussion**	Biological results: No significant immobility of the daphnids was observed up to 500 µg/L at study termination. The single observed immobility of one animal at 250 µg/L was not concentration related and

Section A7.4.1.2	**Acute toxicity to invertebrates**
BPD Annex Point IIA, VII.7.2	7.4.1.2 Acute toxicity to *Daphnia magna* (Flufenoxuron degradate Reg. No. 241208)

		can therefore be considered as a matter of chance. No other effects were observed [see Table 7.4.1.2/131].
5.2.1.	LC_0	500 µg/L
5.2.2.	LC_{50}	654 µg/L
5.2.3.	LC_{100}	Not applicable
5.3.	**Conclusion**	In a 48 hours static acute toxicity study with *Daphnia magna*, the EC_{50} of Reg. No. 241 208 was determined to be 654 µg/L, the EC_0 was 500 µg/L.
5.3.1.	Other Conclusions	None
5.3.2.	Reliability	1
5.3.3.	Deficiencies	No

Section A7.4.1.2	**Acute toxicity to invertebrates**
BPD Annex Point IIA, VII.7.2	7.4.1.2 Acute toxicity to *Daphnia magna* (Flufenoxuron degradate Reg. No. 241208)

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	02/14/2005

Materials and Methods	Applicant's version is acceptable with the following amendments in : - 3.1 Test material : 'Amine' metabolite (Reg. No. 241208) - "3.4.3. Test system" : Static test (48 hours), *4 test concentrations* plus control and solvent control (acetone water mixture), 4 replicates with 5 daphnids in each; assessment of immobility after 24 and 48 h. - "3.4.4. Test conditions" : Synthetic fresh water "M4"; pH 7.8 - *8.1*; oxygen content *9.3 mg/L - 9.4 mg/L* at test initiation, 9*.0 mg/L - 9.7 mg/L* at test termination; glass vessels, test volume 50 mL; no feeding; temperature *19.6 °C - 20.4 °C*; artificial illumination, photoperiod: 16 hours light : 8 hours dark
Results and discussion	Applicant's version is acceptable.
Conclusion	Applicant's version is acceptable.
Reliability	Applicant's reliability indicator is acceptable. Reliability index is : 1.
Acceptability	Acceptable.
Remarks	The following amendments should be done in "1.1. References " : **10) Jatzek H.-J. 2003** Reg.No. 241 208 (metabolite of *BAS 307 I*) - Determination of the acute effect on the swimming ability of the water flea Daphnia magna STRAUS

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.4.1.2/131 **Effects (48 h) of Reg. No. 241 208 on *Daphnia magna* immobility**

Concentration [µg/L] nominal	**Control**	**Solvent control**	**125**	**250**	**500**	**1000**
Immobile (24 hours) [%]	0	0	0	0	0	100
Immobile (48 hours) [%]	0	0	0	5	0	100
Endpoints [µg/L]						
EC_{50} (48 h)	654					
EC_0 (48 h)	500					

Table 7.4.1.2/132 Validity criteria for acute daphnia immobilisation test according to OECD Guideline 202

	Fulfilled	**Not fulfilled**
Immobilisation of control animals <10%	**Yes**	
Control animals not staying at the surface	**Yes**	
Concentration of dissolved oxygen in all test vessels >3 mg/l	**Yes**	
Concentration of test substance ≥80% of initial concentration during test	**Yes**	

Criteria for poorly soluble test substances ergänzen	**Yes**	

Section A7.4.1.2 Acute toxicity to invertebrates

BPD Annex Point IIA, VII.7.2

7.4.1.2 Acute toxicity to *Daphnia magna* (Flufenoxuron degradate Reg. No. 206925)

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**11) Jatzek H.-J. 2003** Reg.No. 206925 (metabolite of Flufenoxuron,) - Determination of the acute effect on the swimming ability of the water flea Daphnia magna STRAUS XXXX. unpublished XXXX	
1.2.	**Data protection**	Yes	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I.	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	EEC 92/32 A V C 2, OECD 202, EPA 850.1010	
2.2.	**GLP**	Yes (laboratory certified by Landesanstalt fuer Pflanzenbau und Pflanzenschutz Rheinland-Pfalz, Mainz)	
2.3.	**Deviations**	No	
		3. MATERIALS AND METHODS	
3.1.	**Test material**		X
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	See chemical glossary	
3.1.3.	Purity	99.6%.	
3.1.4.	Composition of Product	Not applicable	
3.1.5.	Further relevant properties	None	
3.1.6.	Method of analysis	HPLC-UV detection	
3.2.	**Preparation of**	None	

Section A7.4.1.2	**Acute toxicity to invertebrates**
BPD Annex Point IIA, VII.7.2	7.4.1.2 Acute toxicity to *Daphnia magna* (Flufenoxuron degradate Reg. No. 206925)

	TS solution for poorly soluble or volatile test substances		
3.3.	**Reference substance**	No	
3.3.1.	Method of analysis for reference substance	Not applicable	
3.4.	**Testing procedure**		
3.4.1.	Dilution water	Control, 12.5, 25, 50, 100 mg/L (nominal)	
3.4.2.	Test organisms	Water flea (*Daphnia magna* STRAUS), neonates 2 - 24 hours old at test initiation, neonates from in-house culture, stock obtained from Institut National de Recherche Chimique Appliquée, France	
3.4.3.	Test system	Static test (48 hours), 6 test concentrations plus control and solvent control (acetone water mixture), 4 replicates with 5 daphnids in each; assessment of immobility after 24 and 48 h.	X
3.4.4.	Test conditions	Synthetic fresh water "M4"; pH 7.8 - 8.2; oxygen content 8.8 mg/L - 9.1 mg/L at test initiation, 8.7 mg/L - 9.2 mg/L at test termination; glass vessels, test volume 50 mL; no feeding; temperature 20.0 °C - 20.6 °C; artificial illumination, photoperiod: 16 hours light: 8 hours dark	X
3.4.5.	Duration of the test	48-h	
3.4.6.	Test parameter	EC_{50}, based on immobility of daphnids	
3.4.7.	Sampling	Test initiation and termination	
3.4.8.	Monitoring of TS concentration	See 3.4.7	
3.4.9.	Statistics	Descriptive statistics	
		4. RESULTS	
Limit Test		Not performed	
4.1.1.	Concentration	Not applicable	

Section A7.4.1.2	**Acute toxicity to invertebrates**
BPD Annex Point IIA, VII.7.2	7.4.1.2 Acute toxicity to *Daphnia magna* (Flufenoxuron degradate Reg. No. 206925)

4.1.2.	Number/ percentage of animals showing adverse effects	Not applicable
4.1.3.	Nature of adverse effects	Not applicable
Results test substance		
4.1.4.	Initial concentrations of test substance	The measured values ranged from 99.3% to 99.8% of nominal at the beginning of the test and from 97.6% to 99.7% at the end of the test. Therefore the biological results are based on nominal concentrations
4.1.5.	Actual concentrations of test substance	See 4.1.4
4.1.6.	Effect data (Mortality)	See Table 7.4.1.2/133
4.1.7.	Concentration / response curve	See Table 7.4.1.2/133
4.1.8.	Other effects	None
Results of controls		
4.1.9.	Number/ percentage of animals showing adverse effects	See Table 7.4.1.2/133
4.1.10.	Nature of adverse effects	See Table 7.4.1.2/133
Test with reference substance		Not performed

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1.	**Materials and methods**	*Daphnia magna* was exposed for 48-h to a test substance as described under 3.1. The test procedure is detailed under 3.4.
5.2.	**Results and discussion**	Biological results: No immobility of the daphnids was observed in the highest test concentration (100 mg/L) at study termination. The single observed immobility of one animal at 12.5 mg/L was not concentration related [see Table 7.4.1.2/133].

Section A7.4.1.2	**Acute toxicity to invertebrates**
BPD Annex Point IIA, VII.7.2	7.4.1.2 Acute toxicity to *Daphnia magna* (Flufenoxuron degradate Reg. No. 206925)

5.2.1.	LC_0	100 mg/L
5.2.2.	LC_{50}	> 100 mg/L
5.2.3.	LC_{100}	Not applicable
5.3.	**Conclusion**	In a 48 hours static acute toxicity study with Daphnia magna, the EC_{50} of Reg. No. 206 925 was determined to be > 100 mg/L, the EC_0 was 100 mg/L.
5.3.1.	Other Conclusions	None
5.3.2.	Reliability	1
5.3.3.	Deficiencies	No

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	02/14/2005
Materials and Methods	Applicant's version is acceptable with the following amendments in : - 3.1. Test material : 2,6-difluorobenzoic acid (Reg. No. 206 925) - "3.4.3. Test system" : Static test (48 hours), *4 test concentrations plus control*, 4 replicates with 5 daphnids in each; assessment of immobility after 24 and 48 h. - "3.4.4. Test conditions" : Synthetic fresh water "M4"; pH *6.5* - 8.2; oxygen content *8.7 mg/L - 9.0 mg/L* at test initiation, *9.3 mg/L* at test termination; glass vessels, test volume 50 mL; no feeding; temperature *19.4 °C - 21.4 °C*; artificial illumination, photoperiod: 16 hours light: 8 hours dark
Results and discussion	Applicant's version is acceptable.
Conclusion	Applicant's version is acceptable.
Reliability	Applicant's reliability indicator is acceptable. Reliability index is : 1.

Section A7.4.1.2 Acute toxicity to invertebrates

BPD Annex Point IIA, VII.7.2

7.4.1.2 Acute toxicity to *Daphnia magna* (Flufenoxuron degradate Reg. No. 206925)

Acceptability	Acceptable.
Remarks	The following amendments should be done in "1.1. References " : **11) Jatzek H.-J. 2003** Reg.No. 206925 (metabolite of *BAS 307 I*, Flufenoxuron,) - Determination of the acute effect on the swimming ability of the water flea Daphnia magna STRAUS
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.4.1.2/133 Effects (48 h) of Reg. No. 206 925 on *Daphnia magna* immobility

Concentration [mg/L] nominal	**Control**	**12.5**	**25**	**50**	**100**
Immobile (24 hours) [%]	0	0	0	0	0
Immobile (48 hours) [%]	0	5	0	0	0
Endpoints [mg/L]					
EC_{50} (48 h)	> 100				
EC_0 (48 h)	100				

Table 7.4.1.2/134 Validity criteria for acute daphnia immobilisation test according to OECD Guideline 202

	Fulfilled	**Not fulfilled**
Immobilisation of control animals <10%	**Yes**	
Control animals not staying at the surface	**Yes**	
Concentration of dissolved oxygen in all test vessels >3 mg/l	**Yes**	
Concentration of test substance ≥80% of initial concentration during test	**Yes**	

Criteria for poorly soluble test substances ergänzen	**Yes**	

Section A7.4.1.3	**Growth inhibition test on algae**
BPD Annex Point IIA, VII.7.3	7.4.1.3 Green alga (parent, Flufenoxuron)

0.0 Justification of the key study

Pseudokirchneriella subcapitata (syn. Selenastrum capricornutum)

The endpoint studied in tests on *Pseudokirchneriella subcapitata* is inhibition of growth.

Five studies are submitted for this endpoint (5 references).

Two of them are dedicated to the active substance **Flufenoxuron** (BAS 307 I) :

- Reference 1 – XXXX (XXXX, 2003)
  - E_bC_{50} reported is 19228 µg/L
  - E_rC_{50} reported is 71940 µg/L
  - **Reliability Index : 1**
- Reference 2 – XXXX (XXXX, 1987)
  - E_rC_{50} reported is > 2.975 µg/L
  - Reliability Index : 2

In the study of XXXX), only one concentration was tested. This concentration was too low to give relevant data on the toxicity of the substance. Therefore, **reliability index is 2 for this study and the result will be not used to define the hazard of Flufenoxuron.**

Three other studies were conducted with **Flufenoxuron metabolites**

- Reference 3 – XXXX (Hanstveit & Oldersma, 1993)
  - Reg. 4064703 = 4-[2-chloro-4-(trifluoromethhyl) phenoxy]-2-fluoroaniline hydrochloride
  - Reliability Index : 3
- Reference 4 – XXXX (Jatzek, 2003) :
  - Reg. 102719 = 2,6-fluorobenzamid
  - **Reliability Index : 1**
- Reference 5 – XXXX (Jatzek, 2003) :
  - Reg. 4064702 = N-[4-[2-chloro-4-(trifluoromethhyl) phenoxy]-2-fluoro phenyl urea
  - **Reliability Index : 1**

Hanstveit & Oldersma (1993) did not measure concentrations of the metabolite. Therefore, it is not possible to say if CE_{50} is based on actual concentrations or not.

On the contrary, methods employed in studies realized by Jatzek (2003)

Section A7.4.1.3	**Growth inhibition test on algae**
BPD Annex Point IIA, VII.7.3	7.4.1.3 Green alga (parent, Flufenoxuron)

are very close to OECD Guideline 201, concentrations were measured during 72 hours and those concentrations are representative of nominal ones.

The notifier did not propose a key study for inhibition of growth endpoint for *Pseudokirchneriella subcapitata*.

For reasons cited above, RMS proposes to retain as **key study** for inhibition of growth endpoint for *Pseudokirchneriella subcapitata* by

- **Flufenoxuron :**
  - Ref. 1 – XXXX (Kubitza, 2003) – E_rC_{50} = 71.9 mg/L

- metabolites of flufenoxuron : bioassays reported by Jatzek (2003) for two of the metabolites :

- Reg. 102719 : Ref. 4 – XXXX - : E_rC_{50}>100 mg/L
- Reg. 4064702 : Ref. 5 – XXXX : E_rC_{50}=0.107 mg/L

Section A7.4.1.3	**Growth inhibition test on algae**
BPD Annex Point IIA, VII.7.3	7.4.1.3 Green alga (parent, Flufenoxuron)

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**1) Kubitza J. 2003** Effect of BAS 307 I (Flufenoxuron) on the growth of the green alga Pseudokirchneriella subcapitata XXXX. unpublished XXXX	
1.2.	**Data protection**	Yes	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I.	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Yes, OECD 201	
2.2.	**GLP**	Yes (laboratory certified by Landesamt fuer Umweltschutz und Gewerbeaufsicht, Mainz, Germany)	
2.3.	**Deviations**	No	
		3. MATERIALS AND METHODS	
3.1.	**Test material**		X
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	As given in section 2	
3.1.3.	Purity	99.2%	
3.1.4.	Composition of Product	Not applicable	
3.1.5.	Further relevant properties	None	
3.1.6.	Method of analysis	HPLC-UV detection	
3.2.	**Preparation of TS solution for poorly soluble or volatile test**	Not applicable	

Section A7.4.1.3	**Growth inhibition test on algae**
BPD Annex Point IIA, VII.7.3	7.4.1.3 Green alga (parent, Flufenoxuron)

	substances	
3.3.	**Reference substance**	No
3.3.1.	Method of analysis for reference substance	Not applicable
3.4.	**Testing procedure**	
3.4.1.	Culture medium	OECD 201 nutrient solution
3.4.2.	Test organisms	Unicellular fresh water green alga, *Pseudokirchneriella subcapitata* (formerly *Ankistrodesmus bibraianus*) (Reinsch) Korshikov (syn. *Selenastrum capricornutum*), SAG 61.81; stock obtained from Sammlung von Algenkulturen, Göttingen, Germany.
3.4.3.	Test system	Static system, test duration 96 hours, 7 test concentrations, control and solvent control (DMSO), each with 5 replicates plus a solvent control with 10 replicates, daily assessments of growth. Concentration: Control, solvent control, 300, 800, 2000, 5300, 14000, 36000 and 100000 µg a.s./L (nominal).
3.4.4.	Test conditions	pH 7.47 - 7.70, glass Erlenmeyer dimple flasks, continuous shaking, initial cell densities 3 x 10^3 cells/mL, temperature 22 °C ± 1 °C, continuous light at about 8000 lux.
3.4.5.	Duration of the test	96-h
3.4.6.	Test parameter	EC_{50} with respect to growth and biomass after exposure over 96 hours
3.4.7.	Sampling	At study initiation and termination
3.4.8.	Monitoring of TS concentration	See 3.4.7
3.4.9.	Statistics	Descriptive statistics, log-log analysis for determination of the EC_{50} values (siehe auch XXXX).

4. RESULTS

Limit Test		Not performed
4.1.1.	Concentration	Not applicable

Section A7.4.1.3	**Growth inhibition test on algae**
BPD Annex Point IIA, VII.7.3	7.4.1.3 Green alga (parent, Flufenoxuron)

4.1.2.	Number/ percentage of animals showing adverse effects	Not applicable	
Results test substance			
4.1.3.	Initial concentrations of test substance	The analyzed concentrations were initially in a range of 83.1% to 101.7% of nominal. After 96 h of exposure, test item concentrations were in a range of 25.4% - 61.6%. The poor recovery of the analytical results at test termination probably can be explained by adsorption of the a.s. on the glass surface of the test aquaria and/or on biological matrix. Therefore the results are based on the nominal concentrations.	X
4.1.4.	Actual concentrations of test substance	See 4.1.4	
4.1.5.	Growth curves	See Table 7.4.1.3/135	
4.1.6.	Concentration / response curve	See Table 7.4.1.3/135	
4.1.7.	Cell concentration data	See Table 7.4.1.3/135	
4.1.8.	Effect data (cell multiplication inhibition)	See Table 7.4.1.3/135	
4.1.9.	Other observed effects	None	
Results of controls			
Test with reference substance		Not performed	
4.1.10.	Concentrations	Not applicable	
4.1.11.	Results	Not applicable	
		5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1.	**Materials and methods**	Green alga was exposed for 96-h to a test substance as described under 3.1. The test procedure is detailed under 3.4.	
5.2.	**Results and discussion**	Biological results: the test item caused no significant reduction of algal growth up to 36000 µg a.s./L. No morphological effects on the algae could be observed up to 36000 µg a.s./L. The results are summarized in	X

Section A7.4.1.3	**Growth inhibition test on algae**
BPD Annex Point IIA, VII.7.3	7.4.1.3 Green alga (parent, Flufenoxuron)

		Table 7.4.1.3/135.
5.2.1.	NOE_rC	Not determined
5.2.2.	E_bC_{50}	19228 µg a.s./L (mean measured).
5.2.3.	E_rC_{50}	71940 µg a.s./L (mean measured)
5.3.	**Conclusion**	In a 96-hour algae test with Pseudokirchneriella subcapitata, the E_rC_{50} of Flufenoxuron was determined to be 71940 µg a.s./L, the E_bC_{50} was 19228 µg a.s./L (mean measured) (see also XXXX).
5.3.1.	Reliability	1
5.3.2.	Deficiencies	No

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	02/15/2005
Materials and Methods	Applicant's summary acceptable. 3.1 Test material : Flufenoxuron
Results and discussion	Applicant's summary acceptable with the following amendments: 4.1.3 Initial concentrations of test substance : *Therefore the results are based on the ~~nominal~~* **mean-measured** *concentrations.* **Calculations are presented in XXXX (Annex 2 of IIIA 7.6).** **5.2 Results and discussion :** *Biological results: the test item caused no significant reduction of algal growth up to 36000 µg a.s./L* **(nominal)**. *No morphological effects on the algae could be observed up to 36000 µg a.s./L* **(nominal)**. **The nominal concentration of 36000 µg/L corresponds to 26040 µg/L in the mean-measured concentration**. *The results are summarized in Table 7.4.1.3/135.*
Conclusion	Agree with applicant's version.
Reliability	Reliability Index is 1 (study has retained as key study).
Acceptability	Acceptable.
Remarks	Corrections in Tables 7.4.1.3/1 and 2 are indicated in bold and underlined.
	COMMENTS FROM ...

Section A7.4.1.3	**Growth inhibition test on algae**
BPD Annex Point IIA, VII.7.3	7.4.1.3 Green alga (parent, Flufenoxuron)

Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.4.1.3/135 Effect of Flufenoxuron (96 h) on the growth of the green alga *Pseudokirchneriella subcapitata*

Concentration (nominal) [µg a.s./L]	**300**	**800**	**2000**	**5300**	**14000**	**36000**	**100000**
Concentration (mean-measured) [µg a.s./L]	**180**	**510**	**1290**	**3480**	**10370**	**26040**	**80370**
Inhibition in 96 h (biomass) [%]	1.7	26.8	21.1	14.7	51.1	27.2	89.4
Inhibition in 96 h (growth rate) [%]	0.2	5.5	3.8	0.5	11.1	3.6	65.9
Endpoints [µg a.s./L]							
E_rC_{50} (0-96 h)	71940 (mean measured)						
E_rC_{10} (0-96 h)	9500						
E_bC_{50} (0-96 h)	19228 (mean measured)						
E_bC_{10} (0-96 h)	600						

Table 7.4.1.3/136 Validity criteria for algal growth inhibition test according to OECD Guideline 201

	Fulfilled	Not fulfilled
Cell concentration in control cultures increased at least by a factor of 16 within 3 days	**Yes**	
Concentration of test substance ≥80% of initial concentration during test	~~**Yes**~~	**Results are based on mean-measured concentrations**

Criteria for poorly soluble test substances	**Yes**	

Section A7.4.1.3 **Growth inhibition test on algae**

BPD Annex Point IIA, VII.7.3 7.4.1.3 Green alga (parent, Flufenoxuron)

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**2) Croucher E. 1987** WL115110: Acute toxicity to Salmo gairdneri, Daphnia magna and Selenastrum capricornutum XXXX unpublished XXXX	
1.2.	**Data protection**	No	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	No data protection claimed	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	No, description given in the report but in general compliance with OECD 201	
2.2.	**GLP**	Yes (laboratory certified by Department of Health of the Government of the United Kingdom, United Kingdom)	
2.3.	**Deviations**	No	X
		3. MATERIALS AND METHODS	
3.1.	**Test material**		X
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	As given in section 2	
3.1.3.	Purity	96.6% (1986), 93.6% (1987)	
3.1.4.	Composition of Product	Not applicable	
3.1.5.	Further relevant properties	None	
3.1.6.	Method of analysis	HPLC-UV detection	
3.2.	**Preparation of TS solution for poorly soluble or volatile test**	Not applicable	

Section A7.4.1.3 **Growth inhibition test on algae**

BPD Annex Point IIA, VII.7.3 7.4.1.3 Green alga (parent, Flufenoxuron)

	substances		
3.3.	**Reference substance**	No	
3.3.1.	Method of analysis for reference substance	Not applicable	
3.4.	**Testing procedure**		
3.4.1.	Culture medium	OECD 201 nutrient solution	
3.4.2.	Test organisms	Unicellular fresh water green alga, *Pseudokirchneriella subcapitata* (formerly *Ankistrodesmus bibraianus*) (Reinsch) Korshikov (syn. *Selenastrum capricornutum*) ATCC 22662, stock obtained from the American Type Culture Collection, Maryland, USA; cultures maintained in-house	
3.4.3.	Test system	Static system, test duration 96 hours, 1 test concentration plus a control, each with 6 replicates, daily assessments of growth	X
3.4.4.	Test conditions	pH 7.1 - 7.4, glass Erlenmeyer dimple flasks, continuous shaking, initial cell densities 1.3 x 10^4 - 4.1 x 10^4 cells/mL, temperature 22 °C - 28.6 °C, continuous light at 3000 lux.	X
3.4.5.	Duration of the test	96-h	
3.4.6.	Test parameter	EC_{50} with respect to growth and biomass after exposure over 96 hours	
3.4.7.	Sampling	At study initiation	
3.4.8.	Monitoring of TS concentration	See 3.4.7	
3.4.9.	Statistics	Descriptive statistics	
		4. RESULTS	
Limit Test		Performed	
4.1.1.	Concentration	Control, 4.0 µg a.s./L (nominal).	
4.1.2.	Number/ percentage of animals showing adverse effects	See Table 7.4.1.3/137	
Results test substance			
4.1.3.	Initial	Analytical measurements: The concentration of Flufenoxuron in	

Section A7.4.1.3 **Growth inhibition test on algae**

BPD Annex Point IIA, VII.7.3 7.4.1.3 Green alga (parent, Flufenoxuron)

	concentrations of test substance	the culture medium at test initiation was 4.0 µg a.s./L. The results are based on the mean measured concentrations	
4.1.4.	Actual concentrations of test substance	See 4.1.4	X
4.1.5.	Growth curves	Not applicable as one concentration tested	
4.1.6.	Concentration / response curve	Not applicable as one concentration tested	
4.1.7.	Cell concentration data	Not applicable as one concentration tested	
4.1.8.	Effect data (cell multiplication inhibition)	Not applicable as one concentration tested	
4.1.9.	Other observed effects	None	
Results of controls			
Test with reference substance		Not performed	
4.1.10.	Concentrations	Not applicable	
4.1.11.	Results	Not applicable	
		5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1.	**Materials and methods**	Green alga was exposed for 96-h to a test substance as described under 3.1. The test procedure is detailed under 3.4.	
5.2.	**Results and discussion**	Biological results: At test termination (96 h) mean cell number in the control was not significantly different from the mean cell number in the test item concentrations. The results are summarized in Table 7.4.1.3/137	
5.2.1.	NOE_rC	Not determined	
5.2.2.	E_rC_{50}	> 2.975 µg a.s./L (mean measured).	
5.2.3.	E_bC_{50}	> 2.975 µg a.s./L (mean measured)	
5.3.	**Conclusion**	In a 96 hour algae test with *Pseudokirchneriella subcapitata*, the EC_{50} of Flufenoxuron was determined to be > 2.975 µg a.s./L (mean measured) (siehe auch DocID 2006/1004526) .	
5.3.1.	Reliability	1	X

Section A7.4.1.3	**Growth inhibition test on algae**
BPD Annex Point IIA, VII.7.3	7.4.1.3 Green alga (parent, Flufenoxuron)

5.3.2. Deficiencies	No	X

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	02/15/2005

Materials and Methods	**1)** The following amendments should be done to :
	- 3.1 Test material : Flufenoxuron
	- 3.4.3. "Test System" :
	Static system, test duration 96 hours, 1 test concentration plus a control, each with 6 replicates*, assessments of growth were done on days 2 and 4*.
	
	- 3.4.4. "Test Conditions" :
	pH 7.1 - 7.4, glass Erlenmeyer dimple flasks, continuous shaking, initial cell densities 5 x 10^2 cells/mL, temperature 22 °C - 28.6 °C, continuous light at 3000 lux.
	
	2) To be in compliance with OCDE 201 Guideline, following amendments should be done in :
	- 3.4.3. "Test System" :
	  - test duration should be 72 ± 2 hours
	  - number of test concentrations should be at least 5
	  - assessment of growth should be done at least daily
	- 3.4.4. "Test Conditions" :
	- initial cell density should be comprised between 5 x 10^3 and 5 x 10^4 cell.mL^{-1}
	- temperature should be comprised between 21 and 24°C, controlled at ±2°C
	- light intensity should be comprised between 6000 and 10000 lux

Results and discussion	Applicant's summary is acceptable.
Conclusion	Agree with applicant's version.
Reliability	See "Results and discussion" Reliability Index is 2.

Section A7.4.1.3 **Growth inhibition test on algae**

BPD Annex Point IIA, VII.7.3 7.4.1.3 Green alga (parent, Flufenoxuron)

Acceptability	Acceptable Only one concentration tested at the solubility limit.
Remarks	Corrections in Tables 7.4.1.3/3 and 4 are indicated in bold and underlined.
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.4.1.3/137 Effect of Flufenoxuron (96 h) on the growth of the green alga *Pseudokirchneriella subcapitata*

Concentration (initial measured) [µg a.s./L]	**Control**	**4.0 (mean-measured concentration : 2.975)**
Inhibition in 96 h (growth) [%] [1)]	--	4
	Endpoints [µg a.s./L mean measured]	
EC_{50} (0 - 96 h)	> 2.975	

1) calculated based on cell numbers 96 h as % of mean control cell numbers; mean from 6 different cell concentrations.

Table 7.4.1.3/138 Validity criteria for algal growth inhibition test according to OECD Guideline 201

	Fulfilled	**Not fulfilled**
Cell concentration in control cultures increased at least by a factor of 16 within 3 days	**Yes**	
Concentration of test substance ≥80% of initial concentration during test	~~**Yes**~~	**Result is based on mean-measured concentration.**

Criteria for poorly soluble test substances	**Yes**	

Section A7.4.1.3 Growth inhibition test on algae

BPD Annex Point IIA, VII.7.3 7.4.1.3 Green alga (impurity, Reg. No. 406703)

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**3) Hanstveit A.O.,Oldersma H. 1993** Effect of WL 125892 on the growth of alga Selenastrum capricornutum (OECD 201) XXXX unpublished XXXX	
1.2.	**Data protection**	No	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	No data protection claimed	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Yes, OECD 201	
2.2.	**GLP**	Yes	
2.3.	**Deviations**	No	X
		3. MATERIALS AND METHODS	
3.1.	**Test material**		X
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	As given in section 2	
3.1.3.	Purity	97%	
3.1.4.	Composition of Product	Not applicable	
3.1.5.	Further relevant properties	None	
3.1.6.	Method of analysis	No analysis	
3.2.	**Preparation of**	Not applicable	

Section A7.4.1.3 **Growth inhibition test on algae**

BPD Annex Point IIA, VII.7.3 7.4.1.3 Green alga (impurity, Reg. No. 406703)

	TS solution for poorly soluble or volatile test substances		
3.3.	**Reference substance**	No	
3.3.1.	Method of analysis for reference substance	Not applicable	
3.4.	**Testing procedure**		
3.4.1.	Culture medium	OECD 201 nutrient solution	
3.4.2.	Test organisms	Unicellular fresh water green alga, *Pseudokirchneriella subcapitata* (formerly *Ankistrodesmus bibraianus*) (Reinsch) Korshikov (syn. *Selenastrum capricornutum*) ATCC 22662, stock obtained from American Type Culture Collection, Maryland, USA; cultures maintained in-house	
3.4.3.	Test system	Static system, test duration 72 hours, 6 test concentrations, each with 3 replicates plus a control with 6 replicates, daily assessments for growth.	
3.4.4.	Test conditions	pH 7.8 - 8.4, glass Erlenmeyer dimple flasks, continuous shaking, initial cell densities 1.1 x 10^4 cells/mL, temperature 23 °C, continuous light at 60 µmol/s x m^2 - 120 µmol/s x m^2 Concentration : Control, 32, 100, 320, 1000, 3200 and 12000 µg a.s./L (nominal)	X
3.4.5.	Duration of the test	72-h	
3.4.6.	Test parameter	EC_{50} with respect to biomass and NOEC after exposure over 72 h	
3.4.7.	Sampling	Not applicable as no analysis	
3.4.8.	Monitoring of TS concentration	See 3.4.7	
3.4.9.	Statistics	Descriptive statistics	
		4. RESULTS	
Limit Test		Not performed	
4.1.1.	Concentration	No applicable	
4.1.2.	Number/ percentage of	No applicable	

Section A7.4.1.3 **Growth inhibition test on algae**

BPD Annex Point IIA, VII.7.3 7.4.1.3 Green alga (impurity, Reg. No. 406703)

	animals showing adverse effects	
Results test substance		
4.1.3.	Initial concentrations of test substance	Not applicable as no analysis
4.1.4.	Actual concentrations of test substance	See 4.1.4
4.1.5.	Growth curves	See Table 7.4.1.3/139
4.1.6.	Concentration / response curve	See Table 7.4.1.3/139
4.1.7.	Cell concentration data	See Table 7.4.1.3/139
4.1.8.	Effect data (cell multiplication inhibition)	See Table 7.4.1.3/139
4.1.9.	Other observed effects	None
Results of controls		See Table 7.4.1.3/139
Test with reference substance		Not performed
4.1.10.	Concentrations	Not applicable
4.1.11.	Results	Not applicable

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1.	**Materials and methods**	Green alga was exposed for 72-h to a test substance as described under 3.1. The test procedure is detailed under 3.4.
5.2.	**Results and discussion**	Biological results: At low-test item concentrations growth stimulation was found on day 3. After 72 h of exposure, no abnormalities in the test item groups were observed. The results are summarized in Table 7.4.1.3/139.
5.2.1.	NOE_rC	100 µg a.s./L
5.2.2.	E_{r50}	Not determined
5.2.3.	E_bC_{50}	600 µg a.s./L

Section A7.4.1.3	**Growth inhibition test on algae**
BPD Annex Point IIA, VII.7.3	7.4.1.3 Green alga (impurity, Reg. No. 406703)

5.3.	**Conclusion**	In a 72-hour algae test with *Pseudokirchneriella subcapitata,* the E_bC_{50} of Reg No. 406703 was determined to be 600 µg a.s./L, the E_bC_{10} was 360 µg a.s./L and the NOEC was 100 µg a.s./L.	
5.3.1.	Reliability	1	X
5.3.2.	Deficiencies	No	X

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	02/17/2005
Materials and Methods	To be in compliance with OCDE 201 Guideline, following amendments should be done in 3.4.4. "Test Conditions" : Initial cell densities should be comprised between 5 x 10^3 and 5 x 10^4 cells/mL 3.1 Test material : Reg. No. 406703
Results and discussion	Applicant's summary is acceptable.
Conclusion	5.4. Conclusion : The following amendment should be done : In a 72-hour algae test with Pseudokirchneriella subcapitata, the E_bC_{50} of Reg No. *4064703* was determined to be 600 µg a.s./L, the E_bC_{10} was 360 µg a.s./L and the NOEC was 100 µg a.s./L. 5.3.2 Deficiencies : It is reported in OCDE Guideline No. 201 that : "Providing an analytical procedure for determination of the test substance in the concentration range used is available, the test solution should be analysed to verify the initial concentrations and maintenance of the exposure concentrations during the test." The study can not be considered as reliable because concentrations of the substance are not measured. Therefore, it is not possible to know if EC_{50} is based on actual concentrations or not.
Reliability	See deficiencies above. Reliability Index is 3.

Section A7.4.1.3	**Growth inhibition test on algae**
BPD Annex Point IIA, VII.7.3	7.4.1.3 Green alga (impurity, Reg. No. 406703)

Acceptability	Not Acceptable. See above.
Remarks	Correction in Table 7.4.1.3/6 is indicated in bold and underlined.

Section A7.4.1.3 Growth inhibition test on algae

BPD Annex Point IIA, VII.7.3 7.4.1.3 Green alga (impurity, Reg. No. 406703)

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.4.1.3/139 Effect of Reg. No. 406703 (72 h) on the growth of the green alga *Pseudokirchneriella subcapitata*

Concentration [µg a.s./L]	**Control**	**32**	**100**	**320**	**1000**	**3200**	**12000**
Inhibition in 72 h (biomass) [%] [1)]	--	-13	-12	-19	91	97	98
Endpoints [µg a.s./L]							
E_bC_{50} (0 - 72 h)	600						
E_bC_{10} (0 - 72 h)	360						
NOEC	100						

1) Negative values indicate stimulated growth

Table 7.4.1.3/140 Validity criteria for algal growth inhibition test according to OECD Guideline 201

	Fulfilled	**Not fulfilled**
Cell concentration in control cultures increased at least by a factor of 16 within 3 days	**Yes**	
Concentration of test substance ≥80% of initial concentration during test	~~**Yes**~~ **No analysis**	

Criteria for poorly soluble test substances	**Yes**	

Section A7.4.1.3	**Growth inhibition test on algae**
BPD Annex Point IIA, VII.7.3	7.4.1.3 Green alga (Flufenoxuron degradate, Reg. No. 102 719)

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**4) Jatzek H.-J. 2003** Reg.No. 102 719 (metabolite of BAS 307 I) - Determination of the inhibitory effect on the cell multiplication of unicellular green algae XXXX. unpublished XXXX	
1.2.	**Data protection**	Yes	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I.	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Yes, EEC 92/69 A V C 3, OECD 201, EPA 850.5400	
2.2.	**GLP**	Yes (laboratory certified by Landesanstalt fuer Pflanzenbau und Pflanzenschutz Rheinland-Pfalz, Mainz)	
2.3.	**Deviations**	No	
		3. MATERIALS AND METHODS	
3.1.	**Test material**		X
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	See chemical glossary	
3.1.3.	Purity	100%	
3.1.4.	Composition of Product	Not applicable	
3.1.5.	Further relevant properties	None	
3.1.6.	Method of analysis	HPLC-UV detection	
3.2.	**Preparation of TS solution for**	Not applicable	

Section A7.4.1.3	**Growth inhibition test on algae**
BPD Annex Point IIA, VII.7.3	7.4.1.3 Green alga (Flufenoxuron degradate, Reg. No. 102 719)

	poorly soluble or volatile test substances	
3.3.	**Reference substance**	No
3.3.1.	Method of analysis for reference substance	Not applicable
3.4.	**Testing procedure**	
3.4.1.	Culture medium	OECD 201 nutrient solution
3.4.2.	Test organisms	Unicellular fresh water green alga, *Pseudokirchneriella subcapitata* (Reinsch) Korshikov (syn.: *Selenastrum capricornutum* Prinz); SAG 61.81; source: Sammlung Algenkulturen Göttingen; Germany.
3.4.3.	Test system	Static system (72 h); 4 test concentrations, each with 3 replicates plus a control with 5 replicates; daily assessments for growth
3.4.4.	Test conditions	pH 8.0 - 8.9; glass flasks; initial cell densities 1 x 10^4 cells/mL; temperature 23 °C ± 2 °C; continuous light at 60 µE/(m^2 x s) - 120 µE/(m^2 x s) at 400 nm - 700 nm Concentration: Control, 12.5, 25, 50 and 100 mg/L (nominal)
3.4.5.	Duration of the test	72-h
3.4.6.	Test parameter	Effect on biomass and growth rate after exposure over 72 hours
3.4.7.	Sampling	Test initiation and termination
3.4.8.	Monitoring of TS concentration	See 3.4.7
3.4.9.	Statistics	Descriptive statistics, linear regression analysis for determination of the EC_x-values
	4. RESULTS	
Limit Test		Not performed
4.1.1.	Concentration	No applicable
4.1.2.	Number/	No applicable

Section A7.4.1.3	**Growth inhibition test on algae**
BPD Annex Point IIA, VII.7.3	7.4.1.3 Green alga (Flufenoxuron degradate, Reg. No. 102 719)

	percentage of animals showing adverse effects	
Results test substance		
4.1.3.	Initial concentrations of test substance	The analyzed concentrations ranged from 98.9% to 100% of nominal at the beginning and from 101% to 104% at the end of the test. Therefore the results are based on nominal concentrations.
4.1.4.	Actual concentrations of test substance	See 4.1.4.
4.1.5.	Growth curves	See Table 7.4.1.3/141
4.1.6.	Concentration / response curve	See Table 7.4.1.3/141
4.1.7.	Cell concentration data	See Table 7.4.1.3/141
4.1.8.	Effect data (cell multiplication inhibition)	See Table 7.4.1.3/141
4.1.9.	Other observed effects	None
Results of controls		See Table 7.4.1.3/141
Test with reference substance		Not performed
4.1.10.	Concentrations	Not applicable
4.1.11.	Results	Not applicable

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1.	**Materials and methods**	Green alga was exposed for 72-h to a test substance as described under 3.1. The test procedure is detailed under 3.4.
5.2.	**Results and discussion**	Biological results: No significant inhibition of biomass and growth rate was observed. The relative biomass and growth inhibition values at different concentrations of Reg. No. 102719 are depicted below [see

Section A7.4.1.3	**Growth inhibition test on algae**
BPD Annex Point IIA, VII.7.3	7.4.1.3 Green alga (Flufenoxuron degradate, Reg. No. 102 719)

		Table 7.4.1.3/141].	
5.2.1.	NOE_rC	Not determined	
5.2.2.	E_{r50}	> 100 µg a.s./L	X
5.2.3.	E_bC_{50}	> 100 µg a.s./L	X
5.3.	**Conclusion**	In a 72-hour algae test with Pseudokirchneriella subcapitata, the E_bC_{50} and E_rC_{50} of Reg. No. 102719 was determined to be > 100 mg/L.	
5.3.1.	Reliability	1	
5.3.2.	Deficiencies	No	

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	02/17/2005
Materials and Methods	Applicant's version is acceptable with the following amendment : 3.1 Test material : Reg. No. 102719
Results and discussion	Applicant's version is acceptable with the following amendments: 5.2.2 *ErC50 > 100 ~~µg~~* **mg** *a.s./L* 5.2.2 *EbC50 > 100 ~~µg~~* **mg** *a.s./L*
Conclusion	Applicant's version is acceptable.
Reliability	Applicant's version is acceptable. Reliability Index is 1.
Acceptability	Acceptable.
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*

Section A7.4.1.3	**Growth inhibition test on algae**
BPD Annex Point IIA, VII.7.3	7.4.1.3 Green alga (Flufenoxuron degradate, Reg. No. 102 719)

Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.4.1.3/141 Effect of Reg. No. 102719 (72 h) on the growth of the green alga *Pseudokirchneriella subcapitata*

Concentration [mg/L]	**Control**	**12.5**	**25**	**50**	**100**
Inhibition (biomass) [%] [1)]	0	1.18	3.6	-3.39	17.6
Inhibition (growth rate) [%] [1)]	0	0.73	0.44	-0.7	4.1
Endpoints [mg/L]					
E_bC_{50} (72 h)	> 100				
E_bC_{10} (72 h)	77.7				
E_rC_{50} (72 h)	> 100				
E_rC_{10} (72 h)	> 100				

1) Negative values indicate stimulated growth

Table 7.4.1.3/142 Validity criteria for algal growth inhibition test according to OECD Guideline 201

	Fulfilled	**Not fulfilled**
Cell concentration in control cultures increased at least by a factor of 16 within 3 days	**Yes**	
Concentration of test substance ≥80% of initial concentration during test	**Yes**	

Criteria for poorly soluble test substances	**Yes**	

Section A7.4.1.3	**Growth inhibition test on algae**
BPD Annex Point IIA, VII.7.3	7.4.1.3 Green alga (Flufenoxuron degradate, Reg. No. 4064702)

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**5) Jatzek H.-J. 2003** Reg. No. 4064702 (metabolite of BAS 307 I) - Determination of the inhibitory effect on the cell multiplication of unicellular green algae XXXX. unpublished XXXX	
1.2.	**Data protection**	Yes	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I.	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Yes, EEC 92/69 A V C 3, OECD 201, EPA 850.5400	
2.2.	**GLP**	Yes (laboratory certified by Landesanstalt fuer Pflanzenbau und Pflanzenschutz Rheinland-Pfalz, Mainz)	
2.3.	**Deviations**	No	
		3. MATERIALS AND METHODS	
3.1.	**Test material**		X
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	See chemical glossary	
3.1.3.	Purity	95%	
3.1.4.	Composition of Product	Not applicable	
3.1.5.	Further relevant properties	None	
3.1.6.	Method of analysis	HPLC-UV detection	
3.2.	**Preparation of TS solution for**	Not applicable	

Section A7.4.1.3	**Growth inhibition test on algae**
BPD Annex Point IIA, VII.7.3	7.4.1.3 Green alga (Flufenoxuron degradate, Reg. No. 4064702)

	poorly soluble or volatile test substances	
3.3.	**Reference substance**	No
3.3.1.	Method of analysis for reference substance	Not applicable
3.4.	**Testing procedure**	
3.4.1.	Culture medium	OECD 201 nutrient solution
3.4.2.	Test organisms	Unicellular fresh water green alga, *Pseudokirchneriella subcapitata* (Reinsch) Korshikov (syn.: *Selenastrum capricornutum* Prinz) SAG 61.81; source: Sammlung Algenkulturen Göttingen, Germany
3.4.3.	Test system	Static system (72 h); 7 test concentrations, each with 3 replicates plus a control and a solvent control with 5 replicates; daily assessments of growth
3.4.4.	Test conditions	pH 7.8 - 8.1; glass flasks; initial cell densities 1 x 10^4 cells/mL; temperature 23 °C ± 2 °C; continuous light at 60 µE/(m^2 x s) - 120 µE/(m^2 x s) at 400 nm - 700 nm. Concentration: Control, solvent control, 16, 31, 63, 125, 250, 500 and 1000 µg/L (nominal)
3.4.5.	Duration of the test	72-h
3.4.6.	Test parameter	Effect on biomass and growth rate after exposure over 72 hours
3.4.7.	Sampling	Test initiation and termination
3.4.8.	Monitoring of TS concentration	See 3.4.7
3.4.9.	Statistics	Descriptive statistics, linear regression analysis for determination of the EC_x-values

4. RESULTS

Limit Test	Not performed

Section A7.4.1.3	**Growth inhibition test on algae**
BPD Annex Point IIA, VII.7.3	7.4.1.3 Green alga (Flufenoxuron degradate, Reg. No. 4064702)

4.1.1.	Concentration	Not applicable	
4.1.2.	Number/ percentage of animals showing adverse effects	Not applicable	
Results test substance			
4.1.3.	Initial concentrations of test substance	The analyzed concentrations of the test item ranged from 81.5% to 94.6% of nominal at the beginning and from 68.9% to 99.9% at the end of the test. Therefore the results are based on nominal concentrations.	X
4.1.4.	Actual concentrations of test substance	See 4.1.4.	
4.1.5.	Growth curves	See Table 7.4.1.3/143	
4.1.6.	Concentration / response curve	See Table 7.4.1.3/143	
4.1.7.	Cell concentration data	See Table 7.4.1.3/143	
4.1.8.	Effect data (cell multiplication inhibition)	See Table 7.4.1.3/143	
4.1.9.	Other observed effects	None	
Results of controls		See Table 7.4.1.3/143	
Test with reference substance		Not performed	
4.1.10.	Concentrations	Not applicable	
4.1.11.	Results	Not applicable	

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1.	**Materials and methods**	Green alga was exposed for 72-h to a test substance as described under 3.1. The test procedure is detailed under 3.4.

Section A7.4.1.3	**Growth inhibition test on algae**
BPD Annex Point IIA, VII.7.3	7.4.1.3 Green alga (Flufenoxuron degradate, Reg. No. 4064702)

5.2.	**Results and discussion**	Biological results: The relative growth inhibition values at different concentrations of Reg. No. 4064702 are depicted below [see Table 7.4.1.3/143].
5.2.1.	NOE_rC	Not determined
5.2.2.	E_{r50}	107 µg/L
5.2.3.	E_bC_{50}	90 µg/L
5.3.	**Conclusion**	In a 72-hour algae test with *Pseudokirchneriella subcapitata*, the E_bC_{50} of Reg. No. 4064702 was determined to be 90 µg/L, the E_rC_{50} was 107 µg/L.
5.3.1.	Reliability	1
5.3.2.	Deficiencies	No

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	02/17/2005
Materials and Methods	Applicant's version is acceptable with the following amendment: 3.1 Test material : Reg. No. 4064702
Results and discussion	It should be noted that for smallest concentrations 0.016 and 0.031 $mg.L^{-1}$, concentrations measured are only 68.9 and 74.3% of nominal values. In spite of this, study will be considered as reliable because : - those percentages (68.9 and 74.3% of nominal values) are not far from 80% of nominal values, - these concentrations are the nearest to detection limit, - CE_{50} is > 0.063 $mg.L^{-1}$ which is the above nominal concentration well represented by measured concentration (85.9% of nominal values).
Conclusion	Applicant's version is acceptable.
Reliability	Applicant's version is acceptable. Reliability Index is 1.
Acceptability	Acceptable.
Remarks	
	COMMENTS FROM ...

Section A7.4.1.3	**Growth inhibition test on algae**
BPD Annex Point IIA, VII.7.3	7.4.1.3 Green alga (Flufenoxuron degradate, Reg. No. 4064702)

Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.4.1.3/143 Effect of Reg. No. 4064702 (72 h) on the growth of the green alga *Pseudokirchneriella subcapitata*

Concentration [µg/L]	**Control**	**Solvent control**	**16**	**31**	**63**	**125**	**250**	**500**	**1000**
Inhibition (biomass) [%] 1)	-8.45	0	-8.98	-11.1	4.61	92.4	101.3	101.7	101.9
Inhibition (growth rate) [%] 1)	-2.37	0	-1.02	-2.15	-0.19	64.2	150.4	156.9	161.9
Endpoints [µg/L]									
E_bC_{50} (72 h)	90								
E_bC_{10} (72 h)	66								
E_rC_{50} (72 h)	107								
E_rC_{10} (72 h)	70								

1) Negative values indicate stimulated growth

Table 7.4.1.3/144 Validity criteria for algal growth inhibition test according to OECD Guideline 201

	Fulfilled	**Not fulfilled**
Cell concentration in control cultures increased at least by a factor of 16 within 3 days	**Yes**	
Concentration of test substance ≥80% of initial concentration during test	**Yes**	

Criteria for poorly soluble test substances	**Yes**	

Section A7.4.1.4	**Inhibition to microbial activity (aquatic)**
BPD Annex Point IIA, VII.7.4, IIIA, VII.3	7.4.1.4 Activated Sludge – Respiration Inhibition Test

0.0	**Summary**	The only study reported for inhibition of respiration of activated sludge is the one of Lebertz & Yan (2001). This study is completely conform with OCDE Guideline 209 and is therefore considered as reliable. It can be retained as the **key study** for the endpoint : inhibition of respiration of activated sludge.

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**1) Lebertz H.,Yan Z. 2001** Flufenoxuron (BAS 307I): Activated sludge, respiration inhibition test XXXX. unpublished XXXX	
1.2.	**Data protection**	Yes	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I.	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Yes, OEC 209	X
2.2.	**GLP**	Yes (laboratory certified by Hessisches Ministerium fuer Umwelt, Landwirtschaft und Forsten, Wiesbaden)	
2.3.	**Deviations**	No	
		3. MATERIALS AND METHODS	
3.1.	**Test material**		
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	As given in section 2	
3.1.3.	Purity	99.2%	
3.1.4.	Composition of Product	Not applicable	
3.1.5.	Further relevant	None	

Section A7.4.1.4	**Inhibition to microbial activity (aquatic)**	
BPD Annex Point IIA, VII.7.4, IIIA, VII.3	7.4.1.4 Activated Sludge – Respiration Inhibition Test	
	properties	
3.1.6.	Method of analysis	Not applicable
3.2.	**Preparation of TS solution for poorly soluble or volatile test substances**	Not applicable
3.3.	**Reference substance**	Yes, 3.5 dichlorophenol. The reference item was applied at 5, 15 and 30 mg/L.
3.3.1.	Method of analysis for reference substance	No analysis
3.4.	**Testing procedure**	
3.4.1.	Culture medium	As described in OECD guideline
3.4.2.	Inoculum / test organism	Activated sludge from laboratory wastewater plants treating municipal sewage
3.4.3.	Test system	Assessment of the inhibitory effect of the test item on the oxygen consumption rate of aerobic micro-organisms (activated sludge) after short-term exposure of 180 min; the inoculum was aerated during the contact period; 1 replicate for test item and the abiotic control, 2 for the control and the reference item
3.4.4.	Test conditions	Temperature: 20 °C ± 2 °C; pH 7.85; 290 mL - 300 mL test vessels, 8 mL/vessel concentrated OECD medium
3.4.5.	Duration of the test	See 3.4.5 X
3.4.6.	Test parameter	Respiration inhibition
3.4.7.	Analytical parameter	None
3.4.8.	Sampling	Not applicable as no analysis
3.4.9.	Monitoring of TS concentration	See 3.4.9 X
3.4.10.	Controls	See 5.2 X
3.4.11.	Statistics	Descriptive statistic
	4. RESULTS	

Section A7.4.1.4	**Inhibition to microbial activity (aquatic)**	
BPD Annex Point IIA, VII.7.4, IIIA, VII.3	7.4.1.4 Activated Sludge – Respiration Inhibition Test	
Preliminary test	Not performed	
4.1.1. Concentration	Not applicable	
4.1.2. Effect data	Not applicable	
Results test substance		
4.1.3. Initial concentrations of test substance	Not applicable as no analysis	
4.1.4. Actual concentrations of test substance	See 4.1.3	
4.1.5. Growth curves	Not applicable. See 5.2	
4.1.6. Cell concentration data	Not applicable. See 5.2	
4.1.7. Concentration/ response curve	Not applicable. See 5.2	
4.1.8. Effect data	Not applicable. See 5.2	
4.1.9. Other observed effects	None	
Results of controls	Not applicable. See 5.2	
Test with reference substance	Performed	
4.1.10. Concentrations	The reference item was applied at 5, 15 and 30 mg/L.	
4.1.11. Results	See report	
	5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1. Materials and methods	Activated sludge was exposed to a test substance as described under 3.1. The test procedure is detailed under 3.4.	X
5.2. Results and discussion	No significant inhibition of respiration was measured up to the highest tested concentration of 1000 mg a.s./L (nominal).	
5.2.1. EC_{20}	See 5.2	
5.2.2. EC_{50}	>1000 mg a.s./L	
5.2.3. EC_{80}	See 5.2	

Section A7.4.1.4	**Inhibition to microbial activity (aquatic)**
BPD Annex Point IIA, VII.7.4, IIIA, VII.3	7.4.1.4 Activated Sludge – Respiration Inhibition Test

5.3.	**Conclusion**	The EC_{50} of Flufenoxuron in the activated sludge respiration inhibition test is >1000 mg a.s./L. Disturbances in the bio-degradation process of activated sludge are not to be expected if the test substance is correctly introduced into adapted wastewater treatment plants at low concentrations.
5.3.1.	Reliability	1
5.3.2.	Deficiencies	No

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	02/18/2005
Materials and Methods	Applicant's version is acceptable.
Results and discussion	Applicant's version is acceptable.
Conclusion	Applicant's version is acceptable.
Reliability	Applicant's version is acceptable. Reliability Index is 1 (study has retained as key study).
Acceptability	Acceptable
Remarks	No
	COMMENTS FROM DE
Date	7/07/09
Materials and Methods	2.1 Yes, OECD 209 3.4.5 See 3.4.3 3.4.9 See 3.4.3
Results and discussion	5.1 Activated sludge was exposed to a test substance. The test procedure is detailed under 3.4.
Conclusion	Applicant's version is acceptable.
Reliability	Applicant's version is acceptable.
Acceptability	Acceptable
Remarks	No

Section A7.4.3.1 Effects on aquatic organisms, further studies

BPD Annex Point IIIA, XIII.2.1 7.4.3.1 Prolonged toxicity [fish]

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**1) XXXX** Flufenoxuron (Cascade): An early life stage test with the fathead minnow Pimephales promelas (Rafinesque) XXXX unpublished XXXX	
1.2.	**Data protection**	No	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	No data protection claimed	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Yes, EPA 40 CFR Ch. I Part 798, EPA 40 CFR Part 796, EPA 40 CFR Part 797, OECD Guidelines for Testing of Chemicals (Draft Nov. 1988), American Society for Testing and Materials. Standard Guide for Conducting Early Life Stage Toxicity Tests with Fishes (E1241-88 1988)	
2.2.	**GLP**	Yes (laboratory certified by Department of Health of the Government of the United Kingdom, United Kingdom)	
2.3.	**Deviations**	No	
		3. MATERIALS AND METHODS	
3.1.	**Test material**		X
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	As given in section 2	
3.1.3.	Purity	97.6% ± 0.3 (1987), 97.6% (1988), 98.1% (1989)	
3.1.4.	Composition of Product	Not relevant	
3.1.5.	Further relevant properties	None	
3.1.6.	Method of analysis	HPLC-UV	
3.2.	**Preparation of TS**	Not applicable	

Section A7.4.3.1	**Effects on aquatic organisms, further studies**
BPD Annex Point IIIA, XIII.2.1	7.4.3.1 Prolonged toxicity [fish]

	solution for poorly soluble or volatile test substances		
3.3.	**Reference substance**	No	
3.3.1.	Method of analysis for reference substance	Not applicable	
3.4.	**Testing procedure**		
3.4.1.	Dilution water	See 3.4.	
3.4.2.	Test organisms	Fathead minnow (*Pimephales promelas*), embryos (newly fertilized); source: XXXX	
3.4.3.	Test system	Flow through system (34 d); 4 replicates of 30 embryos per test vessel. Embryos were placed in test vessels below the test media inlet, ensuring there was a flow of test item solution over the embryos. The flow rate was nominally 42 mL/min (± 5%)	
3.4.4.	Test conditions	Temperature 23.9 °C - 24.7 °C; pH 7.4 - 7.8; oxygen content 7.3 mg/L - 8.6 mg/L; photoperiod: 16 hours light: 8 hours dark	
3.4.5.	Duration of the test	34 days	
3.4.6.	Test parameter	NOEC, survival, mortality, toxic signs, body weight and length	
3.4.7.	Sampling	See 5.2	
3.4.8.	Monitoring of TS concentration	No	
3.4.9.	Statistics	Descriptive statistics, ANOVA followed by Student t-test for mean dry, wet weights and length ($\alpha = 0.05$).	
		4. RESULTS	
Limit Test		Not performed	X
4.1.1.	Concentration	Not applicable	X
4.1.2.	Number/ percentage of animals showing adverse effects	Not applicable	

Section A7.4.3.1	**Effects on aquatic organisms, further studies**
BPD Annex Point IIIA, XIII.2.1	7.4.3.1 Prolonged toxicity [fish]

4.1.3.	Nature of adverse effects	Not applicable
Results test substance		
4.1.4.	Initial concentrations of test substance	Control, 0.82 µg a.s./L (mean measured)
4.1.5.	Actual concentrations of test substance	The overall mean time-weighted average exposure concentration for the test item treatment was 0.82 µg a.s./L. Measured concentrations of the test item were within a range of 57% - 169% of the overall mean time-weighted average over the exposure period
4.1.6.	Effect data (Mortality)	See Table 7.4.3.1/145.
4.1.7.	Concentration / response curve	Not applicable as only one concentration
4.1.8.	Other effects	See Table 7.4.3.1/145.
Results of controls		
4.1.9.	Number/ percentage of animals showing adverse effects	See Table 7.4.3.1/145.
4.1.10.	Nature of adverse effects	See Table 7.4.3.1/145.
Test with reference substance		Not performed
4.1.11.	Concentrations	Not applicable
4.1.12.	Results	Not applicable

Section A7.4.3.1	**Effects on aquatic organisms, further studies**
BPD Annex Point IIIA, XIII.2.1	7.4.3.1 Prolonged toxicity [fish]

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1.	**Materials and methods**	*Pimephales promelas* (fathead minnow) at embryo stage was exposed for 34-d in a flow through system to a test substance as described under 3.1. The test procedure is detailed under 3.4.	
5.2.	**Results and discussion**	**Embryo and young fish survival was not impaired in the test item group when compared to the control group.** In the test item treatment group, the hatch started and ended nearly simultaneously with the control group. No test item-related effect was observed on the time to hatch in the concentration group. Test item-related toxic signs were not observed. Body weight and length were not statistically significantly reduced compared to the control group (Student t-test, $\alpha = 0.05$). The results are summarized in Table 7.4.3.1/145.	
5.2.1.	LC_0	Not applicable	
5.2.2.	LC_{50}	Not applicable	
5.2.3.	LC_{100}	Not applicable	
5.2.4.	NOEC	$\geq$ 0.82 µg a.s./L	
5.3.	**Conclusion**	In an early life stage study with Flufenoxuron on rainbow trout, an overall NOEC of $\geq$ 0.82 µg a.s./L based on mean measured concentrations was derived from the results.	
5.3.1.	Other Conclusions	None	
5.3.2.	Reliability	1	X
5.3.3.	Deficiencies	No	X

Section A7.4.3.1 Effects on aquatic organisms, further studies

BPD Annex Point IIIA, XIII.2.1 7.4.3.1 Prolonged toxicity [fish]

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	02/21/2005
Materials and Methods	2.3 Deviations : *Yes* Following relevant deviations should be noticed : 4.1.4. Initial concentrations of test substance : Only one concentration was tested in this test, while according to Guideline OCDE 210, number of concentrations should be at least 5, with a separating factor ≤ 3.2. Guideline indicates that it should be relevant, in some cases, to test **less than five concentrations, with smaller intervals between concentrations**, but that this choice **should be justified**. However, in this study, **only one concentration** was tested no justification is provided in the study for testing only one concentration. 3.1 Test material : Flufenoxuron
Results and discussion	4. Results Limit test : RMS proposes that this study should be considered as limit test with mean-measured concentration tested : 0.82 µg/L.
Conclusion	Applicant's summary is acceptable.
Reliability	See deviations above. Reliability Index is 2 (study has retained as key study).
Acceptability	Acceptable. Despite the deficiencies described above, the study is considered acceptable as the NOEC ≥ 0.82 µg/L is a worst case value.
Remarks	Errors in Table 7.4.3.1/2 are corrected in bold and underlined.
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*

Section A7.4.3.1 Effects on aquatic organisms, further studies

BPD Annex Point IIIA, XIII.2.1 7.4.3.1 Prolonged toxicity [fish]

Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.4.3.1/145 Early life stage test (34 d) of Flufenoxuron on fathead minnow (*Pimephales promelas*)

Concentration [µg a.s./L]	**Control**	**0.82**
Start of hatch [day]	3	3
End of hatch [day]	5	5
Mean larvae survival (34 d) [%]	90	95
Symptoms	none	none
Mean wet weight (34 d) [%] 1)	100	102.1
Total wet weight [g]	153.5	156.8
Mean body length [%]	100	98.8
Total length [cm] 1)	2.42	2.39
	Endpoints [µg a.s./L] mean measured	
NOEC (34 d)	0.82	

1) mean from 4 replicates

Table 7.4.3.1/146: Validity criteria for acute fish test according to OECD Guideline 203

	Fulfilled	**Not fulfilled**
Mortality of control animals <10%	**Yes**	
Concentration of dissolved oxygen in all test vessels > 60% saturation	**Yes**	
Concentration of test substance ≥80% of initial concentration during test	5.3.2.1 Yes	**Result is based on mean-measured concentration**

Criteria for poorly soluble test substances	**Yes**	

Section 7.4.3.2	**Effects on reproduction and growth rate of fish**
BPD Annex Point IIIA, XIII 2.2	7.4.3.2 – Fish life cycle

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**1) XXXX** Zebra fish (Danio rerio) static full life cycle test with sediment XXXX. unpublished XXXX	X
1.2.	**Data protection**	Yes	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I.	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Yes, OECD 210, OECD 219 Nagel R. (1986) Untersuchungen zur Eiproduktion beim Zebrabaerbling (Brachydanio rerio Ham.-Buch.) J. Appl. Ichtyol. 4 p. 173-181 Nagel R. (1998) Der vollstaendige Life Cycle Test (complete life cycle test CLC-test) mit dem Zebrabaerbling (Danio rerio vormals Brachydanio rerio) Entwurf. UBA-Texte 58/98: 166-175 Wenzel A. Schaefers C. (2000) Research efforts towards the development and validation of a test method for the identification of endocrine disrupting chemicals. Report to the EU DG 24 B6-7920/98/000015	
2.2.	**GLP**	Yes (laboratory certified by Ministerium fuer Umwelt, Raumordnung und Landwirtschaft des Landes Nordrhein-Westfalen, 40190 Duesseldorf)	
2.3.	**Deviations**	No	X
		3. METHOD	

Section 7.4.3.2	**Effects on reproduction and growth rate of fish**
BPD Annex Point IIIA, XIII 2.2	7.4.3.2 – Fish life cycle

3.1.	**Test material**		X
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	See below	
3.1.3.	Purity	100 g/l	
3.1.4.	Composition of Product	Not a biocidal product, therefore not relevant as data for support of the Annex I listing of flufenoxuron under Council Directive 98/8/EC.	
3.1.5.	Further relevant properties	None	
3.1.6.	Method of analysis	HPLC-UV	
3.2.	**Preparation of TS solution for poorly soluble or volatile test substances**	Not applicable	
3.3.	**Reference substance**	No	
3.3.1.	Method of analysis for reference substance	Not applicable	
3.4.	**Testing procedure**		
3.4.1.	Dilution water	Not applicable, one test concentration using a DC formulation	
3.4.2.	Test organisms	Zebra fish (*Danio rerio* Hamilton-Buchanan 1822), fertilized eggs, juveniles, pre-adult adults at the beginning of reproduction, age of parental fish: about 1.5 years, Origin of the strain used: West Aquarium GmbH, Bad Lauterberg, Germany. Test animals were reared in: XXXX.	
3.4.3.	Handling of embryos and larvae (OECD 210/212)	See 3.4.3	
3.4.4.	Test system	Static system with sediment, 4 test concentrations with 2 replicates (2 applications - 14 day-interval between treatments) plus a control with 4 replicates. Test duration 143 days.	

Section 7.4.3.2	**Effects on reproduction and growth rate of fish**
BPD Annex Point IIIA, XIII 2.2	7.4.3.2 – Fish life cycle

		Simultaneous treatment of fertilized eggs (group A), juveniles (group B) and nearly adult fish (group C) in separate compartments within the test aquaria. Test vessels: 260 L glass aquaria with a water column of 48 cm high and a layer of 3 cm artificial sediment. The aquaria were subdivided in three compartments for the three life stages. The number of fish introduced as (100) fertilized eggs were reduced to 50 at an age of 28 days (juveniles), fish were reduced to 30 at an age of 65 - 70 days (beginning of adult phase). After each reduction, fish were digitally photographed to estimate survival rates and fish lengths, after reduction to 30 individuals, beginning of spawning was recorded; egg production per female and fertilization rate was measured for at least 20 days. For the filial (F1) generation of each group, survival rates and growth until day 28 to 35 of age were observed.
3.4.5.	Test conditions	Temperature 24.5 °C - 27.0 °C, pH-values during study conduct: pH 6.6 - 8.3 (first 36 days), pH 5.3 - 7.7 (day 37 - 67), pH 5.0 - 7.7 (day 68 - 143), oxygen saturation 68% - 134%, total hardness 0.6 - 0.8 mmol/L, photoperiod 12 hours light: 12 hours dark. Artificial sediment according to OECD TG 219, organic carbon content: 2%
3.4.6.	Duration of the test	Life cycle of fish
3.4.7.	Test parameter(s)	Mortality, juvenile growth, spawning performance, fertilization rate, sex ratio.
3.4.8.	Examination / Sampling	See 3.4.3
3.4.9.	Monitoring of TS concentration	Yes, see 4.1.5.
3.4.10.	Statistics	Descriptive statistics ANOVA, followed by Williams's test to calculate NOECs and probit analysis to calculate EC_{50} and EC_{10} values

4. RESULTS

Range finding test	Not performed

Section 7.4.3.2	**Effects on reproduction and growth rate of fish**
BPD Annex Point IIIA, XIII 2.2	7.4.3.2 – Fish life cycle

4.1.1.	Concentrations	Not applicable
4.1.2.	Number/ percentage of animals showing adverse effects	Not applicable
4.1.3.	Nature of adverse effects	Not applicable

Results test substance

4.1.4.	Initial concentrations of test substance	Control, 0.15, 0.5, 1.5 and 4.5 µg a.s./L (nominal)
4.1.5.	Actual concentrations of test substance	With the presence of sediment, the study is a simulation of realistic dissipation of the test item, mimicking exposure following an initial loading resulting from a repeated spray application. **Water phase:** 2 h after the first application, the measured concentrations at all treatment concentrations were 65% - 77% of nominal concentrations, indicating rapid dissipation of the test item from the water column. The dissipation rates were very similar for most aquaria. 6 h after the fisrt application, the measured concentrations were in a range of 47% to 59% of the nominal concentrations, after 1 day 27% - 37% of nominal and after 2 days 16% - 25% of the nominal concentrations. 14 days after the first application, concentrations were below the limit of quantification, except at 4.5 µg a.s./L, at which 3% of the nominal concentration was determined. Dissipation after the second application was more rapid than after the first. Whereas the solutions were analytically confirmed about 10% higher than for the first application, mean values after 2 h, 6 h, 1 d and 2 d decreased to 66%, 44%, 19% and 13%, respectively. After 14 days, 2% remained in the water column of the highest treatment vessels, and after 56 days (70 days after first treatment) the test item was no longer detectable in the water column of even the highest initial concentration. After 2 h of the additional Group C experiment with nominally 0.15 and 4.5 µg a.s./L, analytically detected concentrations

Section 7.4.3.2	**Effects on reproduction and growth rate of fish**
BPD Annex Point IIIA, XIII 2.2	7.4.3.2 – Fish life cycle

		ranged from 65% to 68% of nominal, at later sampling dates the dissipation was 53% - 55% after 6 h, 30% - 38% after 1 d, 12% after 4 d and 6% - 2% after 14 d. During the second application a dosing error resulted in the application of a quantity of the test item that was higher than scheduled by a factor of two. This was 105% for 0.15 µg a.s./L and 90% at 4.5 µg a.s./L (resulting from the limited water solubility of Flufenoxuron). Thus, results are based on initial nominal concentrations. **<u>Sediment phase:</u>** Sediment concentrations increased steadily during the first 6 weeks (4 weeks after the second treatment) up to 4 µg test item equivalents per kg dry sediment. At test termination, concentrations had decreased by 50%. The decrease was mainly for the extractable fraction, whereas the non-extractable fraction increased up to 50% of the residues analyzed at test termination. From day 7 to test termination, the sediment contained between 30% and 50% of the total amount of test item equivalents applied	X
4.1.6.	Effect data	See Table 7.4.3.2/147.	
4.1.7.	Concentration / response curve	See Table 7.4.3.2/147.	
4.1.8.	Other effects	See 5.2	
Results of controls			
4.1.9.	Number/ percentage of animals showing adverse effects	See Table 7.4.3.2/147.	
4.1.10.	Nature of adverse effects	See Table 7.4.3.2/147.	
Test with reference substance		Not performed	
4.1.11.	Concentrations	Not applicable	
4.1.12.	Results	Not applicable	

Section 7.4.3.2	**Effects on reproduction and growth rate of fish**
BPD Annex Point IIIA, XIII 2.2	7.4.3.2 – Fish life cycle

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1.	**Materials and methods**	Danio rerio (zebra fish) were exposed for a life cyle in a static system to a test substance as described under 3.1. The test procedure is detailed under 3.4.
5.2.	**Results and discussion**	Survival and growth: At the tested concentrations, no effect on survival of any life stage of zebra fish, parental or filial, could be observed. Growth was not affected in any of the treatments. Reproduction. No effect on individual reproduction expressed as eggs per female and day and fertilisation rate could be observed. In Group C, sub-optimal test conditions led to decreased hatch at all treatment levels. This lead to inconsistent data on the fertilization rates. In the additional experiment, exposure of adults comprising reproduction and exposure of the filial early life stage did not confirm any reduction of fertilization rates and resulted in high ELS survival rates (above 70%), irrespective of the treatment level. Survival rates of later stages were above 90% except for few small deviations which were considered not to be test item related. Growth resulted in very similar lengths and weights of comparable life-stages of all groups tested at each time-point during the in-life assessment period. Spawned egg numbers were comparable to flow-through studies. Fertilization rates of all groups were above 90%. The results are summarized in Table 7.4.3.2/147.
5.2.1.	NOEC	≥ 1.199 µg a.s./L (mean measured concentration)
5.2.2.	LOEC	Not applicable
5.3.	**Conclusion**	In a higher tier full life-cycle study with zebra fish performed under static conditions including sediment an overall NOEC of ≥ 1.199 µg a.s./L (mean measured concentration) was determined.
5.3.1.	Other Conclusions	None
5.3.2.	Reliability	1
5.3.3.	Deficiencies	No

Section 7.4.3.2 **Effects on reproduction and growth rate of fish**

BPD Annex Point IIIA, XIII 2.2 7.4.3.2 – Fish life cycle

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	02/28/2005
Materials and Methods	Applicant's summary is acceptable, except for the following point : 3.1 Test material : Preparation Flufenoxuron 100 DC (100 g s.a./L) 2.3 Deviations : *Yes* This study was performed in static system with sediment during more than 140 days. Therefore, test conditions are nearer from environmental conditions but very far from test conditions recommended in guidelines, hence interpretation can not be performed the same way. 4.1.5 Actual concentrations of test substance: *Thus, results are based on initial nominal concentrations.* **NOEC was calculated with mean-measured values of the maximal concentration tested (4.5 µg/L nominal – 1.199µg/L mean-measured). Details are presented in DXXXX(Annex 2 of IIIA 7.6).**
Results and discussion	Applicant's summary is acceptable.
Conclusion	Applicant's summary is acceptable.
Reliability	See deviation above. Reliability index is 2.
Acceptability	Acceptable
Remarks	**1/** The following addition should be done to the title of the study in "1.1. Reference" : *Flufenoxuron 100 DC (BAS 307 10 I):* Zebra fish (Danio rerio) static full life cycle test with sediment. **2/** Given that the assay is not done only with water but also with sediment, this test is more likely to be considered as a mesocosm study than a classic bioassay.
	COMMENTS FROM ... *(specify)*
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*

Section 7.4.3.2	**Effects on reproduction and growth rate of fish**
BPD Annex Point IIIA, XIII 2.2	7.4.3.2 – Fish life cycle

Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.4.3.2/147 Higher tier full life-cycle test with zebra fish (*Danio rerio*)

Concentration (nominal) [µg a.s./L]	**Control**	**0.15**	**0.5**	**1.5**	**4.5**
Fish exposed as fertilized eggs - Group A					
End of early life stage period - day 28					
Survival rate (%)	78.0	76.4	71.4	77.9	76.0
Length (cm)	1.194	1.176	1.177	1.152	1.159
End of juvenile growth period - day 69					
Length (cm)	2.588	2.618	2.661	2.642	2.567
Pseudo-specific growth (cm) - between days 28 and 69	1.420	1.437	1.467	1.479	1.415
Reproductive success of Group A fish - between day 78 and 101					
Start of spawning on day	70	70	70	70	70
Eggs per day and female	25.6	24.7	32.6	31.5	44.4
Fertilization rate (%)	94.4	95.8	92.6	93.4	93.0
Results of finale investigation of parental group A fish - day 141					
Length (cm)	3.819	3.805	3.858	3.883	3.883
Weight (g)	0.647	0.625	0.673	0.635	0.633
Sex ratio: females (%)	71.9	66.7	70.0	69.0	70.0
Results of early life stage period of 35 days old filial group A fish - day 143					
Survival rate (%)	73.2	71.0	75.1	76.5	80.2
Length (cm)	1.354	1.407	1.339	1.350	1.382
Weight (g)	0.055	0.060	0.051	0.053	0.051
Fish exposed as juveniles- Group B					
End of juvenile growth period (65 days old fish) - day 30					
Length (cm)	2.577	2.563	2.462	2.518	2.491
Pseudo-specific growth (cm) - between days 28 and 65	1.335	1.293	1.206	1.274	1.243
Reproductive success of Group B fish (66 - 97 days old) - between day 31 and 62					
Eggs per day and female	34.6	23.3	41.2	29.9	36.3
Fertilization rate (%)	95.9	95.4	95.4	94.8	93.1
Results of finale investigation of parental group B fish (119 days old) - day 106					
Length (cm)	3.712	3.704	3.659	3.684	3.690
Weight (g)	0.532	0.523	0.497	0.511	0.521
Sex ratio: females (%)	41.8	56.9	43.1	45.5	48.3
Results of early life stage period of 35 days old filial group B fish - day 112					
Survival rate (%)	86.7	88.4	81.9	87.9	90.3

Table 7.4.3.2/147 Higher tier full life-cycle test with zebra fish (*Danio rerio*)

Concentration (nominal) [µg a.s./L]	**Control**	**0.15**	**0.5**	**1.5**	**4.5**
Length (cm)	1.303	1.381	1.365	1.307	1.300
Weight (g)	0.046	0.053	0.053	0.044	0.044
Fish exposed as pre-adults - Group C					
Reproductive success of Group C fish (87 - 123 days old) - between day 2 and 38					
Start of spawning on day	3.8	2.5	2.0	2.0	2.5
Eggs per day and female	26.1	29.1	36.3	29.2	26.1
Fertilization rate (%)	92.8	89.6	95.7	91.5	87.5
Results of finale investigation of parental Group C fish (184 days old) - day 99					
Length (cm) - day 15	1.977	2.050	2.063	2.108	2.124
Length (cm) - day 99	3.888	3.927	3.824	3.863	3.888
Weight (g) - day 99	0.676	0.658	0.618	0.674	0.666
Sex ratio: females	54.0	58.7	56.0	63.2	67.8
Results of early life stage period of 21 days old filial Group C fish - days 50 and 72					
1. Survival rate (%) - day 50	44.7	64.5	57.8	43.5	58.3
2. Survival rate (%) - day 72	49.2	63.4	36.8	48.1	20.6

Additional experiment Group C fish [1)]			
Concentration (nominal) [µg a.s./L]	**Control**	**0.15**	**4.5**
Reproductive success of Group C fish- observed 1 - 20 days after first exposure			
Eggs per day and female	34.7	28.6	34.5
Fertilization rate (%)	94.7	93.7	95.0
Results of finale investigation of parental Group C fish (28 days old) - day43 after first exposure			
Survival rate (%)	77.6	86.2	93.6
Length (cm)	1.113	1.035	1.199
Weight (g)	0.036	0.032	0.041

1) Parts of the Group C exposure were repeated, since maternal transfer of accumulated substance to yolk potentially is most severe for fish reproducing during or shortly after application

Validity criteria for fish tests according to OECD Guidelines 210/212 & Validity criteria for fish test according to OECD Guideline 215

This study was conducted according to OECD 219 for which all criteria were fulfilled.

Section A7.4.3.3.1	**Bioconcentration in aquatic organisms**
BPD Annex Point IIIA, XIII.2.3	7.4.3.3.1 Fish

0.0 Justification of the key study

The endpoint studied in those tests is bioconcentration of flufenoxuron by organisms.

Three studies are submitted for this endpoint (4 references).

The third one (Junker, 2004) is a microcosm study with two applications of test item, in static conditions. Reliability index of this test is 3.

Oncorhynchus mykiss

The two other studies are dedicated to bioconcentration of **Flufenoxuron** (BAS 307 I) by *Oncorhynchus mykiss*. They are standard bioaccumulation studies, realised according to GLP and in accordance with OECD Guideline 305.

Both of them have reliability index of 2.

On the one hand, in the study of XXXX), two concentrations were tested. Bioconcentration factors in the whole fish were 15700 and 16130.

On the other hand, XXXX, XXXX) did not test two concentrations but bioconcentration factors were obtained with two different radiolabelling. Bioconcentration factors were 25920 and 24187 in whole fish, 19504 and 18426 in edible tissue, 34351 and 32116 in inedible tissue.

It was considered that highest bioconcentration factors in whole fish should be retained as key values. Therefore, RMS proposes to retain as key study XXXX, XXXX) test.

Section A7.4.3.3.1 Bioconcentration in aquatic organisms

BPD Annex Point IIIA, XIII.2.3 7.4.3.3.1 Fish

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**1) XXXX** Flufenoxuron: The accumulation and elimination by rainbow trout (Oncorhynchus mykiss) in a continuous flow test XXXX unpublished XXXX	
1.2.	**Data protection**	No	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	No data protection claimed	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Yes, study based on OECD 305E	
2.2.	**GLP**	Yes (laboratory certified by Department of Health of the Government of the United Kingdom, United Kingdom)	
2.3.	**Deviations**	No	X
		3. MATERIALS AND METHODS	
3.1.	**Test material**		
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	As given in section 2	
3.1.3.	Purity	> 97%	
3.1.4.	Further relevant properties	None	
3.1.5.	Radiolabelling	Not applicable	
3.1.6.	Method of analysis	Macerated fish was mixed with Na2SO4 and extracted with acetone/hexane (1 + 2 v/v) on a steam bath. The extract was decanted, fat was removed by partition with acetonitrile, followed by a clean-up on silica extraction cartridges and a clean-up on reversed phase HPLC. The content of Flufenoxuron was determined by HPLC with UV-detection.	
3.2.	**Reference substance**	No	

Section A7.4.3.3.1	**Bioconcentration in aquatic organisms**
BPD Annex Point IIIA, XIII.2.3	7.4.3.3.1 Fish

3.2.1.	Method of analysis for reference substance	Not applicable
3.3.	**Testing/estimation procedure**	
3.3.1.	Test system/ performance	Flufenoxuron was coated onto glass beds (1.5 mm dia, 1.5 kg) by addition of an acetone solution to the beds in a glass beaker. The acetone was removed by purging with nitrogen. The beds were transferred to a glass column (ca. 50 cm length, 7 cm I.D) that was incorporated into a flow through system. The high dose rate was obtained directly from the column and was close to saturation as could be achieved with a flow-through system (0.71 µg/l at 15 °C, pH 7). The concentration of the test item in the high dose aquarium averaged 0.31 µg/l over the accumulation period. Aerated water was used for dilution (1:10) of the saturated Flufenoxuron-solution for the low-dose aquarium. The concentration of the test item in the low dose aquarium averaged 0.31 µg/l over the accumulation period. The flow through in each aquarium was ca. 21 litres per hour, dechlorinated water, hardness typically 260 – 300 ppm, pH 7.1 – 7.8. **The two accumulation aquaria were each stocked with ca.100 fishes for an accumulation phase of ca. 19 days. Four fishes were removed for analysis at each time point. The accumulation phase continued until the analysis of fish indicated that a steady state was being approached.** Subsequently, fish were moved into new aquaria and exposed to a continuous flow of clean water for 50 days. Analysis of further fish samples during the elimination period enabled the decline in Flufenoxuron residues to be determined.

Section A7.4.3.3.1 **Bioconcentration in aquatic organisms**

Annex Point IIIA, XIII.2.3 7.4.3.3.1 Fish

		4. RESULTS
4.1.	**Experimental data**	
4.1.1.	Mortality/behaviour	See 5.2 below
4.1.2.	Lipid content	
4.1.3.	Concentrations of test material during test	
4.1.4.	Bioconcentration factor (BCF)	
4.1.5.	Uptake and depuration rate constants	
4.1.6.	Depuration time	
4.1.7.	Metabolites	
4.1.8.	Other Observations	
4.2.	**Estimation of bioconcentration**	See 5.2 below
		5. APPLICANT'S SUMMARY AND CONCLUSION
5.1.	**Materials and methods**	Flufenoxuron, as described under 3.1, was tested on fish as procedure detailed in 3.3
5.2.	**Results and discussion**	**When trouts were continuously exposed to concentrations of 0.04 ± 0.1 and 0.31 ± 0.04 µg/l Flufenoxuron in water, residues in whole fish increased rapidly towards calculated equilibrium concentrations of 0.6 and 5.0 µg/g wet weight (21.5 and 227 µg/g lipid weight).** The following data were calculated for whole fish (mean values): BCF: ca. 16000 t_{p95}: ca. 48 days t_{50}: ca. 11 days. The data for whole fish and lipids are summarized in Table 7.4.3.3.1/148.
5.3.	**Conclusion**	Fish were exposed to Flufenoxuron at a nominal exposure level of 0.04 µg/l and 0.31 µg/l for 19 days. After termination of the exposure, radioactivity levels in whole fish decreased with a half-life of 11 days.

Section A7.4.3.3.1	**Bioconcentration in aquatic organisms**	
Annex Point IIIA, XIII.2.3	7.4.3.3.1 Fish	
	Bioconcentration factors in whole fish were 15700 and 16130 for the low dose and the high dose, respectively.	
5.3.1. Reliability	1	X
5.3.2. Deficiencies	No	

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	03/03/2005
Materials and Methods	Applicant's summary is acceptable with the following amendments : 2.3 Deviations : *Yes* In study report (page 17), it is written concerning the lipid data that "The estimates of the bioconcentration factor differ by 27% between the low dose an the high dose experiments" and that "this may result from experimental variability". This should be considered as a deviation because OECD Guideline 305 recommend a variability less than 20%. The duration of the exposure is insufficient to reach the accumulation plateau. Given that, study results should be considered as "reliable with restrictions".
Results and discussion	Applicant's summary is acceptable.
Conclusion	Applicant's summary is acceptable.

Section A7.4.3.3.1 **Bioconcentration in aquatic organisms**

Annex Point IIIA, XIII.2.3 7.4.3.3.1 Fish

Reliability	See deviation above. Reliability Index is 2.
Acceptability	See above.
Remarks	No other.
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Findings	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.4.3.3.1/148 Kinetic parameters for Flufenoxuron in rainbow trout (*Oncorhynchus mykiss*)

Parameter	**DOSE [µG/L]**			
	0.04		0.31	
	Whole fish	Lipids	Whole fish	Lipids
Uptake rate constant k_1 [~~ml~~.g^{-1}.day^{-1}]	1.01	38.1	0.97	43.6
Depuration rate constant k_2 [day^{-1}]	0.06	0.07	0.06	0.06
Bioconcentration factor ($BCF_k = k_1/k_2$)	15700	538400	16130	733100
Time to reach 95% of plateau, t_{p95} [days]	46.6	42.4	49.9	50.3
Depuration half-life t_{50} [days]	10.8	9.8	11.6	11.6

Section A7.4.3.3.1 Bioconcentration in aquatic organisms

BPD Annex Point IIIA, XIII.2.3 7.4.3.3.1 Fish

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**2) XXXX)** Bioaccumulation and metabolism of 14C-BAS 307 I (Flufenoxuron) in Rainbow Trout XXXX unpublished XXXX	
1.2.	**Data protection**	Yes	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I.	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Yes, OECD 305, EPA OPPTS 850. 1730	
2.2.	**GLP**	Yes (laboratory certified by Department of Health of the Government of the United Kingdom, United Kingdom)	
2.3.	**Deviations**	No	X
		3. MATERIALS AND METHODS	
3.1.	**Test material**		
3.1.1.	Lot/Batch number	[Fluoroaniline-ring-U-^{14}C] BAS 307 I [Fluoroaniline-ring-U-^{14}C]-Reg. No. 243154, XXXX, radiochemical purity > 99% [Difluorobenzamide-ring -U-^{14}C] BAS 307 I [difluorobenzamide-ring -U-^{14}C]-Reg. No. 243154, XXXX, radiochemical purity > 99% [Difluoroamide carbonyl-^{13}C] BAS 307 I [Difluoroamide carbonyl-^{13}C] Reg. No. 243154, XXXX, chemical purity 98% Unlabelled: XXXX, purity 99.3%	

Section A7.4.3.3.1	**Bioconcentration in aquatic organisms**
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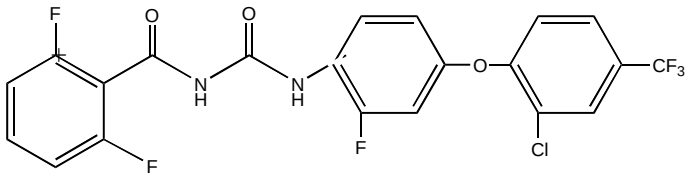
3.1.2.	Specification	As given in section 3.1.1.
3.1.3.	Purity	See 3.1.1.
3.1.4.	Further relevant properties	None
3.1.5.	Radiolabelling *, #	 + denotes ^{14}C fluoroaniline-label * denotes ^{14}C difluorobenzamide-label # denotes ^{13}C-label
3.1.6.	Method of analysis	See report
3.2.	**Reference substance**	No
3.2.1.	Method of analysis for reference substance	Not applicable
3.3.	**Testing/estimation procedure**	
3.3.1.	Test system/ performance	Test Species: Rainbow Trout (*Oncorynchus mykiss*) Supplier: XXXX Weight: ca. 0.7 (0.56 - 0.81) g / Length: 35.1 - 43.0 mm (day 0) (bioconcentration) Weight: ca. 5.7 g (secondary tank for metabolism investigations) Test design: Flow-through system Test concentration: 40 ng a.s./L Test conditions: In the experiments, the test substance concentration was provided using

Section A7.4.3.3.1 **Bioconcentration in aquatic organisms**

BPD Annex Point IIIA, XIII.2.3 7.4.3.3.1 Fish

stock solutions of each radiolabelled form of [^{14}C]-Flufenoxuron prepared in acetone at a target concentration of 396 ng.ml^{-1}. The fluoroaniline labelled form was used without radio-isotopic dilution. In order to assist in structural elucidation, difluorobenzamide labelled [^{14}C]-Flufenoxuron was combined with [^{13}C]-Flufenoxuron in a 1:1 ratio in acetone prior to use. The final specific activities were as follows:

Fluoroaniline-labelled Flufenoxuron = 233400 d.p.m.µg^{-1} equiv.

Difluorobenzamide-labelled Flufenoxuron = 227442 d.p.m.µg^{-1} equiv.

Reconstituted water was mixed with a continuous flow of the acetone stock solution to deliver a nominal concentration of 40 ng a.s./L. The water flowed through each tank of 90 L size at a rate of about 430 L/day (equivalent to a approx. 5 fold water exchange per day). To optimise dissolution of the test item in the dilution water, the tanks were heavily aerated throughout the water column. Three linked aeration devices were placed in the centre of the each tank and acted to distribute water from the lower regions of the tank towards the surface. The apparatus was calibrated to deliver stock and provide a dilution of the stock solution by *ca* 1:10000.

Test fish of ca. 0.7 g size (ca. 200 for each label at day 0) were exposed for a 60 day period followed by a 56 day depuration period in the absence of test substance. The effluent of the tanks were channelled directly into a secondary tank that contained contingency fish for potential isolation of metabolites. This secondary tank was loaded with about 50 fish of approx. 5.7 g size at the beginning of the test. A control experiment was conducted where fish were exposed to acetone and diluent water alone.

Sampling Periods

Five fish were removed from each primary tank on Days 0, 1, 2, 4, 6, 10, 20, 30, 40, 45, 50, 55 and 60 of the uptake phase for analysis of total radioactivity. Four fish were sampled on Days 1, 2, 4, 6, 8, 12, 24, 48 and 56 of depuration for analysis of total radioactivity.

Fifteen fish were sampled from the primary tanks with each radiolabelled form on Days 30 and 60 of the uptake phase for investigations into the nature of the radioactivity. All the fish were sampled from the secondary tanks on Day 60 of the uptake phase as contingency material to support investigations into the nature of the radioactivity.

Ten fish were sampled from the control tank on selected time points of the uptake phase for analysis of lipid content.

Work Up

After sampling, fish were killed and separated into edible tissue (muscle) and inedible tissue (viscera).

3.3.2. Estimation of bioconcentration

Biokinetic Modeling:

Concentrations of radioactivity in whole fish and tissue fractions and

Section A7.4.3.3.1	**Bioconcentration in aquatic organisms**
BPD Annex Point IIIA, XIII.2.3	7.4.3.3.1 Fish

mean concentrations of radioactivity in water were submitted to a Non-Linear-Regression Analysis using a 2-Compartment Model. The following parameters were calculated: uptake and depuration rate constants (k_1 and k_2), kinetic bioconcentration factors (BCF), the depuration half-life (t_{50}) and time to reach 90% depuration (t_{90}).

4. RESULTS

4.1.	**Experimental data**	
4.1.1.	Mortality/behaviour	See 5.2 below
4.1.2.	Lipid content	See 5.2 below
4.1.3.	Concentrations of test material during test	Analysis of total radioactive residues in water samples was taken daily. Due to experimental variations, the test substance concentration throughout the uptake phase ranged between 34 and 53 ng equiv.l^{-1}, in the experiment with the fluoroaniline label and between 34 and 51 ng equiv.l^{-1}, in the experiment with the difluorobenzamide label. The mean exposure concentrations were 42 ng equiv.l^{-1} in each case. The measured variations of the test substance concentrations are acceptable due to guideline requirements. The principal radioactive component in water sampled throughout the uptake phase was unchanged Flufenoxuron.
4.1.4.	Bioconcentration factor (BCF)	See Table 7.4.3.3.1/149.
4.1.5.	Uptake and depuration rate constants	See Table 7.4.3.3.1/149.
4.1.6.	Depuration time	See Table 7.4.3.3.1/149.
4.1.7.	Metabolites	See Table 7.4.3.3.1/149.
4.1.8.	Other Observations	None
4.2.	**Estimation of bioconcentration**	See Table 7.4.3.3.1/149.

Section A7.4.3.3.1 Bioconcentration in aquatic organisms

BPD Annex Point IIIA, XIII.2.3 7.4.3.3.1 Fish

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1. Materials and methods

Flufenoxuron, as described under 3.1, was tested on fish as procedure detailed in 3.3

5.2. Results and discussion

Mean tissue concentrations determined in edible, inedible and whole fish at the end of the uptake phase were 640.2, 977.5 and 792.7 ng equiv.g^{-1} for the fluroaniline label. The corresponding values for the difluorobenzamide label were 630.0, 977.0 and 771.7 ng equiv.g^{-1} respectively.

Biokinetic parameters derived from 2-Compartment Modelling Analysis are summarised in [see Table 7.4.3.3.1/149]. The depuration half-life in whole fish was 21 days. Accordingly, the time to reach 90% clearance (t_{90}) is about 64 - 75 days. Bioconcentration factors obtained by kinetic modelling were about 19000 (edibles) to 33000 (inedibles) and accounted for approximately 25000 in the whole fish. There were no obvious differences in the kinetics of uptake or depuration between the 2 sites of radiolabel. The fit of the model was acceptable (Correlations coefficients are 0.87 - 0.94; Coefficient of variation for k_1 and k_2 are 5.09 % - 11.02 %).

The extractability of the radioactivity in fish was high and accounted for > 90 % in general. All the extracts after 30 and 60 days exposure, from each tissue and each site of radiolabel contained a single radioactive peak. This showed chromatography consistent with unchanged Flufenoxuron in both reversed and normal phase HPLC systems. Therewith it could be demonstrated that Flufenoxuron is metabolically stable in the tested species.

5.3. Conclusion

Fish were exposed to Flufenoxuron at a nominal exposure level of 40 ng a.s./L, for 60 days. After termination of the exposure, radioactivity levels in whole fish decreased with a half-life of 21 days. Bioconcentration factors in whole fish were 25920 and 24187 for the Fluoroaniline label and the Difluorobenzamide label, respectively. Flufenoxuron was metabolically stable in trout. No marked differences between the two sites of radiolabel were observed.

5.3.1. Reliability 1 X

5.3.2. Deficiencies No

Evaluation by Competent Authorities
Use separate "evaluation boxes" to provide transparency as to the comments and views submitted

Section A7.4.3.3.1	**Bioconcentration in aquatic organisms**
BPD Annex Point IIIA, XIII.2.3	7.4.3.3.1 Fish

	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	03/03/2005
Materials and Methods	Applicant's summary is acceptable with the following amendments : 2.3 Deviations : *Yes* Only one concentration tested. This should be considered as a deviation because OECD Guideline 305 recommend to test at least 2 different concentrations so that results can be compared and confirm each other. However, it should be noticed that results obtained with two different radiolabelling can be compared and that they are very close. Given that, study results should be considered as "reliable with restrictions".
Results and discussion	Applicant's summary is acceptable.
Conclusion	Applicant's summary is acceptable.
Reliability	See deviation above. Reliability Index is 2 (study has retained as key study).
Acceptability	See above.
Remarks	Given that both studies have reliability index of 2 and that this test presents higher bioconcentration factors, this study is retain as **key study**.

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Findings	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.4.3.3.1/149 Kinetic parameters

Parameter	Tissue Fraction					
	Fluoroaniline label			Difluorobenzamide label		
	Edible Tissue	Inedible Tissue	Whole Fish	Edible Tissue	Inedible Tissue	Whole fish
Uptake rate constant k_1 [$ml.g^{-1}.day^{-1}$]	659.71	1059.57	846.90	663.19	1007.16	809.6
Depuration rate constant k_2 [day^{-1}]	0.03	0.03	0.03	0.04	0.03	0.03
Bioconcentration factor ($BCF_k = k_1/k_2$)	19504	34351	25920	18426	32116	24187
$BCF_{TRR\ (after\ 60\ days)}$	15243	23274	18874	15000	23262	18374
$BCF_{k,}$ expressed on a lipid basis	722400	715700	700500	682400	669100	653700
Depuration half-life t_{50} [days]	20	22	21	19	22	21
Time to reach 90% depuration, t_{90} [days]	68	75	70	64	73	69

Section A7.4.3.3.1 Bioconcentration in aquatic organisms

BPD Annex Point IIIA, XIII.2.3 7.4.3.3.1 Fish

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**3) XXXX** Bioaccumulation of BAS 307 I (Flufenoxuron) - applied as formulated product BAS 307 QA I - in an Aquatic Ecosystem XXXX. unpublished XXXX	
1.2.	**Data protection**	Yes	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. / b.p. for the purpose of its entry into Annex I.	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	No, description of the method is included in the report	
2.2.	**GLP**	Yes (laboratory certified by Landesamt fuer Umweltschutz und Gewerbeaufsicht, Mainz, Germany)	
2.3.	**Deviations**	No	X
		3. MATERIALS AND METHODS	
3.1.	**Test material**		
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	See below	
3.1.3.	Purity	Batch no. XXXX, containing 103 g/L (nominal 100 g/L) of the a.s.	
3.1.4.	Further relevant properties	None	
3.1.5.	Radiolabelling	Not applicable	
3.1.6.	Method of analysis	The test item concentrations and concentrations of the four main metabolites were analyzed using HPLC with UV-detection for water. Residues of the test item and the metabolites Reg.No.4064702 and Reg.No.241208 were analyzed using LC/MS for test organisms (see report).	
3.2.	**Reference substance**	No	

Section A7.4.3.3.1 **Bioconcentration in aquatic organisms**

BPD Annex Point IIIA, XIII.2.3 7.4.3.3.1 Fish

3.2.1.	Method of analysis for reference substance	Not applicable
3.3.	**Testing/estimation procedure**	
3.3.1.	Test system/ performance	Test species: Pisces: *Lepomis macrochirus*, juveniles obtained from Osage Catfisheries; animals about 13 month old delivered by BASF department of toxicology, GV/T. Mollusca: *Galba palustris* (Gastropoda) individuals collected from nearby natural water body, *Anodonta cygnea* (Bivalvia), obtained from "Zoomax" Mannheim. Arthropoda: *Asellus aquaticus* (Crustacea), individuals collected from nearby natural water body. Periphyton ("Aufwuchs") on glass plates. Macrophyta: *Myriophyllum verticillatum* (Dicotyledoneae), *Ceratophyllum demersum* (Dicotyledoneae), *Potamogeton crispus* (Monocotyledoneae) and *Chara* spec., all macrophytes obtained from "Aquaristik Harster", Speyer. Test design: Two applications, in an interval of two weeks; 2 concentrations (0.31 and 3.05 µg/L, nominal according 0.03 and 0.3 µg a.s. Flufenoxuron/L), each with two replicates plus a control with one replicate; each replicate contained: 30 *Lepomis macrochirus*; 54 *Galba palustris* in cages; *Myriophyllum verticillatum*, *Ceratophyllum demersum, Potamogeton crispus* and *Chara* spec. and 7 glass plates for periphyton. 150 individuals of *Asellus aquaticus* in cages were inserted in the basin of the control and the basins of the concentration of 0.03 µg a.s./L. Two additional basin with a test concentration of 0.03 µg a.s./L were used for testing *Anodonta cygnea*, 7 individuals in each basin. Only *Ceratophyllum demersum* and *Chara* sp. were inserted besides the mussels. Basins were assessed working daily (e.g. for fish mortality and visual symptoms). Test concentrations: Control, 0.03 and 0.3 µg a.s./L (nominal). Test conditions: Microcosm, stainless steel basins (0.96 m x 0.96 m x 0.6 m), about 2 cm natural sediment layer (sandy sediment with 0.6 % TC), about 50 cm natural water layer, pH 7.84 - 10.01, oxygen content 48.3% - 172.7%, total hardness 1.86 - 2.50 mmol/L, conductivity 276 - 670 µS/cm, water

Section A7.4.3.3.1	**Bioconcentration in aquatic organisms**
BPD Annex Point IIIA, XIII.2.3	7.4.3.3.1 Fish

		temperature 9.7 - 25.1 °C during the test, fish foraged on biota within basins, supplemented with zooplankton from nearby ponds. Statistics: Descriptive statistics
3.3.2.	Estimation of bioconcentration	Bioaccumulation factor
		4. RESULTS
4.1	**Experimental data**	
4.1.1	Mortality/behaviour	Not reported
4.1.2	Lipid content	Not reported
4.1.3	Concentrations of test material during test	Not reported
4.1.4	Bioconcentration factor (BCF)	See Table 7.4.3.3.1/149
4.1.5	Uptake and depuration rate constants	See Table 7.4.3.3.1/149
4.1.6	Depuration time	See Table 7.4.3.3.1/149
4.1.7	Metabolites	See Table 7.4.3.3.1/149
4.1.8	Other Observations	None
4.2	**Estimation of bioconcentration**	See Table 7.4.3.3.1/150
		5 APPLICANT'S SUMMARY AND CONCLUSION
5.1	**Materials and methods**	Flufenoxuron, as described under 3.1, was tested on fish as procedure detailed in 3.3
5.2	**Results and discussion**	Analytical measurements: Analytical verification of test item concentration was conducted in the stock solution of both applications by determination of the active ingredient Flufenoxuron. Furthermore, Flufenoxuron was determined in samples of basin water on DAT 0 (shortly after the first application), 2, 7, 14, 15 (shortly after the

Section A7.4.3.3.1 **Bioconcentration in aquatic organisms**

BPD Annex Point IIIA, XIII.2.3 7.4.3.3.1 Fish

second application), 16, 22, 29, 36, 50, 90 and 141 at the high concentration only. The same samples were used to determine additionally the four main degradation products, Reg.No.102719 (CL 211558), Reg.No.206925 (CL 245508), Reg.No.241208 (CL 359882) and Reg.No.4064702 (CL 932338). Only the concentrations of the 0.3 µg a.s./L treatment were determined, as the lowest tested concentration of 0.03 µg/L was below the LoQ of 0.05 µg a.s./L.

The concentration of the four main metabolites were all below LoQ (< 0.05 µg/L) during the complete course of the study.

The measured concentration of Flufenoxuron in the stock solution for the first application was 84.0% and for the second application 88.7%. Further the recovery of 92.0% in basin no. 3 and of 99.0% in basin no. 11 in the highest test concentration after the first application confirmed the correct application of the test item.

The analytical recoveries shows a rapid decrease of Flufenoxuron in the water phase. Flufenoxuron concentrations shortly before the second application were 19.3% in basin No. 3 and 34.1% in basin No. 11 of the initial concentration. Shortly after the second application recoveries of 163.6% in basin no. 11 and 215.2% in basin 3 could be determined in the highest tested concentration. The high recovery value in basin 3 is probably due to an inhomogenity shortly after the application, because one day later the recoveries of both basins were in the same range. Three months after the second application concentrations of Flufenoxuron were below the LoQ. Despite the double application of the insecticide, none of the four main metabolites could be detected in the water phase during the complete course of the study.

Biological results: In general the highest residue of Flufenoxuron in the tested organisms could be observed five days after the second application of the test item. With decreasing concentration of Flufenoxuron in the water phase over time a decrease of Flufenoxuron residues in the organisms could be observed. Only low amounts of the two metabolites Reg.No.4064702 (CL 932338) and Reg.No.241208 (CL 359882) could be determined in some organisms. Only in snails both metabolites could be observed in the high treatment group at the same time. In the second representative of Mollusca, the pond mussel, none of the two metabolites could be determined.

In representatives of primary producers, macrophytes and alga, and in periphyton only a low accumulation of Flufenoxuron could be observed in the highest tested concentration of 0.3 µg a.s./L. No accumulation occurred at a concentration of 0.03 µg a.s./L. The levels observed might dominantly be due to adsorption rather than accumulation.

In snails the bioaccumulation factor values of both tested concentrations were in a comparable range (see Table 7.4.3.3.1/150). In the tested crustacean no accumulation of the test item could be observed.

Fish showed the highest bioaccumulation of Flufenoxuron. Similar to the snails the bioaccumulation factor values for *Lepomis macrochirus* in both

Section A7.4.3.3.1	**Bioconcentration in aquatic organisms**
BPD Annex Point IIIA, XIII.2.3	7.4.3.3.1 Fish

		tested concentrations were in a comparable range (see Table 7.4.3.3.1/150). In comparison to the standard bioconcentration study with a resulting bioconcentration factor of about 18500 (BXXXX) and a mean bioconcentration factor of about 25100 (XXXX) the accumulation under realistic exposure was much lower. Furthermore, rapid elimination of Flufenoxuron was observed in fish and other organism groups. Accordingly, the observed bioaccumulation is largely due to bioconcentration. A significant accumulation along the food chain does not occur. Based on mean measured value of the highest recoveries in water of 0.568 µg a.s./L the bioaccumulation factors would be nearly two times lower in comparison to a nominal concentration of 0.3 µg a.s./L. For example the bioaccumulation factor for fish would be 695 instead of 1316 and for snail 131 instead of 249.	
5.3	**Conclusion**	Bioaccumulation factors for Flufenoxuron under more realistic exposure conditions allowing for combined uptake via medium (bioconcentration) plus potential accumulation via the food chain (biomagnification) are about 14 – 19 times lower than the bioconcentration factor in standard bioaccumulation study. This demonstrated that there is no additional concern for uptake of Flufenoxuron via food chain. In contrast, under more realistic exposure conditions, the maximum concentrations in the biota are much lower as compared to standard worst case laboratory conditions. At the end of the study only minor-, respectively residues below the LoQ of the active ingredient and of the metabolites Reg.No.4064702 (CL 932338) and Reg.No.241208 (CL 359882) could be determined. In addition a rapid decrease of the test item in water could be observed following each application. Three month after the second application the recoveries were below the LoQ of 0.05 µg a.s./L. During the complete course of the study none of the four main metabolites were detected in the water phase.	
5.3.1	Reliability	1	X
5.3.2	Deficiencies	No	X

Section A7.4.3.3.1	**Bioconcentration in aquatic organisms**
BPD Annex Point IIIA, XIII.2.3	7.4.3.3.1 Fish

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	03/03/2005
Materials and Methods	Applicant's summary is acceptable.
Results and discussion	Applicant's summary is acceptable.
Conclusion	5.3.2 Deficiencies : *Yes* **1/** Bioaccumulation studies should preferably be realised with continuous flow. **2/** In study report (page 7 of 68), it is written that "As the amounts of test item introduced into the basins were well documented and confirmed the correct application of test item, the biological results were based on nominal concentrations." It is true to say that amounts of test item confirmed the correct application but it must be noticed that measured concentrations are representatives of nominal concentrations only a few days after applications. In fact, only 19.3% of flufenoxuron is recovered before second application and concentration is below detection limit before the end of the test. Biological results should therefore not be based on nominal values but on measured concentrations. Given that, results of the study can not be considered as reliable.
Reliability	See deficiencies above. Reliability Index is 3.
Acceptability	Not acceptable.

Section A7.4.3.3.1	**Bioconcentration in aquatic organisms**
BPD Annex Point IIIA, XIII.2.3	7.4.3.3.1 Fish

Remarks	**1/** As no guidelines were applied, following amendment should be done to 2.3 Deviations : *Not applicable* **2/** As results are considered unreliable, whole summary of the study was not read
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Findings	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.4.3.3.1/150 Bioaccumulation factors for Flufenoxuron in different organism at nominal concentrations of 0.03 µg a.s./L and 0.3 µg a.s./L

Concentration	**Nominal** **0.03 µg a.s./L**	**Nominal** **0.3 µg a.s./L**
Organism	**Bioaccumulation factor**	
Lepomis macrochirus	1283 (mean)	1316 (mean)
Galba palustris	207	249
Anodonta cygnea	167	not tested
Asellus aquaticus	< LoD	not tested
Macrophytes (*Myriophyllum* verticillatum & *Ceratophyllum demersum)*	< LoD	50
Periphyton	< LoD	28

Section A7.4.3.3.2	**Bioconcentration in aquatic organisms**
BPD Annex Point IIIA, XIII.2.3	7.4.3.3.1 Invertebrate species if direct release on marine environment

	JUSTIFICATION FOR NON-SUBMISSION OF DATA	**Official use only**
Other existing data [ ]	**Technically not feasible [ ] Scientifically unjustified [X]**	
Limited exposure [ ]	**Other justification [ ]**	
Detailed justification:	Not required as no intention for direct release into marine environment	
Undertaking of intended data submission [ ]	Not applicable	

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	03/03/2005
Materials and methods	-
Conclusion	-
Reliability	Applicant's justification is acceptable.
Acceptability	-
Remarks	No.

Section A7.4.3.3.2	**Bioconcentration in aquatic organisms**
BPD Annex Point IIIA, XIII.2.3	7.4.3.3.1 Invertebrate species if direct release on marine environment

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section 7.4.3.4	**Effects on reproduction and growth rate with an appropriate invertebrate species**
BPD Annex Point IIIA, XIII.2.4	7.4.3.4 Chronic toxicity to *Daphnia magna*

Official use only

1. REFERENCE

1.1.	**Reference**	**1) Pearson N., Girling A. 1989** Flufenoxuron: Chronic toxicity to Daphnia magna XXXX unpublished XXXX
1.2.	**Data protection**	No
1.2.1.	Data owner	BASF
1.2.2.	Companies with letter of access	XXXX
1.2.3.	Criteria for data protection	No data protection claimed

2. GUIDELINES AND QUALITY ASSURANCE

2.1.	**Guideline study**	No, method description given in the report.
2.2.	**GLP**	Yes (laboratory certified by the Department of Health and Social Security of the Government of the United Kingdom, United Kingdom)
2.3.	**Deviations**	No

3. METHOD

3.1.	**Test material**	14C-Flufenoxuron
3.1.1.	Lot/Batch number	XXXX
3.1.2.	Specification	See 3.1.3.
3.1.3.	Purity	>99%
3.1.4.	Composition of Product	Not applicable
3.1.5.	Further relevant properties	Not relevant
3.1.6.	Method of analysis	TLC
3.2.	**Preparation of TS solution for poorly soluble or volatile test substances**	Not applicable

Section 7.4.3.4	**Effects on reproduction and growth rate with an appropriate invertebrate species**
BPD Annex Point IIIA, XIII.2.4	7.4.3.4 Chronic toxicity to *Daphnia magna*

3.3.	**Reference substance**	No	
3.3.1.	Method of analysis for reference substance	Not applicable	
3.4.	**Testing procedure**		
3.4.1.	Dilution water	Control, 0.5, 1, 2, 5, 10 and 20 ng a.s./L (nominal)	
3.4.2.	Test organisms	Water flea (*Daphnia magna* STRAUS), neonates, age: less than 24 hours, neonates from in-house culture, stock obtained from Institut National de Recherche Chimique Appliquée, France	
3.4.3.	Handling of embryos and larvae (OECD 210/212)	Not applicable	
3.4.4.	Test system	Semi-static test (21 days), 6 test concentrations plus control, 4 beakers per concentration and control, 10 daphnids were separated and kept individually in beakers containing 500 ml test solution and 10 mL soil extract. Mortality (immobility) rate, reproduction rate and numbers of moulted exoskeletons of each single Daphnia were followed up to the end of the study.	X
3.4.5.	Test conditions	Glass vessels, test volume 500 mL, reconstituted fresh water and soil extract (20 mL/L), pH 7.9 - 8.2, oxygen content: 8.6 mg/L - 9.6 mg/L, temperature: 18 °C - 22 °C, photoperiod: 16 hours light: 8 hours dark, feeding with green algae, no ventilation.	
3.4.6.	Duration of the test	21-days	
3.4.7.	Test parameter(s)	Parent mortality, reproduction capacity.	
3.4.8.	Examination / Sampling	See 3.4.4	
3.4.9.	Monitoring of TS concentration	No	
3.4.10.	Statistics	Descriptive statistics, chi-square analysis for mortality data, ANOVA followed by Dunnett-test ($\alpha = 0.01$; $\alpha = 0.05$) for reproduction data.	

4. RESULTS

Section 7.4.3.4	**Effects on reproduction and growth rate with an appropriate invertebrate species**
BPD Annex Point IIIA, XIII.2.4	7.4.3.4 Chronic toxicity to *Daphnia magna*

Range finding test		Not performed
4.1.1.	Concentrations	Not applicable
4.1.2.	Number/ percentage of animals showing adverse effects	Not applicable
4.1.3.	Nature of adverse effects	Not applicable
Results test substance		
4.1.4.	Initial concentrations of test substance	Control, 0.5, 1, 2, 5, 10 and 20 ng a.s./L (nominal)
4.1.5.	Actual concentrations of test substance	The analyzed concentrations of fresh test item concentrations ranged from 37% to 47% of nominal. The mean added amount was 81% based on stock solution analyses. The results for the used concentrations were in a range of 24% to 27%. Some of the test item present in the test media may have been removed by centrifugation and adsorption to the glass wall. The biological results are based on mean measured concentrations of the test item (see also XXXX or IIIA 7.6).
4.1.6.	Effect data	See Table 7.4.3.4/151.
4.1.7.	Concentration / response curve	See 5.2
4.1.8.	Other effects	See 5.2
Results of controls		
4.1.9.	Number/ percentage of animals showing adverse effects	See Table 7.4.3.4/151.
4.1.10.	Nature of adverse effects	See Table 7.4.3.4/151.
Test with reference substance		Not performed
4.1.11.	Concentrations	Not applicable
4.1.12.	Results	Not applicable

Section 7.4.3.4	**Effects on reproduction and growth rate with an appropriate invertebrate species**
BPD Annex Point IIIA, XIII.2.4	7.4.3.4 Chronic toxicity to *Daphnia magna*

		5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1.	**Materials and methods**	*Daphnia magna* were exposed for 21-day in a semi-static system to a test substance as described under 3.1. The test procedure is detailed under 3.4.	
5.2.	**Results and discussion**	Flufenoxuron caused immobility of the parent daphnids in all test item concentrations and the control. Statistically significant immobility rates were detected in the 2 and 20 ng a.s./L test item concentrations (Dunnett-test, $\alpha = 0.05$; $\alpha = 0.01$). The number of offspring per parent in the control was 32.1. Statistically significant difference in reproduction rate was observed in the highest test item concentration of 20 ng a.s./L (Dunnett-test, $\alpha = 0.01$). The results are summarized in See Table 7.4.3.4/151.	
5.2.1.	NOEC	6.5 ng a.s./L (mean measured, corrected for adsorption and removal by centrifugation) (see also XXXX or IIIA 7.6)	X
5.2.2.	LOEC	Not reported	
5.3.	**Conclusion**	In a 21-day semi-static chronic toxicity study with *Daphnia magna* the NOEC of Flufenoxuron was 6.5 ng a.s./L (mean measured).	
5.3.1.	Other Conclusions	None	
5.3.2.	Reliability	1	X
5.3.3.	Deficiencies	No	X

Section 7.4.3.4	**Effects on reproduction and growth rate with an appropriate invertebrate species**
BPD Annex Point IIIA, XIII.2.4	7.4.3.4 Chronic toxicity to *Daphnia magna*

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	06/05/2010
Materials and Methods	Applicant's summary is acceptable with the following amendments: 3.4.4 test system : *Semi-static test (21 days), 6 test concentrations plus control, 4 beakers per concentration and control, 10 daphnids were* **introduced into each** ~~*separated and kept individually in*~~ *beaker*~~*s*~~ *containing 500 ml test solution and 10 mL soil extract.* **At two day intervals throughout the test, the live Daphnia were transferred to beakers of fresh test media and food.** 3.4.8 Examination/sampling : ~~*See 3.4.4*~~ **At 24h intervals, the numbers of dead Daphnia, moulted exoskeletons, live young and dead immobilised young in each beaker were recoreded. These were then removed and discarded.** 3.4.9 Monitoring of TS concentration : ~~*No*~~ **Chemical analysis was made on four occasions during the test on the fresh medium and the used medium (after an exposure of 48h) for each test concentration except the lowest.**
Results and discussion	Applicant's summary is acceptable. Amendment from the DocID 2006/1004526 : Due to its chemical properties flufenoxuron will adsorb to surfaces in a glass-water-algae system. The fractions of Flufenoxuron were not separately measured in the study. However, the best estimation of what is adsorbed to the glass is provided in a preliminary study (XXXX). In this study media without algae were centrifuged (60 min at 2000 rpm) and losses of 26 to 28% (average 27%) from the initial solution were observed, which may be attributed to sorption to glass. Sorption of Flufenoxuron to algae was also studied in this preliminary study. Media with algae were centrifuged (60 min at 2000 rpm) and a loss of 48% from the intial solution was observed, which may be attributed to sorption to algae but also to glass. Therefore the amount adsorbed to algae is corrected to 48 – 27 = 21%. Thus the actual exposure concentration at the NOEC level is : (8.12 ng/L*(1-0.27))*0.21 + 3.25 ng/L (mean measured concentration) = 4.49 ng/L considering that 8.12 ng/L is measured in stock solution and not in the test solution then additional glass adsorption should be considered in the test vessels. 5.3.3 Deficiencies : Whatever the test concentration, mortality is higher than 20% and the mean number of offsprings/parent is low (less than 35).

Section 7.4.3.4	**Effects on reproduction and growth rate with an appropriate invertebrate species**
BPD Annex Point IIIA, XIII.2.4	7.4.3.4 Chronic toxicity to *Daphnia magna*

Conclusion	Applicant's summary is acceptable. NOEC = 4.49 ng/L
Reliability	See deficiencies above. Reliability index : 2 (study has retained as key study).
Acceptability	See above.
Remarks	As no guidelines were applied, following amendment should be done to 2.3 Deviations : *Not applicable*

	COMMENTS FROM ... *(specify)*
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.4.3.4/151Effects of Flufenoxuron (21 d) on *Daphnia magna* reproduction and parent mortality

Concentration (nominal) [ng a.s./L]	**Control**	**0.5**	**1**	**2**	**5**	**10**	**20**
Concentration (mean-measured) [ng a.s./L]	**Control**	**-**	**0.315**	**0.73**	**1.69**	**3.24**	**6.34**
Mean Offspring/parent	32.1	31.6	32.7	33.2	31.7	34.2	0.3 **
Parent-immobility [%]	7	25	17	27 *	22	25	97 **
Endpoints [ng a.s./L] mean measured							
NOEC (21 d)	**4.49**						

* statistically significant compared to the solvent control (Dunnett-test; $\alpha = 0.05$)

** statistically significant compared to the solvent control (Dunnett-test; $\alpha = 0.01$)

Section 7.4.3.4	**Effects on reproduction and growth rate with an appropriate invertebrate species**
BPD Annex Point IIIA, XIII.2.4	7.4.3.4 Chronic toxicity to *Daphnia magna*

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**2) Harrison E.G. (1988)** Effects of Cascade emulsifiable concentrate (EC) and water dispersable (WDC) formulations on zooplankton in enclosures in experimental ponds XXXX XXXX	
1.2.	**Data protection**	No	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	No data protection claimed	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	No, Method based on Shires S (1983) – Pesticide Science, 14, 475-480 and Stephenson R.R. et al. (1984), Int. J. Environ. Stud., 10, 23-33 Method description given in the report.	
2.2.	**GLP**	Yes (laboratory certified by the Department of Health and Social Security of the Government of the United Kingdom, United Kingdom)	
2.3.	**Deviations**	No	
		3. METHOD	
3.1.	**Test material**		X
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	50 g/l EC & 50 g/l WGC	
3.1.3.	Purity	51.6 g/l & 51 g/l	
3.1.4.	Composition of Product	Not relevant as data to support flufenoxuron Annex I listing in Directive 98/8/EC	
3.1.5.	Further relevant properties	Not relevant	
3.1.6.	Method of analysis	Based on SAMS-445-1, description and results given in the report	
3.2.	**Preparation of TS solution for poorly soluble or volatile**	Not applicable	

Section 7.4.3.4	**Effects on reproduction and growth rate with an appropriate invertebrate species**
BPD Annex Point IIIA, XIII.2.4	7.4.3.4 Chronic toxicity to *Daphnia magna*

	test substances		
3.3.	**Reference substance**	No	
3.3.1.	Method of analysis for reference substance	Not applicable	
3.4.	**Testing procedure**		
3.4.1.	Dilution water	10, 3, 1, 0.3 and 0.1 g ai ha^{-1}	
3.4.2.	Test organisms	*cladoceran,* Daphnia longispina*, two species of Copepoda,* Cyclops strenuus *and* Diaptomus gracilis *and the copepod nauplii.*	
3.4.3.	Handling of embryos and larvae (OECD 210/212)	Not applicable	
3.4.4.	Test system	12 experimental mature ponds, 10 m long on 5 m wide, representing a volume of 0.7 m^3 cylindrical enclosures	X
3.4.5.	Test conditions	Location: Grigg Farm, Headcorn, Kent – IK Meteorlogical data recorded and included in the report [See Figure 56]	
3.4.6.	Duration of the test	Up to 63 days after application	
3.4.7.	Test parameter(s)	Identification and counting of zooplankton Record temperaure, Dissolved oxygene, pH and residues	
3.4.8.	Examination / Sampling	Sampling, -1, 0, 1, 3, 4, 5, 7, 8, 14, 21, 35, 49 and 63 days	
3.4.9.	Monitoring of TS concentration	No	
3.4.10.	Statistics	No	
		4. RESULTS	
Range finding test		Not performed	
4.1.1.	Concentrations	Not applicable	
4.1.2.	Number/ percentage of animals showing adverse effects	Not applicable	
4.1.3.	Nature of adverse	Not applicable	

Section 7.4.3.4	**Effects on reproduction and growth rate with an appropriate invertebrate species**
BPD Annex Point IIIA, XIII.2.4	7.4.3.4 Chronic toxicity to *Daphnia magna*

	effects		
Results test substance			
4.1.4.	Initial concentrations of test substance	Before treatment, concentration in ponds were < 0.01 µg/l (LOD) Spray solution, concentrations within 0.70 to 70 µg/l (average of 3 ponds)	X
4.1.5.	Actual concentrations of test substance	Within 14 days, flufenoxuron was about 20% of the maximum measured concentration [See Figure 57]	X
4.1.6.	Effect data	See 5.2	
4.1.7.	Concentration / response curve	See 5.2	
4.1.8.	Other effects	See 5.2	
Results of controls			
4.1.9.	Number/ percentage of animals showing adverse effects	See tables pages 15 and 16	
4.1.10.	Nature of adverse effects	Only density was recorderd	
Test with reference substance		Not performed	
4.1.11.	Concentrations	Not applicable	
4.1.12.	Results	Not applicable	

Section 7.4.3.4	**Effects on reproduction and growth rate with an appropriate invertebrate species**
BPD Annex Point IIIA, XIII.2.4	7.4.3.4 Chronic toxicity to *Daphnia magna*

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1.	**Materials and methods**	4 Zooplankton populations were exposed for 63-days in a pond system to test substances as described under 3.1. The test procedure is detailed under 3.4.
5.2.	**Results and discussion**	Analysis: Peak concentrations of flufenoxuron in the water were recorded within twenty-four hours of treatment. The maximum mean concentrations of flufenoxuron recorded in the enclosures oversprayed with 1.0, 3.0, and 10.0 g ai ha^{-1} were 0.11, 0.13, and 0.57 µg/L for the WDC formulation and 0.04, 0.16, 0.5 µg/L for the EC formulation respectively. The rate of loss of flufenoxuron from the water was similar in all treated enclosures and within14 days of treatment concentrations of flufenoxuron in the water were approximately 20% of peak concentrations. Biology: Four groups of crustacean zooplankton were sufficiently abundant to allow detection of significant treatment effects. These were the cladoceran, *Daphnia longispina*, two species of Copepoda, *Cyclops strenuus* and *Diaptomus gracilis* and the copepod nauplii. No major differences were recorded between the effects of the two formulations of flufenoxuron. Recovery in the zooplankton population in the enclosures after treatment was within 35 to 63 days after treatment. The no effect dose rates for the zooplankton ranged from 0.1 to 1.0 g ai ha^{-1}. The corresponding no effect concentrations of flufenoxuron in the water ranged from 0.03 to 0.04 µg/L (measured concentrations). Recovery of the zooplankton populations (by latest DAT 63) allows for the derivation of a no observed ecologically adverse effect concentration or NOEAEC of 0.13 to 0.16 µg a.s./L (see also DocID 2006/1004526 or IIIA 7.6)
5.2.1.	NOEC	0.03 to 0.04 µg a.s./L, NOEAEC of 0.13 to 0.16 µg a.s./L (measured concentrations)
5.2.2.	LOEC	Not reported
5.3.	**Conclusion**	In a pond study study with 4 zooplankton populations the $NOEC_{community}$ of Flufenoxuron was 0.03 µg a.s./L and the NOEAEC 0.13 to 0.16 µg a.s./L (both measured concentrations).
5.3.1.	Other Conclusions	None
5.3.2.	Reliability	1
5.3.3.	Deficiencies	No

Section 7.4.3.4	**Effects on reproduction and growth rate with an appropriate invertebrate species**
BPD Annex Point IIIA, XIII.2.4	7.4.3.4 Chronic toxicity to *Daphnia magna*

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	03/03/2005
Materials and Methods	Applicant's summary is acceptable with the following amendments: 3.1 Test material : Two liquid products containing 50 g/L Flufenoxuron. Product XXXX (Emulsifiable concentrate formulation) Product XXXX (Water dispersible concentrate formulation) 3.4.4 Test system : ~~*12*~~ **3** *experimental mature ponds, 10 m long on 5 m wide, ~~representing a volume of 0.7 m^3 cylindrical enclosures.~~* Twelve enclosures of approximatively 1 m diameter and 1.4 m high were placed in each pond. Five enclosures were treated with the serie of doses of the WDC and five similarely with the EC. Two enclosures in each pond were left unsprayed and served as controls.
Results and discussion	Applicant's summary is acceptable with the following amendments: 4.1.4 Initial concentrations of test substance: ~~*Spray solution, concentrations within 0.70 to 70 µg/l (average of 3 ponds)*~~. Concentrations measured in the ponds just after spraying were <0.01, 0.02, 0.11, 0.13, 0.49 µg a.i./L (WDC formulation) and 0.03, 0.03, 0.04, 0.16, 0.50 µg a.i./L (EC formulation) for the tested dose rates of 0.1, 0.3, 1, 3, 10 g a.i./ha. 4.1.2 Actual concentrations: *Within 14 days, flufenoxuron was about 20% of the maximum measured concentration [See Figure 57]*. The mean-measured concentrations over 14 days for the dose rates of 1, 3 and 10 g a.i./ha are respectively 0.054, 0.096 and 0.362 µg a.i./L (WDC product), 0.03, 0.094 and 0.294 µg a.i./L (EC product).
Conclusion	5.3.3. Deficiencies : *Yes*. Concentrations were measured only 5 times until day 14 (while the duration of the test was 63 days) and loss of substance was noticed (until 80% loss after 14 days). NOEC was based on concentrations recorded in the first 24h after application. This study can't be considered as a classic chronic test.
Reliability	See deficiencies above. Reliability index : 3.
Acceptability	Not acceptable.
Remarks	**1/** As no guidelines were applied, following amendment should be done to 2.3 Deviations : *Not applicable* **2/** As results are considered unreliable, whole summary of the study was not read.
	COMMENTS FROM ... *(specify)*

Section 7.4.3.4	**Effects on reproduction and growth rate with an appropriate invertebrate species**
BPD Annex Point IIIA, XIII.2.4	7.4.3.4 Chronic toxicity to *Daphnia magna*

Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Figure 56 – Meteorological data

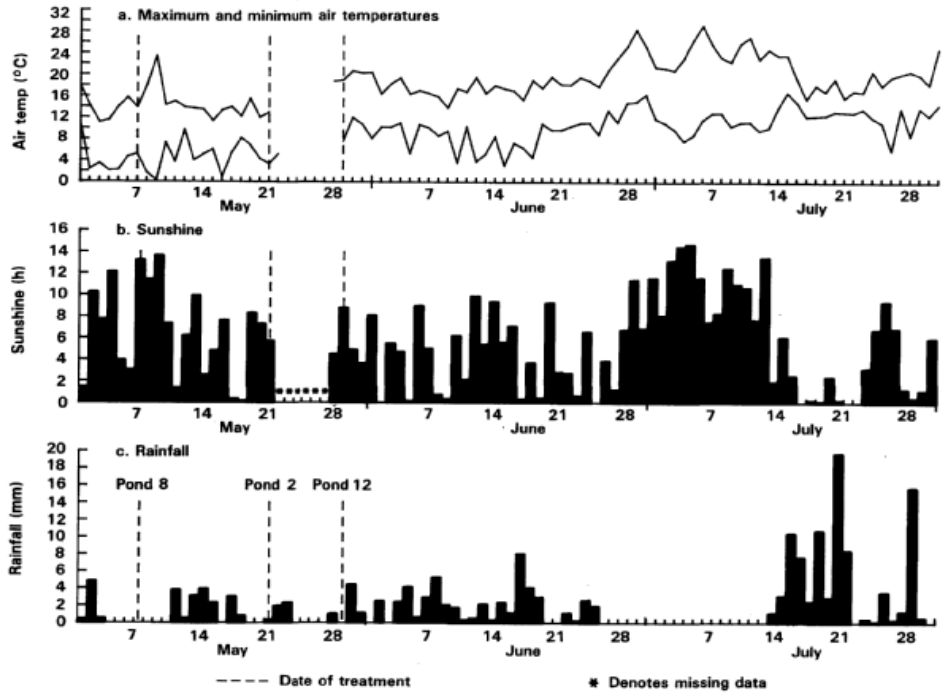
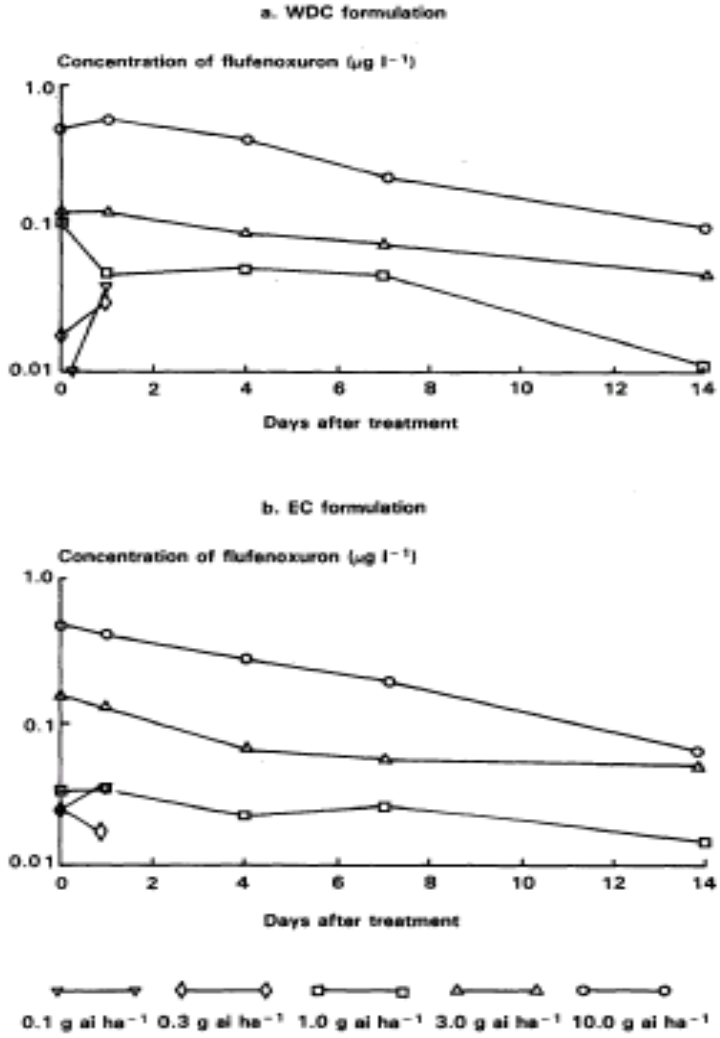


Figure 57 – Test concentration in the ponds (Average)



Mean numbers of Daphnia longispina per litre of pond water

DAT	TREATMENT (g ai ha^{-1})											
	CONTROL1	CONTROL2	EC 10	EC 3	EC 1	EC 0.3	EC 0.1	WDC 10	WDC 3	WDC 1	WDC 0.3	WDC 0.1
-1	30	20	30	27	47	24	20	18	29	21	26	25
0	23	23	60	15	19	20	18	24	35	28	26	22
3	29	20	4.9*	4.8*	22	24	19	5.3*	12*	15	25	28
5	42	36	0.0*	2.1*	18	32	34	0.44*	3.8*	17*	30	29
8	29	34	0.79*	1.2*	13	26	29	0.22*	0.76*	5.3*	17	35
14	39	21	0.11*	0.22*	16	41	28	0.22*	0.67*	6.4*	21	23
21	17	18	0.35*	2.5*	21	27	24	0.37*	0.56*	12	16	21

Mean numbers of nauplii per litre of pond water

DAT	TREATMENT (g ai ha^{-1})											
	CONTROL1	CONTROL2	EC 10	EC 3	EC 1	EC 0.3	EC 0.1	WDC 10	WDC 3	WDC 1	WDC 0.3	WDC 0.1
-1	196	290	220	267	249	223	250	241	246	245	195	266
0	223	268	257	201	263	252	247	213	181	200	200	249
3	181	156	101*	70*	112	142	190	83*	64*	71*	138	180
5	230	172	23*	16*	84	103	167	25*	30*	67*	107	159
8	238	146	2.7*	1.7*	48*	132	181	5.4*	3.9*	12*	86	154
14	76	77	4.6*	10*	63	115	77	3.8*	4.5*	14*	82	94
21	83	103	1.7*	17*	55	115	62	2.7*	14*	30*	72	112
35	139	121	28*	91	185	208	97	19*	67	146	90	156
49	170	129	145	103	356	365	166	30*	63	177	76	180
63	264	180	490	283	319	217	188	268	332	431	143	106

* indicates significant difference from control at 5% level

Mean numbers of Cyclops strenuus (Ponds 2 and 12 only) per litre of pond water

DAT	TREATMENT (g ai ha^{-1})											
	CONTROL1	CONTROL2	EC 10	EC 3	EC 1	EC 0.3	EC 0.1	WDC 10	WDC 3	WDC 1	WDC 0.3	WDC 0.1
-1	59	202	87	59	82	124	86	131	54	69	49	122
0	46	162	116	39	83	82	80	60	40	56	41	99
3	54	92	14	11	26	42	78	21	5.3*	14	19	86
5	25	61	9.2*	2.4*	10*	25	51	9.0*	4.1*	7.0*	14*	41
8	23	20	6.2*	1.8*	1.4*	15	30	2.4*	2.0*	1.6*	8.5	18
14	18	11	1.1*	0.33*	4.2	7.8	7.3	0.35*	0.37*	0.51*	5.0	13
21	7.4	16	0.53*	0.92*	1.5*	17	5.4	0.53*	0.92*	1.4*	3.1*	15
35	30	7.3	13	35	11	40	6.5	6.5	10	29	8.5	55
49	6.3	23	16	2.8	6.1	104	15	2.0	5.0	14	6.7	17
63	36	10	16	10	2.9	5.2	6.1	5.0	5.9	5.5	4.6	5.2

* indicates significant difference from control at 5% level

Mean numbers of Diaptomus gracilis per litre of pond water

DAT	TREATMENT (g ai ha^{-1})											
	CONTROL1	CONTROL2	EC 10	EC 3	EC 1	EC 0.3	EC 0.1	WDC 10	WDC 3	WDC 1	WDC 0.3	WDC 0.1
-1	9.0	7.0	10	8.0	10	7.0	14	8.1	5.5	4.4	5.0	6.9
0	11	11	13	11	7.2	7.7	12	8.9	7.7	13	6.1	10
3	11	8.5	6.2	4.1	4.2	7.1	11	5.1	2.8*	4.0	6.4	7.4
5	9.0	6.1	3.9	2.6*	3.9	11	8.7	3.5*	2.4*	3.6	8.6	8.7
8	7.9	8.5	1.7*	1.5*	3.0*	5.3	10	1.6*	1.9*	1.6*	6.1	7.0
14	4.5	5.5	0.69*	0.44*	1.2*	7.7	6.2	0.45*	0.11*	0.66*	4.4	4.3
21	2.0	3.9	0.12*	0.24*	2.3	7.8	3.6	0.58	0.35	0.12*	6.8	5.7
35	2.2	3.0	1.5	4.5	2.8	2.0	1.1	0.0*	0.87	3.3	2.2	4.7
49	1.1	4.7	1.7	2.8	4.0	4.8	1.7	0.7	1.4	15	4.3	6.3
63	2.3	5.7	5.7	6.0	0.42	2.9	2.3	14	3.9	12	5.4	5.7

* indicates significant difference from control at 5% level

Section 7.4.3.5.1 **Effects on any other species**
BPD Annex Point IIIA, XIII.3.4 7.4.3.5.1 Effects on sediment dwelling organisms

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**1) Mattock S. et al. 2001** Effects of 14C labelled Flufenoxuron on the development of sediment-dwelling larvae of Chironomus riparius in a water-sediment system XXXX unpublished XXXX	
1.2.	**Data protection**	Yes	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I.	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Yes, OECD 207	
2.2.	**GLP**	Yes, (laboratory certified by Department of Health of the Government of the United Kingdom, United Kingdom)	
2.3.	**Deviations**	No	X
		3. METHOD	
3.1.	**Test material**	14C-labeled Flufenoxuron	
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	See 3.1.3.	
3.1.3.	Purity	99.3%	
3.1.4.	Composition of Product	Not relevant	
3.1.5.	Further relevant properties	Not relevant	
3.1.6.	Method of analysis	Analyzed using LSC for overlaying water, pore water and sediment (see report).	

Section 7.4.3.5.1 **BPD Annex Point IIIA, XIII.3.4**	**Effects on any other species** 7.4.3.5.1 Effects on sediment dwelling organisms

3.2.	**Preparation of TS solution for poorly soluble or volatile test substances**	Not applicable
3.3.	**Reference substance**	No
3.3.1.	Method of analysis for reference substance	Not applicable
3.4.	**Testing procedure**	
3.4.1.	Dilution water	0.0065, 0.013, 0.025, 0.05, 0.1 and 0.2 µg a.s./L (nominal).
3.4.2.	Test organisms	*Chironomus riparius*, larvae (first instars, less than 24 hours old); stock originally obtained from a laboratory culture of Covance Laboratories, Harrogate, UK, cultures maintained in-house.
3.4.3.	Handling of embryos and larvae (OECD 210/212)	Not relevant
3.4.4.	Test system	Static system; test duration 28 days; 25 larvae per vessel; 6 test concentrations, a control and a solvent control (Acetone), each with 5 replicates; the larvae were regularly fed with fish food extract. Daily assessments of mortality and emergence. The number and time of emerged adults was recorded.
3.4.5.	Test conditions	OECD 207 artificial standard sediment; dilution water, physico-chemical parameters: pH 6.5 - 6.7; dissolved oxygen: 96%; conductivity: 190 µS - 214 µS; 3.0 L glass beakers were filled with approx. 2 cm layer of artificial sediment and overlaid with test water (approx. 18 cm); temperature 20.6 °C - 21.0 °C; 16 hours light: 8 dark.
3.4.6.	Duration of the test	28 days
3.4.7.	Test parameter(s)	EC_{50}, NOEC
3.4.8.	Examination / Sampling	Not applicable
3.4.9.	Monitoring of TS concentration	Not applicable

Section 7.4.3.5.1 **BPD Annex Point IIIA, XIII.3.4**	**Effects on any other species** 7.4.3.5.1 Effects on sediment dwelling organisms

3.4.10.	Statistics	Descriptive statistics, ANOVA followed by Dunnett-test for emergence data, log transformation and probit analysis for determination of the EC_x values.	
		4. RESULTS	
Range finding test		Not performed	
4.1.1.	Concentrations	Not applicable	
4.1.2.	Number/ percentage of animals showing adverse effects	Not applicable	
4.1.3.	Nature of adverse effects	Not applicable	
Results test substance			
4.1.4.	Initial concentrations of test substance	Control, solvent control, 0.0065, 0.013, 0.025, 0.05, 0.1 and 0.2 µg a.s./L (nominal).	
4.1.5.	Actual concentrations of test substance	Measured test concentrations of the radioactivity in the overlaying water at test initiation were in the range of 34.8% - 67.7% of nominal. Quantities in a range of 4.3% to 29.3% were found in pore water and from 2.0% to 12.9% in the sediment. After 28 d of exposure, test item were found in a range of 2.1% to 2.4% in the water and 13.1% to 27.3% in the sediment extracts. Radioactivity from pore water was not detectable at test end. The biological results are based on the nominal concentrations.	X
4.1.6.	Effect data	See Table 7.4.3.5.1/152	
4.1.7.	Concentration / response curve	See Table 7.4.3.5.1/152.	
4.1.8.	Other effects	See Table 7.4.3.5.1/152.	
Results of controls			
4.1.9.	Number/ percentage of animals showing adverse effects	See Table 7.4.3.5.1/152.	
4.1.10.	Nature of adverse effects	See Table 7.4.3.5.1/152.	

Section 7.4.3.5.1 **BPD Annex Point IIIA, XIII.3.4**	**Effects on any other species** 7.4.3.5.1 Effects on sediment dwelling organisms

Test with reference substance		Not performed	
4.1.11.	Concentrations	Not applicable	
4.1.12.	Results	Not applicable	
		5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1.	**Materials and methods**	Flufenoxuron, as described under 3.1, was applied to dwelling sediment organism as procedure detailed in 3.4.	
5.2.	**Results and discussion**	Flufenoxuron caused no effects on the chironomid emergence up to 0.05 µg a.s./L. No effects on development rate were observed up to 0.1 µg a.s./L. The results are summarized in Table 7.4.3.5.1/152	
5.3.	**Conclusion**	The NOEC for emergence of chironomids was determined to be 0.05 µg a.s./L, the NOEC for development was 0.1 µg a.s./L (nominal).	
5.3.1.	Other Conclusions	None	
5.3.2.	Reliability	1	X
5.3.3.	Deficiencies	No	

Section 7.4.3.5.1
BPD Annex Point IIIA, XIII.3.4

Effects on any other species

7.4.3.5.1 Effects on sediment dwelling organisms

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	03/07/2005
Materials and Methods	**1/** The following amendment should be added to applicant's version : 2.3 Deviations : *Yes* Concentrations were measured but important loss of substance was noticed in the system. It seems actually that loss from water was not only due to adsorption. For example, in the whole system (if percentages of applied radiocativity in overlying water, pore water and sediment are added), at the end of the test (28 days), for nominal concentration of 0.1 $\mu g.L^{-1}$, loss is 84.8%. EC_{50} and NOEC were based on nominal concentration. Given that significant loss was observed and that EC_{50} and NOEC were based on nominal concentrations, the results of the study can not be considered as reliable. **2/** The following remark is done by RMS : **according to "*Guidance on data requirements for active substances and biocidal products*" (page 113),** as Flufenoxuron has a great potentiality of adsorption and is not highly soluble in water, it is not relevant to test sediment dwelling organisms' toxicity *via* a spiked water-sediment system. Therefore, study can not be considered as reliable and **organisms should be exposed to spiked sediment.**
Results and discussion	The following amendment should be added to applicant's version : Measured test concentrations of the radioactivity in the overlaying water at test initiation were in the range of 34.8% - 67.7% of nominal. Quantities in a range of 4.3% to 29.3% were found in pore water and from 2.0% to 12.9% in the sediment. After 28 d of exposure, test item were found in a range of 2.1% to 2.4% in the water and 13.1% to 27.3% in the sediment extracts. Radioactivity from pore water was not detectable at test end. *When those three measured concentrations (overlying water, pore water and sediment) are added, recovery of substance is far less than 80% of nominal concentrations. However,* the biological results are based on the nominal concentrations.
Conclusion	Applicant's summary is acceptable.

Section 7.4.3.5.1 **BPD Annex Point IIIA, XIII.3.4**	**Effects on any other species** 7.4.3.5.1 Effects on sediment dwelling organisms

Reliability	See deviations above. Reliability index : 3. **In view of** mode of action of flufenoxuron, high toxicity of flufenoxuron on *Daphnia magna*, e-fate of flufenoxuron and given that this substance is highly adsorbable and not very soluble in water, given that according to "*Guidance on data requirements for active substances and biocidal products*" (page 113), this study is judged as not reliable and not acceptable by RMS.
Acceptability	Not acceptable. See above.
Remarks	No other.
	COMMENTS FROM ... *(specify)*
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.4.3.5.1/152 Effect of Flufenoxuron (28 d) on *Chironomus riparius*

Concentration [µg a.s./L] nominal	**Control**	**Solvent control**	**0.0065**	**0.013**	**0.025**	**0.05**	**0.1**	**0.2**
Mean daily emergence rates (day 28)	101	97	99	93	92	96	71	19
Development rate [% per day]	5.4	5.4	6.4	5.4	5.5	6.5	6.1	4.7
	Endpoints [µg a.s./L]							
EC_{50}	0.131							
NOEC (emergence rate)	0.05							
NOEC (development rate)	0.1							

Section 7.4.3.5.1 **Effects on any other species**
BPD Annex Point IIIA, XIII.3.4 7.4.3.5.1 Effects on sediment dwelling organisms

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**2) Funk M. 2003** Effect of Reg.No. 4064702 (metabolite of BAS 307 I, Flufenoxuron) on the development of sediment dwelling larvae of Chironomus riparius in a water-sediment system XXXX. unpublished XXXX	
1.2.	**Data protection**	Yes	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I.	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Yes, OECD 207	X
2.2.	**GLP**	Yes (laboratory certified by Landesamt fuer Umweltschutz und Gewerbeaufsicht, Mainz, Germany)	
2.3.	**Deviations**	No	
		3. METHOD	
3.1.	**Test material**	Flufenoxuron degradates	
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	See chemical glossary	
3.1.3.	Purity	95%	
3.1.4.	Composition of Product	Not relevant	
3.1.5.	Further relevant properties	Not relevant	
3.1.6.	Method of analysis	The test item concentrations were analyzed using HPLC with UV-detection for overlaying water and pore water and reversed phase HPLC and by detection by mass spectrometry for sediment (see report).	
3.2.	**Preparation of TS**	Not applicable	

Section 7.4.3.5.1 **BPD Annex Point IIIA, XIII.3.4**	**Effects on any other species** 7.4.3.5.1 Effects on sediment dwelling organisms

	solution for poorly soluble or volatile test substances	
3.3.	**Reference substance**	No
3.3.1.	Method of analysis for reference substance	Not applicable
3.4.	**Testing procedure**	
3.4.1.	Dilution water	Control, solvent control, 100, 200, 400, 800, 1600, 3200 and 6400 µg a.s./L (nominal).
3.4.2.	Test organisms	*Chironomus riparius*, larvae (first instars, up to 3 days old; cultures maintained in-house.
3.4.3.	Handling of embryos and larvae (OECD 210/212)	Not relevant
3.4.4.	Test system	Static system; test duration 28 days; 15 larvae per vessel; 7 test concentrations plus solvent control, each with 4 replicates and a control with 3 replicates; the larvae were regularly fed with fish food extract. Daily assessments of behaviour, mortality and emergence. The number, time and sex of emerged adults is recorded.
3.4.5.	Test conditions	OECD 219 artificial standard sediment, "M4" Elendt medium; physico-chemical parameters: pH 7.21 - 8.78; oxygen content: 5.1 mg/L - 11.3 mg/L; conductivity: 796 µS; 3.0 L glass beakers were filled with approx. 1.5 cm layer of artificial sediment and overlaid with test water (approx. 6 cm); temperature 17.7 °C - 20.6 °C; 16 hours light: 8 dark, light intensity: 493 lux - 837 lux.
3.4.6.	Duration of the test	28 days
3.4.7.	Test parameter(s)	EC_{50}, NOEC
3.4.8.	Examination / Sampling	Not applicable
3.4.9.	Monitoring of TS concentration	Not applicable

Section 7.4.3.5.1 **BPD Annex Point IIIA, XIII.3.4**	**Effects on any other species** 7.4.3.5.1 Effects on sediment dwelling organisms

3.4.10.	Statistics	Descriptive statistics, ANOVA followed by Dunnett-test, Bonferroni-test and Williams-test for emergence and development rates (α = 0.05), logit and probit analysis for determination of the EC_x values	
		4. RESULTS	
Range finding test		Not performed	
4.1.1.	Concentrations	Not applicable	
4.1.2.	Number/ percentage of animals showing adverse effects	Not applicable	
4.1.3.	Nature of adverse effects	Not applicable	
Results test substance			
4.1.4.	Initial concentrations of test substance	Control, solvent control, 100, 200, 400, 800, 1600, 3200 and 6400 µg a.s./L (nominal).	
4.1.5.	Actual concentrations of test substance	Mean measured test concentrations of the radioactivity in the overlaying water at test initiation were in the range of 116.3% - 126.1% of nominal. After 28 d of exposure, test item were found in a range of 7.9% - 13.7% in the water. In sediment concentrations from 4.23 mg/kg - 19.12 mg/kg dry sediment could be detected at 3 sampling dates (1, 7 and 28 d). The measured concentrations from pore water were 2.7% - 5.3% of nominal concentrations. Therefore the biological results are based on the nominal concentrations.	X
4.1.6.	Effect data	See Table 7.4.3.3.1/150.	
4.1.7.	Concentration / response curve	See Table 7.4.3.3.1/150.	
4.1.8.	Other effects	See Table 7.4.3.3.1/150.	
Results of controls			
4.1.9.	Number/ percentage of animals showing adverse effects	SeeTable 7.4.3.3.1/150.	
4.1.10.	Nature of adverse effects	See Table 7.4.3.3.1/150.	

Section 7.4.3.5.1 **BPD Annex Point IIIA, XIII.3.4**	**Effects on any other species** 7.4.3.5.1 Effects on sediment dwelling organisms

Test with reference substance		Not performed
4.1.11.	Concentrations	Not applicable
4.1.12.	Results	Not applicable

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1.	**Materials and methods**	Flufenoxuron degradate, Ref No 4064702, as described under 3.1, was applied to dwelling sediment organism as procedure detailed in 3.4
5.2.	**Results and discussion**	Flufenoxuron caused statistically significant effects in emergence rates at test item concentrations of 1600 µg a.s./L and higher (Dunnett-test, Bonferroni-test and Williams-test, α = 0.05). Statistically significant differences between the overall development rates of the test item concentrations and the controls could be detected in the 3200 and 6400 µg a.s./L test item concentration (Dunnett-test, Bonferroni-test and Williams-test, α = 0.05). The results are summarized in Table 7.4.3.3.1/150.
5.3.	**Conclusion**	The NOEC for emergence rate was determined to be 800 µg a.s./L, the NOEC for development rate was 1600 µg a.s./L (nominal).
5.3.1.	Other Conclusions	None
5.3.2.	Reliability	1
5.3.3.	Deficiencies	No

Section 7.4.3.5.1
BPD Annex Point IIIA, XIII.3.4

Effects on any other species

7.4.3.5.1 Effects on sediment dwelling organisms

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	03/07/2005
Materials and Methods	**1/** The following amendment should be added to applicant's version : 2.1 Guideline study Yes, *OECD 219*. **2/** The following remark is done by RMS : **according to "*Guidance on data requirements for active substances and biocidal products*" (page 113),** as Flufenoxuron has a great potentiality of adsorption and is not highly soluble in water, it is not relevant to test sediment dwelling organisms' toxicity *via* a spiked water-sediment system. Therefore, study can not be considered as reliable and **organisms should be exposed to spiked sediment.**
Results and discussion	**1/** The following amendment should be added to applicant's version : Mean measured test concentrations of the radioactivity in the overlaying water at test initiation were in the range of 116.3% - 126.1% of nominal. After 28 d of exposure, test item were found in a range of 7.9% - 13.7% in the water. In sediment concentrations from 4.23 mg/kg - 19.12 mg/kg dry sediment could be detected at 3 sampling dates (1, 7 and 28 d). The measured concentrations from pore water were 2.7% - 5.3% of nominal concentrations. *When those three measured concentrations (overlying water, pore water and sediment) are added, recovery of substance is more than 80% of nominal concentrations*. Therefore the biological results are based on the nominal concentrations. **2/** The following remark is done by RMS : According to Figure 1 (page 6 of 47 of Final Report in Doc IVA), the metabolite is completely adsorbed onto sediment approximately on day 7, which means that chironoms are exposed to substance only for 3 days, given that emergence normally appears on day 10.
Conclusion	Applicant's version is acceptable.
Reliability	See above. Reliability index is 3.
Acceptability	Not acceptable
Remarks	No.
	COMMENTS FROM ... *(specify)*

Section 7.4.3.5.1 **Effects on any other species**
BPD Annex Point IIIA, XIII.3.4 7.4.3.5.1 Effects on sediment dwelling organisms

Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.4.3.5.1/153 Effect of Flufenoxuron (28 d) on *Chironomus riparius*

Concentration [µg a.s./L] nominal	**Control**	**Solvent control**	**100**	**200**	**400**	**800**	**1600**	**3200**	**6400**
Emergence rates % reduction	0.867 -13.0	0.767 --	0.817 -6.5	0.767 0	0.717 6.5	0.667 13.0	0.15 * 80.5 *	0.15* 80.5*	0.05 * 96.5 *
Development rates % reduction	0.07 2.2	0.0716 --	0.0722 -0.8	0.0675 5.7	0.0681 4.9	0.0636 11.2	0.0627 12.4	0.049* 31.6*	0.0161* 77.5*

Endpoints [µg a.s./L]	
EC_{50} (emergence rate)	1200
EC_{50} (development rate)	4610
NOEC (emergence rate)	800
NOEC (development rate)	1600

* statistically significant differences compared to the controls (Bonferroni-test, Williams-test, Dunnett-test; $\alpha = 0.05$)

Section A7.4.3.5.1 Effects on sediment dwelling organisms

Annex Point IIIA, XIII.3.4 *Chironomus riparius*

			Official use only
		1 REFERENCE	
1.1.	**Reference**	**3) Toy, R. 1993** Flufenoxuron: Toxic effects of soils treated with CASCADE 100 g/l DC (SF07055) on *Chironomus riparius* XXXX, unpublished Report No.: XXXX, Date: 1993-04-20 XXXX	
1.2.	**Data protection**	Yes	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I.	
		2. GUIDELINES AND QUALITY ASSURANCE	
1.3.	**Guideline study**	No common guideline available at the time, the study was conducted.	
1.4.	**GLP**	Yes, (laboratory certified by Department of Health of the Government of the United Kingdom, United Kingdom)	
1.5.	**Deviations**	Not applicable	
		2. MATERIALS AND METHODS	
2.1.	**Test material**	CASCADE 100 g/L DC	
2.1.1.	Lot/Batch number	XXXX	
2.1.2.	Specification	See 3.1.3.	
2.1.3.	Purity	99.5 g a.i./L (flufenoxuron)	
2.1.4.	Composition of Product	Not applicable	
2.1.5.	Further relevant properties	Not relevant	
2.1.6.	Method of analysis	HPLC	
2.2.	**Preparation of TS solution for poorly soluble or volatile test substances**	Not applicable	
2.3.	**Reference**	No	

Section A7.4.3.5.1 Effects on sediment dwelling organisms

Annex Point IIIA, XIII.3.4 *Chironomus riparius*

	substance	
2.3.1.	Method of analysis for reference substance	-
2.4.	**Testing procedure**	
2.4.1.	Dilution water, Test sediment	Details on dilution water see Table 7.4.3.5.1/3. The soil was a silty clay soil containing 3.9% organic matter. It was treated by sieving it through a 4 mm mesh, spreading it in a 3 cm layer, and pouring onto it a suspension of CASCADE 100 g/L DC made up in tap water. The soil was then dried and thoroughly mixed. The nominal concentration of flufenoxuron on this dosed soil was 25 mg/kg. A control soil was prepared in the same way except that clean water was used instead of a suspension of CASCADE 100 g/L DC.
2.4.2.	Test organisms	*Chironomus riparius*, see Table 7.4.3.5.1/4
2.4.3.	Test system	see Table 7.4.3.5.1/5
2.4.4.	Test conditions	see Table 7.4.3.5.1/6
2.4.5.	Duration of the test	32 days
2.4.6.	Test parameter	The survival of larvae after 10 days and the number of emerging adult flies was recorded after 32 days.
2.4.7.	Sampling	After 10 days the contents of one dish at each concentration were examined and the number of live larvae was recorded. The contents of these dishes were then discarded. The number of adult flies emerging from the remaining dishes was recorded each day until no adults had emerged for five days. Emerged adults were removed daily. At the end of the test the contents of the dishes were inspected for larval *C. riparius.* The temperature of water in a flask adjacent to the test vessels was monitored at hourly intervals by a computer controlled thermocouple System. The pH, concentration of dissolved oxygen and total hardness of the reconstituted water used at the start of the test were also measured.
2.4.8.	Monitoring of TS concentration	Measured concentrations of flufenoxuron in the treated soil were used to calculate the exposure concentrations in the test, using the proportion of soil used to prepare the stock slurries. No direct measurement of flufenoxuron in the test vessels was made.
2.4.9.	Statistics	The 10 day LC_{50} was calculated using the moving average angle method (U.S. Environmental Protection Agency, 1985). The 32 day LC_{50} value was calculated by probit analysis using log. transformed concentration values (Finney, 1971). The highest concentration causing no observed effect (NOEC) on adult emergence was calculated using Williams‘ test

Section A7.4.3.5.1 Effects on sediment dwelling organisms

Annex Point IIIA, XIII.3.4 *Chironomus riparius*

		(Williams, 1971). The NOEC for larval survival was determined from the data without the use of statistical analysis.
		3. RESULTS
3.1.	**Limit Test**	Not performed
3.1.1.	Concentration	-
3.1.2.	Number/ percentage of animals showing adverse effects	-
3.1.3.	Nature of adverse effects	-
3.2.	**Results test substance**	
3.2.1.	Initial concentrations of test substance	Concentrations based on measurements of the spiked soil: 7.9, 25, 79, 260 and 770 µg a.i./kg of soil and a control
3.2.2.	Actual concentrations of test substance	No direct measurements of Flufenoxuron in the test vessels were made. The measured concentration of Flufenoxuron in the dosed soil ("stock slurry") was 26 mg a.i./kg soil.
3.2.3.	Effect data	Pre-imaginal development, see Table 7.4.3.5.1/7 Cumulative adult emergence at 32 days, see Table 7.4.3.5.1/8
3.2.4.	Concentration / response curve	A concentration-response-curve is given in the report. A concentration-response relationship was observed with a no observed effect concentration of 79 µg flufenoxuron per kg of soil (0.3% of dosed soil).
3.2.5.	Other effects	-
3.3.	**Results of controls**	In the control test vessel more than 30 live larvae were recovered. The nominal number of larvae added to the test vessels at the start of the test was 30. The fact that on day10 more larvae were found than initially added, may have resulted from the difficulty in counting the < 24 h old larvae at the start of the test. The number of adult *C. riparius* to emerge from the control vessels was on average 90% of the nominal number of larvae added to the vessel.
3.4.	**Test with reference substance**	Not performed
3.4.1.	Concentrations	-
3.4.2.	Results	-

Section A7.4.3.5.1 Effects on sediment dwelling organisms

Annex Point IIIA, XIII.3.4 *Chironomus riparius*

4. APPLICANT'S SUMMARY AND CONCLUSION

4.1. Materials and methods

The effects on the pre-imaginal development and adult emergence of the midge *Chironomus riparius* of CASCADE 100 g/L DC, containing 99.5 g flufenoxuron/L, adsorbed to soil have been determined.

A suspension of CASCADE DC was poured onto a silty clay soil known never to have been treated with pesticide. Reconstituted fresh water was then added to produce a soil 'slurry', containing nominal 25 mg Flufenoxuron/kg soil. Portions of this dosed slurry were diluted with a slurry of untreated soil to produce a series of test slurries containing nominal concentrations of flufenoxuron ranging from 7.9 to 770 µg/kg of soil. These slurries were added to the test vessels and further diluted with water such that each test vessel contained approximately 77 mL of water and 33 g of soil.

The test was initiated with <24 h old larvae. The survival of larvae after 10 days and the number of emerging adult flies was recorded.

Exposure concentrations are expressed on the basis of measured concentrations of flufenoxuron on the soils used to prepare the test media.

4.2. Results and discussion

The number of surviving larvae after 10 days is presented in Table 7.4.3.5.1/7, In the control and in the 0.1 and 0.3 % dosed soil test vessels more than 30 larvae were recorded which may have resulted from the difficulty in counting the < 24h old larvae at the start of the test. In vessels in which more than 30 larvae were found, survival was set to be 100%. A clear dose-response relationship was observed with a no observed effect concentration of 79 µg of flufenoxuron per kg of soil (0.3% of dosed soil). The LC_{50} (10 days) was 170 µg a.i./kg soil.
The emergence of adult *C. riparius* after 32 days is shown in Table 7.4.3.5.1/8. Most adults emerged over a 10 day period starting 13 days after the start of the test. Most adults were observed resting on the side of the test vessel or flying in the space between the water and the cling-film covering the vessel. From all vessels only 6 adults were found dead. The NOEC was determined to be 79 µg a.i./kg soil, the EC_{50} (32 days) was 130 µg a.i./kg soil.

The LC_{50} and NOEC values are summarised in Table 7.4.3.5.1/9.

4.3. Conclusion

The test was not conducted according to a guideline as no common guideline was available in the year 1993. Furthermore, no analytical measurements of the test substance in the overlying water or pore water were conducted. Nevertheless, the results are considered reliable and may be used for the risk assessment.

4.3.1.	Reliability	2	X
4.3.2.	Deficiencies	See 5.3	

Section A7.4.3.5.1 Effects on sediment dwelling organisms

Annex Point IIIA, XIII.3.4 *Chironomus riparius*

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	February 2007
Materials and Methods	Agree with the applicant's version
Results and discussion	Agree with the applicant's version
Conclusion	Agree with the applicant's version
Reliability	Reliability index 3 No analytical measurements of the test substance were carried out in the overlying water and pore water. Moreover, test substance was quantified only in the stock soil (at the concentration of 25 mg a.i./kg) used to prepare the different concentrations of treated sediments, and never during the 32 days of the test. For these reasons, the study is considered as unreliable.
Acceptability	Not acceptable See above
Remarks	As results are considered unreliable, whole summary of the study was not read in detail.
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.4.3.5.1/3: Dilution water

Criteria	Details
Source	The water used for the culturing and testing of *C. riparius* is reconstituted fresh water prepared by dissolving Analar grade salts in glass-distilled deionised water or Millipore, Milli-Q filtered water. The salts are prepared in three stock solutions and quantities of these stock solutions are combined and diluted to produce the reconstituted water.
Alkalinity	-
Hardness	150 ≤ 10 mg/L $CaCO_3$
pH	adjusted to 7.0 ± 0.5 using acid or alkali
Ca / Mg ratio	-
Na / K ratio	-
Oxygen content	9.2 mg/L
Conductance	-
Holding water different from dilution water	No

Table 7.4.3.5.1/4: Test organisms

Criteria	Details
Strain	*Chironomus riparius* Meigen
Source	Egg ropes were taken from a laboratory culture derived from animals obtained from the University of Wales, Cardiff.
Age (at start of the study)	1st instars < 24 h old
Breeding method	Approximately eight egg ropes are used to initiate new cultures. The cultures are held in a temperature controlled room, 18-22°C under artificial light with a 16 h light, 8 h dark cycle.
Kind of food	Light sprinkling of finely crushed Tetramin (Tetra Werke, Germany)
Amount of food	Approximately 25 mg per vessel
Feeding frequency	About 3 times a week
Pretreatment	The test was initiated with <24 h old larvae. Egg ropes were removed from the culture and placed in petri dishes in reconstituted water. Approximately 24 h later actively moving young were removed and added to the test vessels.
Feeding of animals during test	The test animals were fed approximately three times a week with approximately 25 mg per vessel of finely ground Tetramin during the test.

Table 7.4.3.5.1/5: Test system

Criteria	Details
Static test	Portions of the stock slurries were added to 8 cm diameter crystallizing dishes and reconstituted water was added such that each dish contained 30-33 g of soil and approximately 77 g of reconstituted water. Three dishes were set up at each treatment and three control dishes were set up containing control slurry and reconstituted water. The dishes were set up on 9th September 1991, the following day when the contents of the dishes had settled the depth of sediment was 7 to 10 mm.
Volume of test vessels	-
Volume water/animal	-
Number of animals/vessel	30
Number of vessels/ concentration	3 replicates per test concentration
Test performed in closed vessels due to significant volatility of TS	No, but the dishes were covered with PVC film ("cling-film") to reduce evaporation.

Table 7.4.3.5.1/6: Test conditions

Criteria	Details
Test temperature	20 ± 2 °C
Dissolved oxygen	9.2 mg/L
pH	7.0
Adjustment of pH	pH is adjusted to 7.0 ± 0.5 using acid or alkali when preparing the dilution/culturing water
Aeration of dilution water	Yes, gentle aeration
Quality/Intensity of irradiation	artificial light
Photoperiod	16:8 light-dark-cycle

Table 7.4.3.5.1/7: *Chironomus riparius* larval survival after 10 days

Percentage of dosed soil	conc. * [mg a.i./kg soil]	No. of inserted larvae/test vessel	No. of larvae alive after 10 days	% Survival**
Control	Control	30	31	100
0.03	7.9	30	30	100
0.1	25	30	31	100
0.3	79	30	38	100
1.0	260	30	2	6.7
3.0	770	30	0	0

* Flufenoxuron concentration based upon analytical measurements of soils used to make the slurries. The relative spacing differs slightly from that of nominal percentages of dosed soil as test vessels of different concentrations received slightly different quantities of soil (range 30 - 33 g).
** Nominal 30 larvae added to each vessel, recovery of > 30 larvae taken to be 100 % survival.

Table 7.4.3.5.1/8: Cumulative number of adult *C. riparius* emerging during the test

Percentage of dosed soil	conc. * [mg a.i./kg soil]	Cumulative emergence (day 32) as % of nominal no. of larvae added at the start of the test
Control	Control	90
0.03	7.9	72
0.1	25	77
0.3	79	72
1.0	260	6.7
3.0	770	0

* Flufenoxuron concentration based upon analyses of soils used to make the slurries.

Table 7.4.3.5.1/9: NOEC and LC_{50} values for *Chironomus riparius* exposed to flufenoxuron in the sediment phase.

	Endpoints	
	NOEC [µg a.i./kg soil]	LC_{50}/EC_{50} [µg a.i./kg soil]
Larval survival after 10 days	79	170
Cumulative adult emergence at 32 days	79	130

n.d. = not determined

Section 7.4.3.5.1
BPD Annex Point IIIA, XIII.3.4

Effects on any other species

7.4.3.5.1 Effects on sediment dwelling organisms

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**4) Egeler, P. and Seck, C. 2006** Flufenoxuron (BAS 307 I): Chronic toxicity to the aquatic Oligochaete *Lumbriculus variegatus* exposed to spiked sediment in a 28 d study. XXXX unpublished XXXX	
1.2.	**Data protection**	Yes	
1.2.1.	Data owner	BASF AG	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	Data submitted to the MS after 14 May 2000 on existing a.s. for the purpose of its entry into Annex I	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	For this study no standard guideline is available. The design of this study takes into account aspects of the following methods: - Egeler P., Meller M., Schallnaß, H.-J., and Gilberg, D. (2005): Validation of a sediment toxicity test with the endobenthic aquatic oligochaete *Lumbriculus variegatus* by an international ring test. In co-operation with R. Nagel and B. Karaoglan. Technical Report, R&D No.: 202 67 429. Federal Environmental Agency (Umweltbundesamt), Berlin, Germany.	
2.2.	**GLP**	Yes	
2.3.	**Deviations**	No	
		3. MATERIALS AND METHODS	
3.1.	**Test material**	Flufenoxuron (BAS 307 I)	
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	See 3.1.3.	
3.1.3.	Purity	99.2 %	
3.1.4.	Composition of Product	Not relevant	
3.1.5.	Further relevant properties	Not relevant	
3.1.6.	Method of	The concentrations of Flufenoxuron (BAS 307 I) and its	

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	analysis	metabolite CL 932338 in water and sediment samples from the toxicity test were determined. The analyses of Flufenoxuron (BAS 307 I) and its metabolite CL 932338 in **sediment** were based on the Study "Validation of method RLA 12637 for the analysis of BAS 307 I and CL 932338 in soil down to a LOQ of 0.001 mg/kg", XXXX, by Richard Smalley on October 2002, XXXX. The quantification limit (LOQ) in sediment samples was 10 µg/kg (dry weight). The limit of detection was estimated at 5 µg/kg (dry weight). The analyses of Flufenoxuron (BAS 307 I) and its metabolite CL 932338 in **water** were based on XXXX "Method for the Analysis of Flufenoxuron and its Metabolites in Water by LC-MS-MS" by A. Donn on May 15, 2003, XXXX. The quantification limit (LOQ) in water samples was 0.01 µg/L. The limit of detection was estimated at 0.002 µg/L.	X
3.2.	**Preparation of TS solution for poorly soluble or volatile test substances**	A stock solution (S1) of nominal 264.3 mg/L was prepared by dissolving 26.5 mg of the test item in 100 mL of acetone (actual concentration: 265.0 mg/L). Thereafter a second stock solution (S2) of nominal 13.22 mg/L was prepared by diluting 5 mL of S1 in 100 mL of acetone (actual concentration: 13.25 mg/L). All further calculations of nominal concentrations are based on 13.22 mg/L. This stock solution (S2) was shaken manually for 30 seconds and directly used thereafter. The test solutions for application of the test item to the sediment were obtained by diluting the stock solution or application solutions with acetone. From these test solutions an appropriate volume was mixed with an appropriate amount of quartz sand for each treatment (10 g of quartz sand per replicate). The acetone was evaporated to dryness before the sediment of each concentration level was prepared. The amount of sand provided by the test-item-and-sand mixture was taken into account when preparing the formulated sediment. To ensure that the test item added to sediment was evenly distributed within the sediment, the bulk formulated sediments were thoroughly mixed. From these bulk concentration levels, the sediment was distributed to the individual replicates of each concentration level.	
3.3.	**Reference substance**	No	
3.3.1.	Method of analysis for reference	Not applicable	

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	substance		
3.4.	**Testing procedure**		
3.4.1.	Dilution water, Test sediment	Reconstituted water (table A7_4_3_5_1-1) and artificial sediment (table A7_4_3_5-1a) were used as media.	
3.4.2.	Test organisms	See table A7_4_3_5_1-2	
3.4.3.	Test system	Prior to application of the test item, the formulated pre-sediment was conditioned for 7 days with reconstituted water (sediment-water volume ratio: 1 : 3.5 - 4.5) and was incubated under a light and temperature regime comparable to the conditions in the subsequent test. On day of application, the overlying water was carefully decanted and discarded. The spiked quartz sand (10 g per replicate), and feed was mixed with the formulated pre-sediment. Thereafter the formulated sediment was distributed to the test vessels and topped with new overlying water. For further details on the test system *cf.* table A7_4_3_5_1-3.	X
3.4.4.	Test conditions	See table A7_4_3_5_1-4	
3.4.5.	Duration of the test	28 days	
3.4.6.	Test parameter	Endpoints are reproduction and biomass (dry weight) (EC_X and NOEC/LOEC), i.e., total number of worms, dry weight of worms. For assessment of the biological effects at the end of the test, the worms were sieved from the sediment (500 µm mesh), rinsed in reconstituted water and counted. Worms that did not react to a gentle stimulus or showed signs of decomposition were considered dead. The number of living and dead individuals, the number of adults (complete worms), and the number of worms with regenerated body regions (i.e., with new posterior part, with new anterior part, and with both new posterior and anterior parts), and the number of small, incomplete worms (i.e., freshly fragmented worms with non-regenerated body regions) per replicate were recorded. The worms found in each replicate were then transferred to dried, pre-weighed weigh boats (one per replicate), and immobilised using a few drops of ethanol per weigh pan. The weigh pans were placed in a drying oven at 100 ± 5°C to dry overnight, after which they were weighed and worm dry weight was determined.	
3.4.7.	Sampling	At least three times a week the test vessels were observed in order to assess visually any behavioural differences compared with the control.	

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		The following physical-chemical parameters were determined during the test: **Environmental parameters:** light intensity was measured once during the test and room temperature was monitored continuously throughout the test. **Overlying water:** Temperature, dissolved oxygen, and pH were determined in one test vessel of each concentration level and one test vessel of the controls once per week and at the start and the end of the exposure period. Total water hardness was measured in one replicate of the controls and one test vessel at the highest concentration at the start and the end of the exposure period. Ammonium content was determined in one replicate of the controls and one test vessel of each concentration level at the start of the exposure period, and subsequently 3 x per week. **Sediment:** Dry weight on day -7 and on the sampling dates in all replicates of each concentration level to be used for later supporting chemical analysis. Total organic carbon content (TOC) was determined in 4 samples after preparation of sediment (day -7). The pH was recorded on day -7 of the study in all concentration levels.
3.4.8.	Monitoring of TS concentration	For chemical analysis of the active ingredient additional parallel replicates were prepared for analytical purposes only. The concentration of Flufenoxuron was analysed in sediment, pore water and overlying water, at start and at end of exposure. The samples or test concentrations used for chemical analysis were from control, the highest and one intermediate treatment.
3.4.9.	Statistics	ANOVA and multiple comparison tests (Dunnett‘s t-test). As there was no concentration-response relationship, EC-values were not calculated. The statistical software package ToxRat Professional 2.09 was used for these calculations.
		4. RESULTS
4.1.	**Range finding test**	Not performed
4.1.1.	Concentrations	Not applicable
4.1.2.	Number/ percentage of animals showing adverse effects	Not applicable
4.1.3.	Nature of adverse effects	Not applicable

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4.2.	**Results test substance**		
4.2.1.	Initial concentrations of test substance	Concentrations tested: 25, 50, 100, 200, and 400 µg/kg sediment dry weight (nominal)	X
4.2.2.	Actual concentrations of test substance	The measured initial recovery of the test item in the test system varied between 61.8 and 76.5% of the nominal concentrations. At the end of the exposure period (day 28) the measured recovery varied between 79.6 and 69.0% of the nominal concentrations. Until the end of the exposure period, the main fraction of the test item applied to the system was associated to the sediment. Only minor amounts were measured in samples of pore water and overlying water. Minor amounts of a metabolite (CL 932338) were found in the overlying water on day 28, which were below 0.5% of the nominal test item concentration The measured initial concentrations in the sediment (based on measured concentrations in pore water and sediment) were 61.7 µg/kg dry sediment (at nominal 100 µg/kg dry sediment), and 305.9 µg/kg dry sediment (at nominal 400 µg/kg dry sediment) on day 0 of the exposure phase. Since no effects were found up to 400 µg/kg dry sediment, the biological results were calculated based on the initially measured concentrations at the highest concentration level. See individual values in table A7_4_3_5_1-6.	
4.2.3.	Effect data	After 28 days of exposure, no mortality was observed up to the highest concentration level. In all replicates 10 or more worms were found. The total number of worms (including adult and regenerated worms) found at the end of the test was evaluated as parameter of reproduction. This endpoint showed also no effects at the highest concentration tested. For biomass no effects were observed too. See table A7_4_3_5_1-5.	X
4.2.4.	Concentration / response curve	Not applicable	
4.2.5.	Other effects	-	
4.3.	**Results of controls**	No effects	
4.4.	**Test with reference substance**	Not performed	

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4.4.1.	Concentrations	Not applicable
4.4.2.	Results	Not applicable
		5. APPLICANT'S SUMMARY AND CONCLUSION
5.1.	**Materials and methods**	The study was conducted in order to determine the potential impact of the test item on the survival, reproduction and biomass of the aquatic oligochaete *Lumbriculus variegatus* at the end of the exposure phase. To achieve this aim, adult worms of synchronised physiological state were exposed to a series of toxicant concentrations applied to the sediment phase of a sediment-water system. Artificial sediment and reconstituted water were used as media. Test vessels without the addition of the test item served as controls. The test item was spiked into the sediment in bulk for each concentration level in order to minimise variability between replicates of each concentration level, and the test organisms were subsequently introduced into the test vessels in which the sediment and water concentrations had been equilibrated for 7 days. The equilibration was carried out at the same test conditions as the exposure phase. The test animals were exposed to the sediment-water systems for a period of 28 days. The preferred endpoints of this study were the no observed effect concentration (NOEC) and the lowest observed effect concentration (LOEC) for survival, reproduction, and biomass reduction, respectively, compared to the control. To verify the nominally applied concentrations, samples were taken and analysed during the test.
5.2.	**Results and discussion**	With respect to reproduction and biomass, no concentration-dependent effects were found. Therefore no EC-values were calculated. There were no mortalities up to the highest concentration level. NOEC (reproduction and biomass): ≥ 306 µg/kg LOEC (reproduction and biomass): > 306 µg/kg The results are related to the initially measured concentrations at the highest concentration level (400 µg/kg dw sediment). Recoveries at the beginning of the test were between 61.8 and 76.5% of the nominal concentrations. At the end of the test were 79.6 and 69.0%.
5.3.	**Conclusion**	The validity criteria are fulfilled, *cf.* table A7_4_3_5_1-7.
5.3.1.	Other Conclusions	None
5.3.2.	Reliability	1

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5.3.3. Deficiencies No

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	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	*Give date of action*
Materials and Methods	Agree with applicant's version **Revisions/amendments :** 3.1.6 Method of analysis : … *the Study "Validation of method RLA 12637 for the analysis of BAS 307 I and CL 932338 in soil down to a LOQ of 0.001 mg/kg", BASF study number 148828,* **XXXX (refer to Section 4.2/5)** *Report number 4872, by Richard Smalley on October 2002, XXXX* The methods for the detection of Flufenoxuron and its metabolite in water and sediment were validated with average recoveries into the required 70 – 110 % range and a standard deviation below 20 %.
Results and discussion	Agree with applicant's version. **Revisions/amendments :** 4.2.1 Initial concentrations of test substance : *Concentrations tested:* **0 (water), 0 (solvent),** *25, 50, 100, 200, and 400 µg/kg sediment dry weight (nominal)*
Conclusion	Agree with applicant's version. Flufenoxuron has no effect on the reproduction and biomass of *Lumbriculus variegates* at the maximal dose rate tested (306 µg/kg dry weight - actual concentration). NOEC (reproduction and biomass): ≥ 306 µg/kg LOEC (reproduction and biomass): > 306 µg/kg In taking into account a total organic carbon of 2.42% in the experimental sediment, the results normalized for a standard sediment (containing 5% of organic carbon) are the following : NOEC (reproduction and biomass): ≥ 632 µg/kg LOEC (reproduction and biomass): > 632 µg/kg
Reliability	1
Acceptability	Acceptable
Remarks	Errors in Tables A7_4_3_5_1-3, A7_4_3_5_1-5 were corrected in bold and underlined
	COMMENTS FROM …
Date	*Give date of comments submitted*

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Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table A7_4_3_5_1-1: Dilution water

Criteria	**Details**
Source	Reconstituted water according to OECD guideline No. 203 (OECD 1992); sediment-water volume ratio approx. 1: 4 The final concentrations of the salts in the reconstituted water were: $CaCl_2$*2 H_20 294.0 mg/L $MgSO_4$*7 H_2O 123.0 mg/L $NaHCO_3$ 64.8 mg/L KCl 5.75 mg/L
Alkalinity	Not specified
Hardness	Between 17.0 – 17.7 °dH (304-316 mg $CaCO_3$/L) as measured on day 0 and 28.
PH	See table A7_4_3_5_1-4
Ca / Mg ratio	See above
Na / K ratio	See above
Oxygen content	See table A7_4_3_5_1-4
Conductance	623 µS/cm
Holding water different from dilution water	No

Table A7_4_3_5_1-1a: Test sediment

Sediment characterisation	Details
Particle size distribution	Spiked artificial sediment according to OECD guideline No. 218 (OECD 2004) was used. The final composition of the formulated sediment is as follows (figures refer to sediment dry weight): - Peat: Sphagnum moss peat, air dried, no visible plant remains, finely ground (particle size ≤ 0.5 mm); 5 ± 0.5% of sediment dry weight - Quartz sand: grain size > 50% of the particles in the range of 50- 200 µm; 75 – 76% of sediment dry weight - Kaolinite clay: 20 ± 1% (kaolinite content ≥ 30%) - Urtica powder: 0.2 – 0.25% (*Folia urticae*; Caelo Caesar & Loretz GmbH, Hilden, in addition to dry sediment, finely ground (particle size ≤ 0.5 mm)) - Cellulose powder: 0.2 – 0.25% (α-Cellulose, in addition to dry sediment) - Organic carbon: 2% ± 0.5 (adjusted by addition of peat and sand) - Calcium carbonate ($CaCO_3$): 0.05 – 1% (pulverised, chemically pure, in addition to dry sediment) - Deionised water: 30 – 50% (in addition to dry sediment)
Organic carbon (%)	2% ± 0.5
Water content (%)	30 – 50% dw sediment
pH	With calcium carbonate the pH value was adjusted to 6.5 – 7.0
Cation exchange capacity	No data
TOC (Total organic carbon)	On day –14 of the test it was determined to be 2.42 ± 0.05% (average ± standard deviation, n = 4) of sediment dry weight (without feed).

Table A7_4_3_5_1-2: Test organisms

Criteria	Details
Strain	*Lumbriculus 524ariegates* (Müller) In contrast to epibenthic organisms, *L. 524ariegates* burrows in the sediment, and ingests sediment particles below the sediment surface. This allows exposure of the test system to the test item via all possible uptake routes.
Source	The animals were originally obtained from Fischfutter Etzbach (D-53894 Mechernich-Bergheim, Germany).
Age (at start of the study)	Synchronised adult worms of similar size
Breeding method	The species has been cultured at ECT Oekotoxikologie GmbH since Jan. 1998. *Lumbriculus 524ariegates* was cultured in glass containers containing of a layer of quartz sand as used for the artificial sediment, and reconstituted water. The oligochaetes were held at room temperature with a natural photoperiod. In the culture, the worms were fed with TetraMin. The worms to be used for measurement of biological effects at the end of the test were "synchronised" before the start of the test. These worms were artificially fragmented, the worms were placed onto a glass slide in a drop of culture water, and dissected in the median body region with a scalpel. The posterior ends were left to regenerate for 14 days at 20 ± 2°C until start of exposure. The test organisms were therefore considered to be in a similar physiological state. This synchronisation was performed to avoid "uncontrolled" regeneration and subsequent high variation in test results. This variation can occur, when some worms, which have fragmented and therefore do not feed for a certain time period, are less exposed to the test item than other worms, which do not fragment during the test. The worms were fed with a suspension of 50 mg/mL finely ground TetraMin on day 7 after synchronisation.
Kind of food	During the test feed was in sediment (Urtica powder and cellulose)
Amount of food	Nutrient content of the artificial sediment was 0.4 – 0.5% of sediment dry weight
Feeding frequency	Not applicable
Pretreatment	No
Feeding of animals during test	Feed was in sediment

Table A7_4_3_5_1-3: Test system

Criteria	Details
Static test	Test glass vessels were covered by plastic lids. Test vessels contained 80 or 200 g ww sediment, depending on vessel type (depth of sediment layer was of 1.8 – 1.9 cm) and 205 or 570 mL overlying water **in order to respect the sediment-water volume ratio of approx. 1:4.**
Volume of test vessels	Glass vessels, 250 mL (6 x 11.5 cm) for biological measurements, and 1 L (10 x 15 cm) for analytical samples
~~Volume water/animal~~ **Number of animals/test vessels**	~~250 mL test water/10 animals for treatment~~ ~~1L/25 animals for analytical samples~~ **10 animals/250 mL test vessel (treatment)** **25 animals/1L test vessel (analytical sample)**
Number of animals/vessel	10 in replicates for biological measurements (25 in replicates for analytical measurements)
Number of vessels/ concentration	4 replicates per test concentration and for the control plus 6 for the solvent control and additional vessels for chemical analysis
Test performed in closed vessels due to significant volatility of TS	No

Table A7_4_3_5_1-4: Test conditions

Criteria	Details
Test temperature of the overlying water	19.8°C (mean value of 35 measurements; 19.3 – 20.0°C)
Dissolved oxygen of the overlying water	Mean values during the test: 8.20 – 8.52 mg/L (90.4 to 94.0% of the air saturation value)
pH of the overlying water	Mean values during the test: 8.20 – 8.28
Adjustment of pH	Yes (only in sediment)
Aeration of dilution water	Gentle aeration during acclimation and exposure
Quality/Intensity of irradiation	307 lux (mean value of 5 measurements; min: 283 lux, max: 337 lux)
Photoperiod	16:8 light-dark-cycle

Table A7_4_3_5_1-5: Reproduction and biomass (dry weight) results of the bioassay after 4 weeks of exposure

Nominal concentration [µg/kg sed dw]	Reproduction		Biomass (dry weight)	
	Mean [Total number/replicate]	Std dev.	Mean [mg/replicate]	Std dev.
Control	33.5	3.4	39.40	11.43
Solvent control	33.7	3.1	41.73	9.25
25	30.3	1.7	39.98	4.58
50	33.5	2.1	34.60	3.62
100	33.8	5.7	40.93	5.93
200	34.3	4.8	42.63	4.61
400	32.0	2.8	33.58	4.35

Table A7_4_3_5_1-6: Recoveries (% of nominal concentrations) of the test item in sediment, pore water and overlying water samples

Nom. concentration	Test period	Recovery of test item in % of nominal concentration			Sum of recoveries
µg/kg (dw)	(days)	Sediment (%)	Pore water (%)	Overlying water (%)	Total test system
0 100 400	0 0 0	n.a. 61.7 76.4	n.a. 0.01 0.05	n.a. 0.10 0.03	n.a. 61.8 76.5
0 100 400	28 28 28	n.a. 79.1 69.0	n.a. 0.02 0.01	n.a. 0.48 0.01	n.a. 79.6 69.0

Table A7_4_3_5_1-7: Validity criteria for sediment toxicity test with the endobenthic aquatic oligochaete *Lumbriculus variegatus*

	Fulfilled	Not fulfilled
Number of worms in the control vessels at the end of exposure at least 80% higher than at the start of exposure	**X**	
pH of the overlying water between 6 and 9 at the start and at the end of the test	**X**	
Dissolved oxygen concentration measured in at least one replicate per concentration level and control > 60% of the air saturation value (ASV)	**X**	

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			Official use only
		1. REFERENCE	
1.1.	**Reference**	**5) Weltje, L. and Pupp, A. 2007** Chronic toxicity of flufenoxuron (BAS 307 I) to the non-biting midge *Chironomus riparius* exposed via spiked-sediment. XXXX. unpublished XXXX	
1.2.	**Data protection**	Yes	
1.2.1.	Data owner	BASF AG	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	Data submitted to the MS after 14 May 2000 on existing a.s. for the purpose of its entry into Annex I	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	OECD Guideline 218 (adopted 2004) "Sediment-water chironomid toxicity test using spiked sediment".	
2.2.	**GLP**	Yes	
2.3.	**Deviations**	No	
		3. MATERIALS AND METHODS	
3.1.	**Test material**	Flufenoxuron (BAS 307 I)	
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	See 3.1.3	
3.1.3.	Purity	99.2 %	
3.1.4.	Composition of Product	Not relevant	
3.1.5.	Further relevant properties	Not relevant	
3.1.6.	Method of analysis	HPLC-MS/MS	
3.2.	**Preparation of TS solution for poorly soluble or volatile test substances**	For the application, a stock solution of flufenoxuron was prepared by dissolving 8.57 mg BAS 307 I in 1000 mL acetone. For the test concentration of 150.0 µg/kg dry sediment, 10.0 mL of the stock solution were added to 80 g of quartz sand and mixed homogeneously. After an evaporation time of about 2 h under the fume hood, the spiked quartz sand was added to 620 g sediment	

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		and mixed again thoroughly. In order to include potentially remaining residues from the vessel in which the quartz sand and the test item were mixed, the vessel was rinsed with 100 mL deionised water, which were carefully added to the sediment. Afterwards, the moisture content of the sediment was approximately 30%. Then, 100 ± 2 g of the spiked sediment was added to each of five 600 mL glass beakers (one for chemical analysis and 4 for exposure). For the lower concentrations the exact same procedure was repeated using dilutions of the above-mentioned stock solution.	
3.3.	**Reference substance**	Lindane	
3.3.1.	Method of analysis for reference substance	No data	
3.4.	**Testing procedure**		
3.4.1.	Dilution water, Test sediment	Reconstituted water (table A7_4_3_5_1-1) and artificial sediment (table A7_4_3_5-1a) were used as media.	
3.4.2.	Test organisms	See table A7_4_3_5_1-2	
3.4.3.	Test system	The test system was allowed to stabilise for 2 days before addition of the larvae. The following definitions therefore apply: DAT: day after treatment. DAI: day after insertion of the larvae. For further details on the test system *cf.* table A7_4_3_5_1-3.	
3.4.4.	Test conditions	See table A7_4_3_5_1-4	X
3.4.5.	Duration of the test	28 days	
3.4.6.	Test parameter	**Development rate**: development time represents the time span between the insertion of the larvae (DAI 0) and the emergence of the adult midges. The development rate is the reciprocal of the development time (day^{-1}) and represents the portion of larval development taking place per day. **Emergence rate** is the ratio of the emerged insects (imagines) to introduced larvae. **NOEC** is the highest concentration of the test item at which no significant effects (on emergence or development rate or other observations) occur relative to the (water, solvent or pooled) control. The LOEC is the next higher concentration, i.e. the lowest concentration at which a significant effect was determined.	

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		EC_{50} is the concentration causing a 50% effect on the parameter under consideration. It is usually determined mathematically (e.g. via probit, logit or log-log analysis).	
3.4.7.	Sampling	Before emergence of the first midge occurs observations on behaviour and mortality were made at least 3 times a week, and observed irregularities were recorded. From the onset of emergence observations on behaviour, mortality and emergence were made at least once each working day. Daily, the emerged adults were removed from the vessels, and their number and sex was recorded.	X
3.4.8.	Monitoring of TS concentration	One additional vessel for each treatment group was set up for chemical analysis of sediment on DAT 2. In the treatments 80.0 and 150.0 µg/kg dry sediment (nominal), overlaying and pore water was also analysed on DAT 2. The analysis of sediment of the 80.0 and the 150.0 µg/kg dry sediment treatment (nominal) at DAT 30 (end of the test), as well as the analysis of pore water and overlaying water of these treatments at DAT 30 were conducted in the same test vessels as used for the biological assessments.	
3.4.9.	Statistics	Statistical determination of the NOEC for both endpoints is done by analysis of variance (ANOVA), followed by Bonferroni's or Williams' post test ($\alpha = 0.05$) to test for significant differences between the treatment and the solvent control. The EC_{50} was determined using an appropriate model (for example probit, logit or log-log). The calculations were conducted on a PC using the commercial software package TOXSTAT, Version 3.5 (Western Ecosystems Technology, Inc., 2003 Central Avenue, Cheyenne, WY 82001, USA).	
		4. RESULTS	
4.1.	**Range finding test**	Not performed. A previous GLP test (XXXX) was taken into account for selection of test concentrations.	X
4.1.1.	Concentrations	-	
4.1.2.	Number/ percentage of animals showing adverse effects	-	
4.1.3.	Nature of adverse effects	-	

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4.2.	**Results test substance**		
4.2.1.	Initial concentrations of test substance	Based on the results of a previous GLP test (XXXX) the following target concentrations were selected: 30.0, 60.0, 80.0, 100.0 and 150.0 µg/kg dry sediment. Additionally a solvent free (or water) control and solvent (acetone) control were included.	
4.2.2.	Actual concentrations of test substance	Analytical confirmation of the sediment concentrations by HPLC-MS/MS at the start of exposure yielded values of 26.4, 58.6, 72.3, 98.1 and 154.6 µg/kg dry sediment for the nominal 30.0, 60.0, 80.0, 100.0 and 150.0 µg/kg dry sediment treatment. Hence, the recovery of the test item was between 88.0 and 103.1%. At test end (DAT 30) 88.1 and 175.9 µg/kg dry sediment were found for the nominal 80.0 and 150.0 µg/kg dry sediment treatment (recovery between 110.1 to 117.3%). Therefore, the endpoint calculations are based on nominal sediment concentrations. Overlaying water concentrations, measured in the nominal 80.0 and 150.0 µg/kg dry sediment treatment were 0.344 and 0.352 µg/L on DAT 2 and 0.345 and 0.360 µg/L on DAT 30. The pore water concentrations were 0.409 and 0.536 µg/L on DAT 2 and 0.324 and 0.344 on DAT 30 for the nominal 80.0 and 150.0 µg/kg dry sediment treatment. The results of the chemical analyses of the test item in sediment, overlaying water and pore water are summarised in table A7_4_3_5_1-6.	
4.2.3.	Effect data	On DAI 13 (= DAT 15), the first emerged midges were observed, which is normal under the conditions of this test system. In vessel 10 of the 30 µg/kg dry sediment treatment only 7 midges emerged. In the other vessels of this treatment and also in higher ones (up to 80 µg/kg dry sediment) 16 to 20 midges emerged. The low number of emerged midges may have been caused by the use of contaminated glassware or the insertion of too few larvae in this vessel. Since this observation is clearly an outlier and not related to the test item concentration, this vessel was excluded from further (statistical) evaluations. See table A7_4_3_5_1-5 for individual values.	
4.2.4.	Concentration / response curve	A clear concentration-response relation was observed. The effect of test substance on no. of emerged midges per test substance concentration are plotted in p. 18 of the report.	X
4.2.5.	Other effects	-	
4.3.	**Results of controls**	See table A7_4_3_5_1-5 for results	X

Section 7.4.3.5.1 **BPD Annex Point IIIA, XIII.3.4**	**Effects on any other species** 7.4.3.5.1 Effects on sediment dwelling organisms

4.4.	**Test with reference substance**	A study with the reference item lindane was completed in December 2006 under study code 177181_1 (XXXX). The study director was XXXX.	
4.4.1.	Concentrations	No data	
4.4.2.	Results	The NOEC for the development rate was 2.0 µg/L (nominal) and for the emergence rate 6.0 µg/L (nominal). The results were within the expected range.	X
		5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1.	**Materials and methods**	A chronic static toxicity test with *C. riparius* was conducted. Five concentrations: 30.0, 60.0, 80.0, 100.0 and 150.0 µg/kg dry sediment (nominal target values), with four replicates, plus a solvent (acetone) control with six and a solvent free (water) control with four replicates were used. Artificial sediment and reconstituted water were used as media. Twenty *C. riparius* first instar larvae were added to each vessel. The endpoints observed were emergence rate and development rate. The test animals were exposed to the sediment-water systems for a period of 28 days. To verify the nominally applied concentrations, samples were taken and analysed during the test.	X
5.2.	**Results and discussion**	The NOEC for both development and emergence rate was 80.0 µg/kg dry sediment (nominal value) as determined by ANOVA, followed by Bonferroni's or Williams' test ($p < 0.05$). A log-log analysis of the emergence data against the nominal concentrations yielded an EC_{50} (95% confidence interval) of 142.7 (131.7 – 154.6) µg/kg dry sediment.	
5.3.	**Conclusion**	The validity criteria are fulfilled, *cf.* table A7_4_3_5_1-7.	
5.3.1.	Other Conclusions	None	
5.3.2.	Reliability	1	
5.3.3.	Deficiencies	No	

Section 7.4.3.5.1
BPD Annex Point IIIA, XIII.3.4

Effects on any other species

7.4.3.5.1 Effects on sediment dwelling organisms

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	March 2007
Materials and Methods	Agree with applicant's version. **Comments:** 3.4.4 Test conditions : There are no information on the depth of sediment, the volume of pore water, the weight of wet sediment with pore water. **Revision/amendments:** 3.4.4 Test conditions : *See table A7_4_3_5_1-4* Measurements of pH, oxygen and temperature in overlaying water have been taken on DAI 0, 7, 14, 22 and 28 for each vessel. 3.4.7 ~~*Sampling*~~ Observation conditions
Results and discussion	Don't agree with applicant's version concerning point 4.4.2 Results : *'The NOEC for the development rate was 2.0 µg/L (nominal) and for the emergence rate 6.0 µg/L (nominal). The results were within the expected range.'* must be replaced by : 'Biological results are based on nominal dry sediment concentrations of BAS 307 I. The NOEC for both development and emergence rate was 80.0 µg/kg dry sediment (ANOVA with Bonferroni's or William's test, $p < 0.05$). The EC50 (95% confidence interval) for emergence rate was 142.7 (131.7 – 154.6) µg/kg dry sediment (log-log analysis).' **Revision/amendments:** • 4.1 Range finding test : *Not performed. A previous GLP test (XXXX) was taken into account for selection of test concentrations.* **Refer to Section 7.4.3.5.1/3 (Toy, 1993).** • 4.2.4 Concentration/response curve : *A clear concentration-response relation was observed. ~~The effect of test substance on no. of emerged midges per test substance concentration are plotted in p. 18 of the report~~* • 4.3 Results of controls : **No significant difference was noted between the water control and the acetone control.** *See table A7_4_3_5_1-5 for results*

Section 7.4.3.5.1 **BPD Annex Point IIIA, XIII.3.4**	**Effects on any other species** 7.4.3.5.1 Effects on sediment dwelling organisms

Conclusion	Adopt applicant's version : After an exposure of *C. riparius* first instar larvae to Flufenoxuron in a water/sediment system for a period of 28 days, the NOEC for both development and emergence rate was 80.0 µg/kg dry sediment (nominal value). ~~In taking into account a percentage of organic matter of 5% (sphagnum peat content), corresponding to 2.94% of organic carbon, in the experimental sediment, the normalized value of NOEC for a standard sediment containing 5% organic carbon is 136 µg/kg dry sediment.~~ **Revision/amendments:** 5.1 Materials and methods : *To verify the nominally applied concentrations, samples were taken and analysed ~~during the test~~* **at the beginning and at the end of the test.**
Reliability	1
Acceptability	Acceptable
Remarks	Unnecessary comments in Table A7.4.3.5.1-1 were crossed out. Additional comments in Tables A7.4.3.5.1-3 and A7.4.3.5.1-4 were added in bold and underlined.

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table A7_4_3_5_1-1: Dilution water

Criteria	Details
Source	Synthetic medium (reconstituted water, M4 according to Elendt) was used for the test. ~~The composition of the medium is given in detail on page 11 of the report.~~ The medium was prepared on the basis of ultrapure deionized water, at least 24 hours before use to allow stabilisation of the solution. It was constantly aerated.
Alkalinity	0.95 mmol/L
Hardness	2.47 mmol/L (up to pH 4.3) for pure reconstituted water 2.937 to 3.204 mmol/L during the test.
pH	7.95 for pure reconstituted water. See table A7_4_3_5_1-4 for values during the test.
Ca / Mg ratio	Not specified
Na / K ratio	Not specified
Oxygen content	9.1 mg/L for pure reconstituted water. See table A7_4_3_5_1-4 for values during the test.
Conductance	662 µS/cm
Holding water different from dilution water	No data

Table A7_4_3_5_1-1a: Test sediment

Sediment characterisation	Details
Particle size distribution	The artificial substrate as described in OECD guideline 218 is used as sediment. It is composed as follows: ca. 5% finely ground sphagnum peat ca. 20% kaolin clay (kaolinite content > 30%) ca. 0.75% $CaCO_3$ (Merck 2069) ca. 75% quartz sand (ISS-0-VAC, Fa. Gebr. Willersinn) > 80% has a particle size > 0.09 and < 0.18 mm
Organic carbon (%)	No data
Water content (%)	The moisture content was 27.7%
pH	The pH was determined to be 6.66
Cation exchange capacity	No data
TOC (Total organic carbon)	No data

Table A7_4_3_5_1-2: Test organisms

Criteria	Details
Strain	Non-biting midge *Chironomus riparius*
Source	House laboratory culture, which was established with egg-ropes obtained from the Zoological Institute of the J.W. Goethe university in Frankfurt am Main, Germany.
Age (at start of the study)	Larvae up to 3 days old
Breeding method	No data
Kind of food	Commercially available fish food, TetraMin
Amount of food	The food was finely ground and suspended in M4 water. An amount of food suspension corresponding to about 0.25 - 1.0 mg TetraMin per larva per day (i.e. 5 - 20 mg/vessel/day) was added for each day up to DAI 27. Depending on the smell of the overlaying water and the amount of green algae grown in the test vessels, feeding was adjusted or completely stopped
Feeding frequency	Daily
Pretreatment	Two days prior to addition of the larvae, fresh egg masses were collected from the culture and transferred to small vessels with standard M4-water, containing a small amount of green algae. About two days later the first larvae start hatching. Two days after preparing the vessels with spiked sediment, 20 1st instar larvae (not older than 3 days) were added to the test vessels. During addition of the larvae and for about 24 h afterwards, the aeration was stopped to give the larvae the opportunity to settle into the sediment.
Feeding of animals during test	Yes, up to day 27 after insertion of the larvae

Table A7_4_3_5_1-3: Test system

Criteria	Details
Static test	Test glass vessels were covered to reduce evaporation and to avoid the escape of emerging midges. Test vessels contained 100 +/- 2 g wet artificial sediment and ca. 400 mL M4 water (Elendt medium) corresponding to a water layer of about 8.0 cm.
Volume of test vessels	Glass vessels, 600 mL
Volume water/animal	400 mL / 20 larvae
Number of animals/vessel	20 larvae / vessel
Number of vessels/ concentration	For each test concentration and the solvent free (or water) control four replicates were used. **One additional vessel for each treatment group was set up for chemical analysis on DAT 2.** In addition, a solvent (acetone) control with six replicates was included.
Test concentrations (nominal)	**0, 30, 60, 80, 100, 150 µg/kg dry weight**
Test performed in closed vessels due to significant volatility of TS	No

Table A7_4_3_5_1-4: Test conditions

Criteria	Details
Test temperature of the overlying water	19.9 - 21.4°C during the test
Dissolved oxygen of the overlying water	6.68 - 9.97 mg/L (> 60% air saturation value)
pH of the overlying water	7.65 - 9.20
Ammonium	**DAI 0 : 0.2 mg/L (control and solvent control)** **0.1 mg/L (150 µg/kg dry sediment treatment)** **DAI 28 : 0 mg/L (control and solvent control)** **0 mg/L (150 µg/kg dry sediment treatment)**
Adjustment of pH	No
Aeration of dilution water	Slight aeration; gentle aeration of the water was provided to each vessel via a glass Pasteur pipette of which the outlet was situated a few cm above the sediment.
Quality/Intensity of irradiation	580 - 760 lux
Photoperiod	16:8 light-dark-cycle

Table A7_4_3_5_1-5: Emergence rate (ER) and development rate (DR) with their respective standard deviations (SD)

Nominal concentration [µg/kg d.s.]	ER (SD)	DR (SD)
water control	0.9375 (0.0629)	0.0625 (0.0013)
solvent control	0.9167 (0.0816)	0.0650 (0.0028)
30.0	0.8500 (0.0500)	0.0637 (0.0024)
60.0	0.9125 (0.0629)	0.0630 (0.0022)
80.0	0.9000 (0.0707)	0.0644 (0.0016)
100.0	0.7000 (0.1225)*	0.0611 (0.0046)*
150.0	0.4000 (0.0408)*	0.0617 (0.0029)*

d.s. = dry sediment, * indicates significant difference from the solvent control

Table A7_4_3_5_1-6: Measured concentrations of BAS 307 I in the sediment, overlaying water, and pore water at different times after application

Sediment, DAI 0			
Nominal sediment conc. [µg/kg dry weight]	**Sediment humidity [%]**	**Mean concentration found [µg/kg dry weight]**	**Mean recovery [%]**
0 (water control)	16.60	< LoQ	-
0 (solvent control)	16.76	< LoQ	-
30.0	16.70	26.4	88.0
60.0	16.81	58.6	97.6
80.0	16.30	72.3	90.3
100.0	15.85	98.1	98.1
150.0	15.95	154.6	103.1

LoQ = limit of quantitation; 1 µg/kg

Sediment, DAI 28			
Nominal sediment conc. [µg/kg dry weight]	**Sediment humidity [%]**	**Mean concentration found [µg/kg dry weight]**	**Mean recovery [%]**
80.0	16.50	88.1	110.1
150.0	16.05	175.9	117.3

Overlaying water and pore water, DAI 0 and 28			
Nominal sediment conc. [µg/kg dry weight]	**Time [DAI]**	**Overlaying water [µg/L]**	**Pore water [µg/L]**
80.0	0	0.344	0.409
	28	0.345	0.324
150.0	0	0.352	0.536
	28	0.360	0.344

Table A7_4_3_5_1-7: Validity criteria according to OECD guideline 218

	Fulfilled	**Not fulfilled**
The emergence of the controls was ≥ 70%	**X**	
Emergence in the controls occurred between 12 and 23 days after insertion of the larvae	**X**	
The oxygen concentration was ≥ 60% of the ASV (air saturation value)	**X**	
The pH of the water was in the range 6 to 9*	**X**	
The water temperature did not differ more than ± 1.0°C	**X**	

* It was observed that in the vessels 13, 16, 17 and 18 the pH of the overlaying water at test end (DAI 28) was slightly above 9 (maximum measured value 9.20). There was no relation with the test item concentration, since the vessels are all from different treatments. Although strictly speaking these values are in breach of the validity criterium it is argued that there were no effects on the development or emergence of the midges. This is based on the fact that: i) in these vessels emergence at DAI 22 was (nearly) complete with values between 85% and 100%, ii) no further emergence occurred after DAI 22, iii) pH values in these vessels on DAI 22 were between 8.54 and 8.70, and iv) the increase in pH is expected to have occurred slowly and was therefore probably above 9 only during the last few test days.

Section A7.5.1.1	**Inhibition to microbial activity (terrestrial)**
BPD Annex Point IIA, VII.7.4	7.5.1.1 N-transformation (parent)

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**1) Koelzer U. 2003** Assessment of the side effects of BAS 307 QA I on the activity of the soil microflora, nitrogen turnover XXXX. unpublished XXXX	
1.2.	**Data protection**	Yes	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I.	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Yes, OECD 216 (2000)	
2.2.	**GLP**	Yes (laboratory certified by Ministerium fuer Umwelt und Verkehr Baden-Wuerttemberg, Stuttgart)	
2.3.	**Deviations**	No	X
		3. MATERIALS AND METHODS	
3.1.	**Test material**		
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	Active substance prepared as 100 g/l dispersible concentrate (supported product under Directive 91/414/EEC review program)	
3.1.3.	Purity	103 g/L (measured).	
3.1.4.	Composition of Product	Not a biocide product, however data to support Annex I listing for Flufenoxuron under Council Directive 98/8/EC.	
3.1.5.	Further relevant properties	Not applicable	
3.1.6.	Method of analysis	See report.	
3.2.	**Reference substance**	Yes	

Section A7.5.1.1	**Inhibition to microbial activity (terrestrial)**
BPD Annex Point IIA, VII.7.4	7.5.1.1 N-transformation (parent)

3.2.1.	Method of analysis for reference substance	Reported in Study code XXXX, available upon request.
3.3.	**Testing procedure**	
3.3.1.	Soil sample / inoculum / test organism	Biologically active agricultural soil: loamy sand soil
3.3.2.	Test system	Determination of the N-transformation (NO_3-nitrogen production) in soil enriched with lucerne meal (concentration in soil 0.5%). Comparison of test item treated soil with a non-treated soil. 3 replicates per treatment and concentration. NH_4-nitrogen formed from organically bound nitrogen and NO_3-nitrogen from the nitrification process was determined by using calibrated ion-selective electrodes connected to an Orion expandable ion-analyzer model EA 940.
3.3.3.	Application of TS	Not relevant
3.3.4.	Test conditions	Soil moisture: 45% of its maximum water holding capacity; pH 6.89 - 7.07. Soil samples were incubated at 20 °C ± 2 °C while stored in glass bottles in the dark.
3.3.5.	Test parameter	Effects on O_2-consumption after 28 days of exposure and NO_3 - nitrogen production after 28 and 91 days of exposure.
3.3.6.	Analytical parameter	See 3.3.5
3.3.7.	Duration of the test	28 days
3.3.8.	Sampling	0, 7, 14 and 28 days after treatment
3.3.9.	Monitoring of TS concentration	No
3.3.10.	Controls	Control without test substance.
3.3.11.	Statistics	Descriptive statistics.
	4. RESULTS	
Range finding test		Not performed
4.1.1.	Concentration	Not applicable
4.1.2.	Effect data	Not applicable

Section A7.5.1.1	**Inhibition to microbial activity (terrestrial)**
BPD Annex Point IIA, VII.7.4	7.5.1.1 N-transformation (parent)

Results test substance

4.1.3.	Initial concentrations of test substance	Control, 1.696 mg Flufenoxuron 100 g/L DC per kg dry soil (corresponding to an application rate of 1.214 L/ha) and 16.96 mg Flufenoxuron 100 g/L DC per kg dry soil (corresponding to an application rate of 12.14 L/ha).
4.1.4.	Actual concentrations of test substance	No measurement
4.1.5.	Growth curves	Not applicable
4.1.6.	Cell concentration data	Not applicable
4.1.7.	Concentration/ response curve	Not applicable
4.1.8.	Effect data	See Table 7.5.1.1/154
4.1.9.	Other observed effects	No long term effect on C- and N-transformation.

Results of controls

Test with reference substance		Performed
4.1.10.	Concentrations	3.33, 6.67 and 13.3 mg/kg dry soil. Test concentrations related to a soil depth of 5 cm and a soil density of 1.5 g/cm^3
4.1.11.	Results	Effect on N-transformation were 12.5%, 37.1% and 92.9% at 3.33, 6.67 and 13.3 mg/kg, respectively, in the loamy sand soil

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1.	**Materials and methods**	Flufenoxuron, as described under 3.1, was applied to soil. Procedure is detailed in 3.4
5.2.	**Results and discussion**	For the 7 and 14 day values the deviation between the control and the treated soil for both concentrations were more than 25%. No influence of Flufenoxuron 100 g/L DC on nitrogen turnover measured as NO_3-N production could be observed in the loamy sand soil at both application rates 28 days after application. After 28 days no adverse influences of Flufenoxuron 100 g/L DC on the nitrate production could be observed in both field soils at both application rates. Only slight deviations from the control of +12.6% and +6.92% in the loamy sand soil were measured. The results are summarized in Table 7.5.1.1/154.

Section A7.5.1.1	**Inhibition to microbial activity (terrestrial)**
BPD Annex Point IIA, VII.7.4	7.5.1.1 N-transformation (parent)

5.2.1.	NOEC	Not relevant	X
5.2.2.	EC_{10}	Not relevant	
5.2.3.	EC_{50}	Not relevant	
5.3.	**Conclusion**	Based on the results of this study in accordance with OECD guideline 216, Flufenoxuron 100 g/L DC caused no no long-term effects on the soil N-transformation (measured as NO_3-N production, deviations from the untreated control ≤ 25%) in a field soil tested up to a concentration of 16.96 mg Flufenoxuron 100 g/L DC per kg dry soil, corresponding to nominally 1.7 mg Flufenoxuron/kg dry soil (equivalent to a field rate of about 1.28 kg a.s./ha).	
5.3.1.	Reliability	1	X
5.3.2.	Deficiencies	No	

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	03/08/2005
Materials and Methods	Applicant's summary is acceptable. The test was realized according to guideline for plant protection product and not for biocides (2 concentrations tested instead of 5) and no effect was recorded.
Results and discussion	Applicant's summary is acceptable with the following amendment : 5.2.1 NOEC : *1.696 mg/kg dry soil*
Conclusion	Applicant's summary is acceptable.
Reliability	See deviation above Reliability Index is 2.
Acceptability	Given that relevant deviation, study should not be considered as reliable and should be redone with 5 concentrations. However, results of the study are judged "**acceptable**" as **NOEC** reported (1.696 mg/kg dry soil) is considered as a **worst case**.
Remarks	No other.

Section A7.5.1.1	**Inhibition to microbial activity (terrestrial)**
BPD Annex Point IIA, VII.7.4	7.5.1.1 N-transformation (parent)

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.5.1.1/154 Effect on N-transformation in soil exposed to BAS 307 QA I (day 7, 14, 28)

Soil	**% Deviation from the control [1)]**	
	1.696 mg BAS 307 QA I per kg dry soil	16.96 mg BAS 307 QA I per kg dry soil
Loamy sand (7 d)	+46.6	+28.6
Loamy sand (14 d)	+29.2	+20.8
Loamy sand (28 d)	+12.6	+6.92

1) based on NO_3-nitrogen production; - = inhibition; + = stimulation

Section A7.5.1.1	**Inhibition to microbial activity (terrestrial)**
BPD Annex Point IIA, VII.7.4	7.5.1.1 Soil respiration (parent)

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**2) Koelzer U. 2003** Assessment of the side effects of BAS 307 QA I on the activity of the soil microflora, short-term respiration XXXX. unpublished XXXX	
1.2.	**Data protection**	Yes	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I.	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Yes, OECD 217 (2000)	
2.2.	**GLP**	Yes (laboratory certified by Ministerium fuer Umwelt und Verkehr Baden-Wuerttemberg, Stuttgart)	
2.3.	**Deviations**	No	X
		3. MATERIALS AND METHODS	
3.1.	**Test material**		
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	Active substance prepared as 100 g/l dispersible concentrate (supported product under Directive 91/414/EEC review program)	
3.1.3.	Purity	103 g/L (measured).	
3.1.4.	Composition of Product	Not a biocide product, however data to support Annex I listing for flufenoxuron under Council Directive 98/8/EC	
3.1.5.	Further relevant properties	Not applicable	
3.1.6.	Method of analysis	See 3.1.6.	
3.2.	**Reference substance**	Yes	

Section A7.5.1.1	**Inhibition to microbial activity (terrestrial)**
BPD Annex Point IIA, VII.7.4	7.5.1.1 Soil respiration (parent)

3.2.1.	Method of analysis for reference substance	Reported in Study code 20021167/01-ABMF, available upon request
3.3.	**Testing procedure**	
3.3.1.	Soil sample / inoculum / test organism	Biologically active agricultural soil: loamy sand soil
3.3.2.	Test system	Determination of C-transformation in soil after addition of glucose. Comparison of test item treated soil with a non-treated soil. 3 replicates per treatment and concentration. An OxyTop® system was used to measure the O_2-consumption over a period of 24 hours at different sampling intervals.
3.3.3.	Application of TS	Not relevant
3.3.4.	Test conditions	Soil moisture: 45% of its maximum water holding capacity; pH 6.53 - 6.77. Soil samples were incubated at 20 °C ± 2 °C while stored in glass bottles in the dark.
3.3.5.	Test parameter	Effects on O_2-consumption after 28 days of exposure.
3.3.6.	Analytical parameter	See 3.3.5
3.3.7.	Duration of the test	28 days
3.3.8.	Sampling	0, 7, 14 and 28 days after treatment.
3.3.9.	Monitoring of TS concentration	No
3.3.10.	Controls	Control without test substance
3.3.11.	Statistics	Descriptive Statistics

4. RESULTS

Range finding test		Not performed
4.1.1.	Concentration	Not applicable
4.1.2.	Effect data	Not applicable

Results test substance

Section A7.5.1.1	**Inhibition to microbial activity (terrestrial)**
BPD Annex Point IIA, VII.7.4	7.5.1.1 Soil respiration (parent)

4.1.3.	Initial concentrations of test substance	Control, 1.696 mg BAS 307 QA I per kg dry soil (corresponding to an application rate of 1.214 L BAS 307 QA I/ha) and 16.96 mg BAS 307 QA I per kg dry soil (corresponding to an application rate of 12.14 L BAS 307 QA I/ha).	
4.1.4.	Actual concentrations of test substance	No measurement	
4.1.5.	Growth curves	Not applicable	
4.1.6.	Cell concentration data	Not applicable	
4.1.7.	Concentration/ response curve	Not applicable	
4.1.8.	Effect data	See Table 7.5.1.1.2/155.	
4.1.9.	Other observed effects	None	
Results of controls		See Table 7.5.1.1.2/155.	
Test with reference substance			
4.1.10.	Concentrations	3.33, 6.67 and 13.3 mg/kg dry soil. Test concentrations related to a soil depth of 5 cm and a soil density of 1.5 g/cm^3	
4.1.11.	Results	An effect of the C-transformation of -28.8%, -35.6% and -29.5% at 3.33, 6.67 and 13.3 mg/kg, respectively, in the loamy sand soil	
		5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1.	**Materials and methods**	Flufenoxuron, as described under 3.1, was applied to soil. Procedure is detailed in 3.4	
5.2.	**Results and discussion**	No adverse effects of Flufenoxuron 100 g/L DC on soil respiration could be observed in the loamy sand soil at both tested rates (single and ten-fold application rate) after 28 days. Only slightly reduced respiration rates of -0.86% in the 1.696 mg/kg and -3.66% in the 16.96 mg/kg dry soil were observed as compared to the control data. The results are summarized in Table 7.5.1.1.2/155.	
5.2.1.	NOEC	Not relevant	X
5.2.2.	EC_{10}	Not relevant	
5.2.3.	EC_{50}	Not relevant	

Section A7.5.1.1	**Inhibition to microbial activity (terrestrial)**
BPD Annex Point IIA, VII.7.4	7.5.1.1 Soil respiration (parent)

5.3.	**Conclusion**	Based on the results of this study in accordance with OECD guideline 217, Flufenoxuron 100 g/L DC caused no short-term and long-term effects on C-transformation (tested as O_2-consumption, deviations from the untreated control ≤25%) in a field soil tested up to a concentration of 16.96 mg Flufenoxuron 100 g/L DC per kg dry soil, corresponding to nominally 1.7 mg Flufenoxuron/kg dry soil (equivalent to a field rate of about 1.28 kg a.s./ha).	
5.3.1.	Reliability	1	X
5.3.2.	Deficiencies	No	

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	03/08/2005
Materials and Methods	Applicant's summary is acceptable. The test was realized according to guideline for plant protection product and not for biocides (2 concentrations tested instead of 5) and no effect was recorded. Finally, it should be noticed that more than 15% deviation (15.5%) was found between replicates of controls after 14 days treatment.
Results and discussion	Applicant's summary is acceptable with the following amendment : 5.2.1 NOEC : *1.696 mg/kg dry soil*
Conclusion	Applicant's summary is acceptable.
Reliability	See deviation above Reliability Index is 2.
Acceptability	Given those relevant deviations, study should not be considered as reliable and should be redone with 5 concentrations. However, results of the study are judged "**acceptable**" as **NOEC** reported (1.696 mg/kg dry soil) is considered as a **worst case**.
Remarks	No other.

Section A7.5.1.1	**Inhibition to microbial activity (terrestrial)**
BPD Annex Point IIA, VII.7.4	7.5.1.1 Soil respiration (parent)

	COMMENTS FROM ...
Date	Give date of comments submitted
Materials and Methods	Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion. Discuss if deviating from view of rapporteur member state
Results and discussion	Discuss if deviating from view of rapporteur member state
Conclusion	Discuss if deviating from view of rapporteur member state
Reliability	Discuss if deviating from view of rapporteur member state
Acceptability	Discuss if deviating from view of rapporteur member state
Remarks	

Table 7.5.1.1.2/155 Effect on C-transformation in soil exposed to BAS 307 QA I (day 7, 14, 28)

Soil	**% Deviation from the control [1)]**	
	1.696 mg Flufenoxuron 100 g/L DC per kg dry soil	16.96 mg Flufenoxuron 100 g/L DC per kg dry soil
Loamy sand (7 d)	+7.2	-4.18
Loamy sand (14 d)	-2.34	-6.73
Loamy sand (28 d)	-0.86	-3.66

1) Based on O_2 consumption; - = inhibition; + = stimulation

Section A7.5.1.1	**Inhibition to microbial activity (terrestrial)**
BPD Annex Point IIA VII.7.4	7.5.1.1 N-transformation (Flufenoxuron degradate, Reg No. 4064702)

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**3) Koelzer U. 2003** Effects of CL 932338 (metabolite of BAS 307 I) on the activity of the soil microflora, nitrogen transformation test XXXX. unpublished XXXX	
1.2.	**Data protection**	Yes	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I.	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Yes, OECD 216 (2000)	
2.2.	**GLP**	Yes (laboratory certified by Ministerium fuer Umwelt und Verkehr Baden-Wuerttemberg, Stuttgart)	
2.3.	**Deviations**	No	X
		3. MATERIALS AND METHODS	
3.1.	**Test material**		
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	See chemical glossary	
3.1.3.	Purity	95%	
3.1.4.	Composition of Product	Not applicable	
3.1.5.	Further relevant properties	None	
3.1.6.	Method of analysis	See 3.2.1.	
3.2.	**Reference substance**	Yes	
3.2.1.	Method of	Reported in Study code XXXX, available upon request.	

Section A7.5.1.1	**Inhibition to microbial activity (terrestrial)**
BPD Annex Point IIA VII.7.4	7.5.1.1 N-transformation (Flufenoxuron degradate, Reg No. 4064702)

	analysis for reference substance	
3.3.	**Testing procedure**	
3.3.1.	Soil sample / inoculum / test organism	Biologically active agricultural soil: loamy sand soil.
3.3.2.	Test system	Determination of the N-transformation (NO_3-nitrogen production) in soil enriched with lucerne meal (concentration in soil 0.5%). Comparison of test item treated soil with a non-treated soil; 3 replicates per treatment and concentration. NH_4-nitrogen formed from organically bound nitrogen and NO_3-nitrogen from the nitrification process was determined by using calibrated ion-selective electrodes connected to an Orion expandable ion-analyzer EA 940.
3.3.3.	Application of TS	Not relevant
3.3.4.	Test conditions	Soil moisture: 45% of its maximum water holding capacity; pH 5.73 - 6.36. Soil samples were incubated at 20 °C ± 2 °C while stored in glass bottles in the dark.
3.3.5.	Test parameter	Effects on NO_3 - nitrogen production after 28 days of exposure.
3.3.6.	Analytical parameter	See 3.3.5
3.3.7.	Duration of the test	28 days
3.3.8.	Sampling	0, 7, 14 and 28 days after treatment.
3.3.9.	Monitoring of TS concentration	No
3.3.10.	Controls	Control without test substance.
3.3.11.	Statistics	Descriptive statistics

4. RESULTS

Range finding test		Not performed
4.1.1.	Concentration	Not applicable

Section A7.5.1.1	**Inhibition to microbial activity (terrestrial)**
BPD Annex Point IIA VII.7.4	7.5.1.1 N-transformation (Flufenoxuron degradate, Reg No. 4064702)

4.1.2.	Effect data	Not applicable
Results test substance		
4.1.3.	Initial concentrations of test substance	Control, 0.00761 mg CL 932338 (Reg. No. 4064702) per kg dry soil (corresponding to the single application rate of 0.04 kg a.s./ha) and 0.0761 mg CL 932338 per kg dry soil (corresponding to the 10-fold application rate of 0.4 kg a.s./ha). Transformation rate of 20% was calculated, including Mol-factor. Test concentrations related to a soil depth of 5 cm and a soil density of 1.5 g/cm^3
4.1.4.	Actual concentrations of test substance	No measurement
4.1.5.	Growth curves	Not applicable
4.1.6.	Cell concentration data	Not applicable
4.1.7.	Concentration/ response curve	Not applicable
4.1.8.	Effect data	See Table 7.5.1.1/156.
4.1.9.	Other observed effects	None
Results of controls		See Table 7.5.1.1/156.
Test with reference substance		Performed
4.1.10.	Concentrations	3.33, 6.67 and 13.3 mg/kg dry soil. Test concentrations related to a soil depth of 5 cm and a soil density of 1.5 g/cm^3
4.1.11.	Results	12.5%, 37.1% and 92.9% at 3.33, 6.67 and 13.3 mg/kg, respectively, in the loamy sand soil.

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1.	**Materials and methods**	Flufenoxuron degradate CL 932338 (Reg No. 4064702), as described under 3.1, was applied to soil. Procedure is detailed in 3.4.
5.2.	**Results and**	No adverse effect on the nitrate production was detectable during

Section A7.5.1.1	**Inhibition to microbial activity (terrestrial)**
BPD Annex Point IIA VII.7.4	7.5.1.1 N-transformation (Flufenoxuron degradate, Reg No. 4064702)

	discussion	the whole test period at both application rates. Only slight deviations from the control were measured in the loamy sand soil after 28 days. The results are summarized in Table 7.5.1.1/156.	
5.2.1.	NOEC	Not relevant	X
5.2.2.	EC_{10}	Not relevant	
5.2.3.	EC_{50}	Not relevant	
5.3.	**Conclusion**		
5.3.1.	Reliability	1	X
5.3.2.	Deficiencies	No	

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	03/08/2005
Materials and Methods	Applicant's summary is acceptable. The test was realized according to guideline for plant protection product and not for biocides (2 concentrations tested instead of 5) and no effect was recorded. Finally, it should be noticed that more than 15% deviation (23.9%) was found between replicates of controls after 7 days treatment.

Section A7.5.1.1	**Inhibition to microbial activity (terrestrial)**
BPD Annex Point IIA VII.7.4	7.5.1.1 N-transformation (Flufenoxuron degradate, Reg No. 4064702)

Results and discussion	Applicant's summary is acceptable with the following amendment : 5.2.1 Considering a Student t-test, no difference of the means was observed between control and test concentration of 0.00761 mg/kg dry soil. But a difference of mean was observed between control and test concentration of 0.0731 mg/kg dry soil. So, according to the discussion in biocidal technical meeting II-09, RMS considered the NOEC as the lowest concentration test as a worst case. NOEC : *0.00761 mg/kg dry soil*
Conclusion	Applicant's summary is acceptable.
Reliability	See deviation above Reliability Index is 2.
Acceptability	Given those relevant deviations, study should not be considered as reliable and should be redone with 5 concentrations. However, results of the study are judged "**acceptable**" as **NOEC** reported (0.00761 mg/kg dry soil) is considered as a **worst case**.
Remarks	No other.

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.5.1.1/156 Effect on N-transformation in soil exposed to CL 932 338, Reg. No. 4064702 (day 7, 14, 28)

Soil	% deviation from the control [1)]	
	0.00761 mg CL 932 338 per kg dry soil	0.0761 mg CL 932 338 per kg dry soil
Loamy sand (7 d)	-6.52	-41.5
Loamy sand (14 d)	-11.7	-19.4
Loamy sand (28 d)	-17.2	-17.2

1) Based on NO_3-nitrogen production; - = inhibition; + = stimulation

Section A7.5.1.2	**Earthworm, acute toxicity test**
BPD Annex Point IIIA, XIII.3.2	7.5.1.2 Acute toxicity test (parent)

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**1) Hillaby J.M. 1987** The toxicity of WL115110 to the earthworm, Eisenia foetida L. (Oligocheata: Lumbriculidae) in laboratory tests XXXX unpublished XXXX	
1.2.	**Data protection**	No	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	No data protection claimed	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Yes, OECD (1984); Edwards, 1984	X
2.2.	**GLP**	No, at the time the study was conducted GLP was not compulsory. However the study was conducted according to the principle of Good Laboratory Practices.	
2.3.	**Deviations**	No	
		3. METHOD	
3.1.	**Test material**	As given in section 2	
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	As given in section 2	
3.1.3.	Purity	99% ±1%	
3.1.4.	Composition of Product	Not applicable	
3.1.5.	Further relevant properties	None	
3.1.6.	Method of analysis	No measurement	
3.2.	**Reference substance**	Yes	X

Section A7.5.1.2	**Earthworm, acute toxicity test**
BPD Annex Point IIIA, XIII.3.2	7.5.1.2 Acute toxicity test (parent)

3.2.1.	Method of analysis for reference substance	No analysis.
3.3. Testing procedure		
3.3.1.	Preparation of the test substance	Test substance diluted in test solvant
3.3.2.	Application of the test substance	Mixed with the artificial soil
3.3.3.	Test organisms	Earthworm (*Eisenia foetida*), adult worms, (with clitellum and weight 510 mg - 810 mg), 2 - 3 months old; source: British Ground Baits, Four Elms Farm, Braintree, Essex
3.3.4.	Test system	14-d exposure in treated artificial soil; different concentrations of the test item were mixed homogeneously into the soil which is filled in glass vessels before the earthworms are introduced on top of the soil; 4 variants (1 test item concentration, control, solvent control, reference item); 5 replicates for the test item, 4 replicates/variant for the controls and the reference item; 10 worms each. Assessment of worm mortality and weight change as sub-lethal parameter after 14 d.
3.3.5.	Test conditions	Artificial soil according to OECD 207, water content: 22% (of soil dry weight), temperature: 20 °C ± 3 °C, continuous illumination.
3.3.6.	Test duration	14-days
3.3.7.	Test parameter	Mortality of earthworms after exposure over 14 days, weight change.
3.3.8.	Examination	See 3.3.4
3.3.9.	Monitoring of test substance concentration	No
3.3.10.	Statistics	Descriptive statistics

Section A7.5.1.2	**Earthworm, acute toxicity test**
BPD Annex Point IIIA, XIII.3.2	7.5.1.2 Acute toxicity test (parent)

4. RESULTS

Filter paper test		Not performed
4.1.1.	Concentration	Not applicable
4.1.2.	Number/ percentage of animals showing adverse effects	Not applicable
4.1.3.	Nature of adverse effects	Not applicable
Soil test		
4.1.4.	Initial concentrations of test substance	1000 mg/kg soil dry weight
4.1.5.	Effect data (Mortality)	See Table 7.5.1.2/1
4.1.6.	Concentration / effect curve	Not applicable
4.1.7.	Other effects	None
Results of controls		
4.1.8.	Mortality	See Table 7.5.1.2/1
4.1.9.	Number/ percentage of earthworms showing adverse effects	Not applicable
4.1.10.	Nature of adverse effects	Not applicable
Test with reference substance		Performed
4.1.11.	Concentrations	8, 16, 33, 65 and 130 mg/kg soil dry weight.
4.1.12.	Results	See Table 7.5.1.2/1.

Section A7.5.1.2	**Earthworm, acute toxicity test**
BPD Annex Point IIIA, XIII.3.2	7.5.1.2 Acute toxicity test (parent)

		5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1. Materials and methods		Flufenoxuron, as described under 3.1, was mixed to soil. Test procedure is detailed in 3.3	
5.2. Results and discussion		After 14 days of exposure, a mortality rate of 2.5% was observed in the control, no mortality could be detected in the solvent control and test item group. The biomass development was slightly decreased in all variants and can probably ascribed to the poor nutritional quality of the test substrate. The results are summarized in Table 7.5.1.2/1.	
5.2.1.	LC_0	Not applicable	
5.2.2.	LC_{50}	Not applicable	X
5.2.3.	LC_{100}	1000 mg/kg soil dry weight	X
5.3. Conclusion		In a 14-d toxicity study with Flufenoxuron to earthworms (*Eisenia foetida*) the LC_{50} was > 1000 mg a.s./kg soil dry weight. NOEC could be determined to be 1000 mg a.s./kg soil dry weight.	
5.3.1.	Other Conclusions	No	
5.3.2.	Reliability	1	
5.3.3.	Deficiencies	No	

Section A7.5.1.2	**Earthworm, acute toxicity test**
BPD Annex Point IIIA, XIII.3.2	7.5.1.2 Acute toxicity test (parent)

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	08/03/2005
Materials and Methods	Applicant's summary is acceptable but following amendment should be done : - 2.1 Guideline study : Yes, OECD *207* (1984); Edwards, 1984 - 3.2 Reference substance : Yes *(Chloroacetamide)*
Results and discussion	Applicant's summary is acceptable with following amendments : 5.2.2. LC_{50}: *> 1000 mg/kg soil dry weight* 5.2.3. LC_{100} : *Not applicable*
Conclusion	Applicant's summary is acceptable with following amendments : *5.3.1 Other conclusions : No effect at highest concentration tested. Therefore, it can be assumed as a worst case that NOEC is 1000 mg/kg soil dry weight and that LC_{50} is > 1000 mg/kg soil dry weight.*
Reliability	Applicant's methods are applied according to OECD Guideline 207. Therefore, applicant's results can be considered as reliable. Reliability index is 1.
Acceptability	See above.
Remarks	No other.

	COMMENTS FROM ... *(specify)*
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.5.1.2/1 Effect of Flufenoxuron on earthworm (*Eisenia fetida)* mortality and biomass (14 d)

Concentration [mg a.s./kg soil dry weight]	**Control**	**Solvent control**	**1000**
Mortality [%] [1)]	2.5	0	0
Weight change [%] [1)]	-4.92	-2.58	-2.26
	Endpoints [mg a.s./kg soil dry weight]		
LC_{50}	> 1000		

1) values recalculated from original data, based on means of 4 replicates for control and solvent control and 5 replicates for the test item

Table 7.5.1.2/ 2 Validity criteria for acute earthworm test according to OECD 207

	Fulfilled	**Not fulfilled**
Mortality of control animals < 10%	**Yes**	

Section A7.5.1.2	**Earthworm, acute toxicity test**
BPD Annex Point IIIA, XIII.3.2	7.5.1.2 Acute test (Flufenoxuron degradate, Reg. No. 4064702)

			Official use only
		1. REFERENCE	
1.1. Reference		**2) Staebler D. 2003** Acute toxicity of CL 932 338 (metabolite of BAS 307 I) on earthworms, Eisenia fetida using an artificial soil test XXXX. unpublished XXXX	
1.2. Data protection		Yes	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I.	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1. Guideline study		Yes, OECD 207	
2.2. GLP		Yes (laboratory certified by Ministerium fuer Umwelt und Verkehr Baden-Wuerttemberg, Stuttgart)	
2.3. Deviations		No	
		3. METHOD	
3.1. Test material			
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	See chemical glossary	
3.1.3.	Purity	95%	
3.1.4.	Composition of Product	Not applicable	
3.1.5.	Further relevant properties	None	
3.1.6.	Method of analysis	No analysis	
3.2. Reference substance		None	X
3.2.1.	Method of analysis for	Not applicable	X

Section A7.5.1.2	**Earthworm, acute toxicity test**
BPD Annex Point IIIA, XIII.3.2	7.5.1.2 Acute test (Flufenoxuron degradate, Reg. No. 4064702)

	reference substance	
3.3. Testing procedure		
3.3.1.	Preparation of the test substance	No specific preparation
3.3.2.	Application of the test substance	Mixed with artificial soil
3.3.3.	Test organisms	Earthworm (*Eisenia foetida*), from in-house culture, adult worms (with clitellum and weight > 300 mg < 600 mg), less than 1 year old.
3.3.4.	Test system	14-d exposure in treated artificial soil; different concentrations of the test item were mixed homogeneously into the soil which is filled in glass vessels before the earthworms are introduced on top of the soil; 7 variants (5 test item concentrations, control, reference item); 4 replicates/variant with 10 worms each. Assessment of worm mortality and behavioural effects after 7 and 14 d, assessment of weight change as sub-lethal parameter after 14 d.
3.3.5.	Test conditions	Artificial soil according to OECD 207, pH 5.7 - 6.0, water content: 33.0% - 35.1% (of soil dry weight) at test initiation, 31.3% - 34.1% (of soil dry weight) at test termination, temperature: 19 °C – 21 °C, continuous illumination.
3.3.6.	Test duration	14-days
3.3.7.	Test parameter	LC_{50} (50% mortality of earthworms after exposure over 14 days), behavioural effects, weight change.
3.3.8.	Examination	See 3.3.4
3.3.9.	Monitoring of test substance concentration	No
3.3.10.	Statistics	Descriptive statistics, ANOVA followed by Dunnett-test for weight change ($\alpha = 0.05$)

4. RESULTS

Filter paper test	Not performed

Section A7.5.1.2	**Earthworm, acute toxicity test**
BPD Annex Point IIIA, XIII.3.2	7.5.1.2 Acute test (Flufenoxuron degradate, Reg. No. 4064702)

4.1.1.	Concentration	Not applicable
4.1.2.	Number/ percentage of animals showing adverse effects	Not applicable
4.1.3.	Nature of adverse effects	Not applicable
Soil test		
4.1.4.	Initial concentrations of test substance	Control, 100, 178, 316, 562 and 1000 mg /kg soil dry weight.
4.1.5.	Effect data (Mortality)	See table
4.1.6.	Concentration / effect curve	Not applicable
4.1.7.	Other effects	None
Results of controls		
4.1.8.	Mortality	See Table 7.5.1.2/157.
4.1.9.	Number/ percentage of earthworms showing adverse effects	See Table 7.5.1.2/157.
4.1.10.	Nature of adverse effects	See Table 7.5.1.2/157.
Test with reference substance		Not performed
4.1.11.	Concentrations	Not applicable
4.1.12.	Results	Not applicable

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1. Materials and methods	Reg. No. 4064702, Flufenoxuron soil metabolites, as described under 3.1, was mixed to soil. Test procedure is detailed in 3.3
5.2. Results and discussion	The LC_{50} was determined to be >1000 mg/kg soil dry weight. After 14 days of exposure, no mortality was observed in the

Section A7.5.1.2	**Earthworm, acute toxicity test**
BPD Annex Point IIIA, XIII.3.2	7.5.1.2 Acute test (Flufenoxuron degradate, Reg. No. 4064702)

		control and the test item concentrations. The biomass development was statistically significant affected at 562 mg and 1000 mg CL 932 338/kg, the two highest concentrations tested (Dunnett test; α = 0.05). The results are summarized in Table 7.5.1.2/157.
5.2.1.	LC_0	Not applicable
5.2.2.	LC_{50}	> 1000 mg/kg
5.2.3.	LC_{100}	Not applicable
5.3. Conclusion		In a 14-d toxicity study with Reg. No. 4054702 to earthworms (*Eisenia foetida*) the LC_{50} was determined to be >1000 mg/kg soil dry weight. The NOEC could be determined as 316 mg CL 932 338/kg soil dry weight.
5.3.1.	Other Conclusions	None
5.3.2.	Reliability	1
5.3.3.	Deficiencies	No

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	08/03/2005

Section A7.5.1.2	**Earthworm, acute toxicity test**
BPD Annex Point IIIA, XIII.3.2	7.5.1.2 Acute test (Flufenoxuron degradate, Reg. No. 4064702)

Materials and Methods	Applicant's summary is acceptable but following amendment should be done : - 3.2 Reference substance : *Yes (2-Chloroacetamide)* - 3.2.1 Method of analysis for reference substance : *No analysis*
Results and discussion	Applicant's version is acceptable.
Conclusion	Applicant's version is acceptable with following amendments : *Other conclusions : NOEC for growth endpoint is 316 mg/kg soil dry weight*
Reliability	Reliability Index is 1.
Acceptability	Acceptable.
Remarks	No other.

	COMMENTS FROM ... *(specify)*
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.5.1.2/157 Effect of CL 932 338 on earthworm (*Eisenia fetida)* mortality and biomass (14 d)

Concentration [mg/kg soil dry weight]	**Control**	**100**	**178**	**316**	**562**	**1000**
Mortality [%]	0	0	0	0	0	0
Weight change [%] [1)]	-18.4	-21.9	-23.6	-23.9	-30.7 *	-41.7 *
	Endpoints [mg CL 932 338/kg soil dry weight]					
LC_{50}	> 1000					

Table 7.5.1.2/157 Effect of CL 932 338 on earthworm (*Eisenia fetida)* mortality and biomass (14 d)

Concentration [mg/kg soil dry weight]	**Control**	**100**	**178**	**316**	**562**	**1000**
NOEC	316					

1) results represent rounded values (% mean of 4 replicates)

* Statistically significant differences compared to the control (Dunnett-test, $\alpha = 0.05$)

Table 7.5.1.2/158: Validity criteria for acute earthworm test according to OECD 207

	Fulfilled	**Not fulfilled**
Mortality of control animals < 10%	**Yes**	

Section 7.5.1.3 Terrestrial plant toxicity
Annex Point IIIA XIII 3.4

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**1) Sack, D. 2003** BAS 307 QA I: Effects on non-target plants in the greenhouse - A limit test XXXX unpublished XXXX	
1.2.	**Data protection**	Yes	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I.	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Yes, OECD Proposal for Revision of Guideline 208 (2000): ”Terrestrial (Non-Target) Plant Testing (Part B) Vegetative Vigour Test”	
2.2.	**GLP**	Yes (certified laboratory)	
2.3.	**Deviations**	No	
		3. METHOD	
3.1.	**Test material**		
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	See 3.1.3.	
3.1.3.	Purity	103 g a.s./L (nominal: 100 g Flufenoxuron/L)	
3.1.4.	Composition of Product	Not applicable	
3.1.5.	Further relevant properties	None	
3.1.6.	Method of analysis	No measurement	
3.2.	**Preparation of TS solution for poorly soluble or volatile test substances**	Not applicable	

Section 7.5.1.3 Terrestrial plant toxicity
Annex Point IIIA XIII 3.4

3.3.	**Reference substance**	No
3.3.1.	Method of analysis for reference substance	Not applicable
3.4.	**Testing procedure**	
3.4.1.	Dilution water	For mixing of the spray solution, the demanded amount of test substance was diluted with the demanded amount of deionized water.
3.4.2.	Test plants	2 Monocotyledonae: oats (*Avena sativa*); onion (*Allium cepa*) 4 Dicotyledonae: cabbage (*Brassica oleracea*); pea (*Pisum sativum*); carrot (*Daucus carota*); sunflower (*Helianthus annuus*) see also Table A7_5_1_3-3
3.4.3.	Test system	Limittest in the greenhouse, see Table 7.5.1.3/4
3.4.4.	Test conditions	see Table 7.5.1.3/5
3.4.5.	Test duration	The test substance was applied post emergence in the latest six weeks after seeding at growth stage BBCH 11 to 14 of the plants (depending on plant species). The application was done using a laboratory spray cabin which simulated an application in agricultural practice. Following the application the plants were cultivated for 15 days in the greenhouse.
3.4.6.	Test parameter	Assessments for phytotoxicity were done 7 days and 15 days after application. At study termination, 15 days after application, the fresh weight of the aerial parts above ground was determined.
3.4.7.	Sampling	-
3.4.8.	Method of analysis of the plant material	-
3.4.9.	Quality control	-
3.4.10.	Statistics	For all observations mean values and standard deviations were calculated. For metric parameters (plant biomass) an analysis of variance (ANOVA) was done. To detect significant differences to the control group the Dunnett test ($\alpha = 0.05$) was applied. The assumption of homogeneity of variance was tested using the Kruskal-Wallis-test ($\alpha = 0.05$). All calculations were done using either Microsoft Excel (version 97-SR2, mainly used for calculation of mean values and standard deviation) or SAS release 6.12 (mainly used for ANOVA and Dunnett‘s test). Spot checks for mean values and standard

Section 7.5.1.3 Terrestrial plant toxicity
Annex Point IIIA XIII 3.4

		deviations showed identical results for Excel and SAS. All calculations were done using the maximum number of digits available for each software program. The results were rounded to the given number of digits.
		4. RESULTS
4.1.	**Results test substance**	
4.1.1.	Applied initial concentration	Two application rates were tested: 0.4 L/ha (equivalent to 40 g a.s./ha) and 0.8 L/ha (equivalent to 80 g a.s./ha).
4.1.2.	Phytotoxicity rating	After treatment no injuries could be seen at study termination and no phytotoxic potential to non-target plants was found.
4.1.3.	Plant height	Not measured
4.1.4.	Plant dry weights	Not measured
4.1.5.	Root dry weights	Not measured
4.1.6.	Root length	Not measured
4.1.7.	Number of dead plants	No dead plants occurred during the study.
4.1.8.	Effect data	Phytotoxicity: Plant development was normal in all treatments. Neither the lower nor the higher tested rate caused any symptoms of phytotoxicity Biomass (Fresh Weight): For all plant species a normal development of plant weight in the control groups was observed. No statistically significant differences (Dunnett-test, $\alpha = 0.05$) between the control groups and the BAS 307 QA I treated groups were observed. The maximum observed reduction compared to the control was 4.0 % (pea, higher rate). see also Table 7.5.1.3/6
4.1.9.	Concentration / response curve	No graph of the concentration-response curve at test termination is given in the report.
4.1.10.	Other effects	-
4.2.	**Results of controls**	
4.2.1.	Number/ percentage of plants showing adverse effects	No adverse effects occurred in the control plants.

Section 7.5.1.3 Terrestrial plant toxicity
Annex Point IIIA XIII 3.4

4.2.2.	Nature of adverse effects	Not applicable as no adverse effects occurred in the control plants.
4.3.	**Test with reference substance**	Not performed
4.3.1.	Concentrations	-
4.3.2.	Results	-

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1.	**Materials and methods**	The objective of the study was to identify in a limit test if the test substance BAS 307 QA I (containing 103 g Flufenoxuron/L) has any phytotoxic potential. Therefore, the test substance was applied at two rates to six terrestrial plant species that had been cultivated in the greenhouse. These species represented six different plant families widely used for non target plant testing. Assessments for phytotoxicity were done 7 days and 15 days after application. At study termination, 15 days after application, the fresh weight of the aerial parts above ground was determined. The test was conducted according to OECD Proposal for Revision of Guideline 208 (2000):"Terrestrial (Non-Target) Plant Testing (Part B) Vegetative Vigour Test".
5.2.	**Results and discussion**	BAS 307 QA I showed no phytotoxic potential to non-target plants if applied at a rate of 0.8 L a.s./ha, as no injuries could be seen at study termination. For all plant species the plant weight was at the same level as the weight of the control plants. Statistically significant differences were not observed. The ER_{25} (rate which causes 25% effect) for plant weight is therefore > 0.8 L a.s./ha (highest rate tested) for all tested plant species. The NOAER (no observed adverse effect rate) for all species was 0.8 L/ha, which corresponds to 80 g a.s./ha. By using a 5 cm soil depth, the batch purity (103 g a.s./L) and an average soil densitiy of 1.5 g/cm^3, this rate was recalculated into a NOEC for soil of 110 µg a.s./kg (see XXXX).
5.2.1.	EC_{25}	> 0.8 L a.s./ha
5.2.2.	EC_{50}	-
5.2.3.	EC_{80}	-
5.3.	**Conclusion**	The validity criteria can be considered fulfilled according to the above mentioned OECD guideline (OECD 208 (2000), (Part B) Vegetative Vigour Test)
5.3.1.	Reliability	1

Section 7.5.1.3 Terrestrial plant toxicity
Annex Point IIIA XIII 3.4

5.3.2. Deficiencies No

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	May 2007
Materials and Methods	Applicant's version is acceptable.
Results and discussion	Applicant's version is acceptable
Conclusion	Applicant's version is acceptable
Reliability	1
Acceptability	Acceptable
Remarks	The test has been carried out by spraying the soil surface with the test solution which is a method of application adapted to crop protection products. The result obtained doesn't allow to define the hazard of the molecule to plants as this limit test employed the maximal concentrations used for crop protection which are without effect on plants.
	COMMENTS FROM ... *(specify)*
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.5.1.3/1: Preparation of TS solution for poorly soluble or volatile test substances

Criteria	**Details**
Dispersion	Not applicable
Vehicle	Not applicable
Concentration of vehicle	Not applicable
Vehicle control performed	Not applicable
Other procedures	Not applicable

Table 7.5.1.3/2: Dilution water

Criteria	**Details**
Source	For mixing of the spray solution, the demanded amount of test substance was diluted with the demanded amount of deionized water.
Alkalinity / Salinity	Not reported
Hardness	Not reported
pH	Not reported
Oxygen content	Not reported
Conductance	Not reported
Holding water different from dilution water	Not applicable

Table 7.5.1.3/3: Test plants

	Family	**Species**	**Common name**	**Source (seed/plant)**
Dicotyledonae	Brassicaceae	*Brassica oleracea*	Cabbage	Seeds
	Leguminosae	*Pisum sativum*	Pea	Seeds
	Umbelliferae	*Daucus carota*	Carrot	Seeds
	Asteraceae	*Helianthus annuus*	Sunflower	Seeds
Monocotyledonae	Poaceae	*Avena sativa*	Oats	Seeds
	Liliaceae	*Allium cepa*	Onion	Seeds

Table 7.5.1.3/4: Test system

<table>
<tr><th>Criteria</th><th>Details</th></tr>
<tr><td>Test type</td><td>Limit-Test in the greenhouse</td></tr>
<tr><td>Container type</td><td>Plastic pots, 8 cm diameter, 7 cm height</td></tr>
<tr><td>Seed germination potential</td><td>Not reported</td></tr>
<tr><td>Identification of the plant species</td><td>Not reported</td></tr>
<tr><td>Number of replicates</td><td>6</td></tr>
<tr><td>Numbers of plants per replicate per dose</td><td>Each replicate comprised one pot of plants with at least three plants (3-5 plants, depending on plant species)</td></tr>
<tr><td>Date of planting</td><td>November 27, 2002</td></tr>
<tr><td>Plant density</td><td>Plants per pot
<table>
<tr><td>Cabbage</td><td>Carrot</td><td>Sun-flower</td><td>Pea</td><td>Oats</td><td>Onion</td></tr>
<tr><td>3</td><td>4</td><td>4</td><td>3</td><td>4</td><td>5</td></tr>
</table></td></tr>
<tr><td>Date of test substance application</td><td>January 08, 2003</td></tr>
<tr><td>High of plants at application</td><td>Growth stage at application (BBCH code)
<table>
<tr><td>Cabbage</td><td>Carrot</td><td>Sun-flower</td><td>Pea</td><td>Oats</td><td>Onion</td></tr>
<tr><td>13</td><td>14</td><td>12</td><td>14</td><td>13</td><td>11</td></tr>
</table></td></tr>
<tr><td>Date of phytotoxicity rating or harvest</td><td>Assessments for phytotoxicity were done 7 days and 15 days after application. At study termination, 15 days after application (January 23, 2003), the fresh weight of the aerial parts above ground was determined.</td></tr>
<tr><td>Dates of analysis</td><td>Not applicable</td></tr>
</table>

Table 7.5.1.3/5: Test conditions

<table>
<tr><th>Criteria</th><th>Details</th></tr>
<tr><td>Test type</td><td>Limit-Test in the greenhouse</td></tr>
<tr><td>Method of application</td><td>The test substance and water, respectively, were applied using a laboratory spraying cabin constructed by Fa. Schmitt, Sondermaschinenbau, Gau Algesheim, Germany. Before application the sprayer was adjusted to an output of 400 L/ha.
All plants of one treatment rate were placed in the central area of the cabin for which a sufficient homogeneity of the spray cover was guaranteed. Then the spray was applied with one nozzle moving once above the pots (spray pressure 2.5 bar; distance 14 - 42 cm, depending on plant species). After spraying the pots were placed in a ventilation chamber until the plants were dry. Then the plants were transported into the glass house.</td></tr>
<tr><td>Application levels</td><td>Treatment rates
<table>
<tr><th>Test sub-stance</th><th>Rate [g a.s./ha]</th><th>Rate [L product/ha]</th><th>Amount of water [L/ha]</th></tr>
<tr><td>Control</td><td>-</td><td></td><td rowspan="3">400</td></tr>
<tr><td rowspan="2">BAS 307 QA I</td><td>40</td><td>0.4</td></tr>
<tr><td>80</td><td>0.8</td></tr>
</table></td></tr>
<tr><td>Dose rates</td><td>0.4 and 0.8 L/ha</td></tr>
<tr><td>Substrate characteristics</td><td>Substrate: Compost (steam sterilized)
Type of soil: Loamy Sand
Organic Carbon: 5.4%
pH: 6.7%</td></tr>
<tr><td>Watering of the plants</td><td>According to need. First watering 24 h after application of the test substance</td></tr>
<tr><td>Temperature</td><td>Day: 20°C - 31°C
Night: > 14°C</td></tr>
<tr><td>Thermoperiod</td><td>See above</td></tr>
<tr><td>Light regime</td><td>16/8 hrs day/night. Plants were illuminated with additional light to ensure 4500 LUX at top of the plants (Radium HRJ-T Planta, 400W).</td></tr>
<tr><td>Relative humidity</td><td>80%</td></tr>
</table>

Table A7.5.1.3/5: Test conditions (continued)

Wind volatility	Not applicable
Observation periods and duration of test	For measuring of plant damages, mainly of reduction of plant mass, caused by the active ingredient tested, the fresh weight of the shoots was determined 15 days after application. The plants were cut directly above the ground and weighed immediately after cutting to avoid any weight loss by wilting. Additionally, a visual assessment was performed. Following the application all plants were assessed for morphological symptoms of phytotoxicity 7 days and 15 days after application. Phytotoxicity was rated in % (0%-100%, 0% = no effect, 100% = total effect, plant dead).
Pest control	Not applicable
Any other treatments and procedures	Fertilisers according to need

Table 7.5.1.3/6: Effects of BAS 307 QAI on plant biomass and plant condition (visible damage), 15 days after application (test termination)

Treatment	Cabbage	Carrot	Sunflower	Pea	Oats	Onion
Mean plant weight [% of control]						
Control	100	100	100	100	100	100
0.4 L/ha	103	111	114	98	113	116
0.8 L/ha	107	97	115	96	118	106
Mean visible damage [% damage compared to control]						
Control	0	0	0	0	0	0
0.4 L/ha	0	0	0	0	0	0
0.8 L/ha	0	0	0	0	0	0

No statistical significant differences compared to the control (Dunnett test or Kruskal-Wallis test, $\alpha = 0.05$)

Table 7.5.1.3/7:Validity criteria for terrestrial plant toxicity according to OECD Guideline 208, Part B (Vegetative Vigour Test, 2000)

	Fulfilled	Not fulfilled
Plant growth does not exhibit visible phytotoxic effects (e.g. chlorosis, necrosis, wilting,leaf and stem deformation);	x	
Mean plant survival is at least 90% at the end of the test.	x	

Section A7.5.2.1 **BPD Annex Point IIIA, XIII.3.2**	**Reproduction study with non-target soil macro-organisms** 7.5.2.1 Sub-lethal effect on earthworm (Flufenoxuron)

			Official use only
		1. REFERENCE	
1.1. Reference		**1) Luehrs U. 2001** Effects of Flufenoxuron technical (AC 811678) on reproduction and growth of earthworms Eisenia fetida (Savigny 1826) in artificial soil XXXX. unpublished XXXX	
1.2. Data protection		Yes	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I.	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1. Guideline study		Yes, BBA VI 2-2	X
2.2. GLP		Yes (laboratory certified by Hessisches Ministerium fuer Umwelt, Landwirtschaft und Forsten, Wiesbaden)	
2.3. Deviations		No	X
		3. METHOD	
3.1. Test material			
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	As given in section 2	
3.1.3.	Purity	94.9%	
3.1.4.	Composition of Product	Not applicable	
3.1.5.	Further relevant properties	None	
3.1.6.	Method of analysis	No measurement	
3.2. Reference substance		Yes	X
3.2.1.	Method of analysis for	Not applicable	X

Section A7.5.2.1 **BPD Annex Point IIIA, XIII.3.2**	**Reproduction study with non-target soil macro-organisms** 7.5.2.1 Sub-lethal effect on earthworm (Flufenoxuron)

	reference substance			
3.3. Testing procedure				
3.3.1.	Preparation of the test substance	No test substance preparation		
3.3.2.	Application of the test substance	Mixed with the artificial soil		
3.3.3.	Test organisms	Earthworm (Eisenia foetida andrei Savigny 1826), from in-house culture, adult worms (with clitellum and weight 300 mg - 500 mg), about 10-11 months old.		
3.3.4.	Test system	Different concentrations of the test item were mixed homogeneously into the soil before worms were placed on soil surface. 4 variants (2 test item concentrations, control, reference item); 4 replicates/variant with 10 worms each. Assessment of worm mortality and biomass development; offspring were maintained for additional 4 weeks; at the end of the test the number of surviving juveniles are counted to assess the reproduction rate.	X	
3.3.5.	Test conditions	Artificial soil according to OECD 207 amended with cow manure; pH 6.2 - 6.8; water content 55.5% - 62.8% (of water holding capacity); temperature: 18 °C - 21 °C; photoperiod: 16 hours light: 8 hours dark; light intensity 465 lux - 761 lux.	X	
3.3.6.	Test duration	56 day		
3.3.7.	Test parameter	Mortality, weight change, behavioural effects and reproduction rate.		
3.3.8.	Examination	See 3.3.4		
3.3.9.	Monitoring of test substance concentration	No		
3.3.10.	Statistics	Descriptive statistics, ANOVA followed by Dunnett-test for body weight and reproduction data, Fisher's exact test for mortality (α = 0.05).		

4. RESULTS

Section A7.5.2.1 **BPD Annex Point IIIA, XIII.3.2**	**Reproduction study with non-target soil macro-organisms** 7.5.2.1 Sub-lethal effect on earthworm (Flufenoxuron)	
Filter paper test	Not performed	
4.1.1. Concentration	Not applicable	
4.1.2. Number/ percentage of animals showing adverse effects	Not applicable	
4.1.3. Nature of adverse effects	Not applicable	
Soil test		
4.1.4. Initial concentrations of test substance	Control, 1.0 and 5.0 mg a.s./kg soil	X
4.1.5. Effect data (Mortality)	See Table 7.5.2.1/159.	
4.1.6. Concentration / effect curve	Not applicable	
4.1.7. Other effects	None	
Results of controls		
4.1.8. Mortality	See Table 7.5.2.1/159.	
4.1.9. Number/ percentage of earthworms showing adverse effects	Not applicable	X
4.1.10. Nature of adverse effects	Not applicable	
Test with reference substance	Performed	
4.1.11. Concentrations	7 mg Derosal S5 36 (31.1%w/w carbenazim)	
4.1.12. Results	Validity criteria for the study were met. For details on test reference results, see report.	
	5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1. Materials and methods	Flufenoxuron, as described under 3.1, was mixed to soil. Test procedure is detailed in 3.3	

Section A7.5.2.1 **BPD Annex Point IIIA, XIII.3.2**	**Reproduction study with non-target soil macro-organisms** 7.5.2.1 Sub-lethal effect on earthworm (Flufenoxuron)

5.2. Results and discussion		Flufenoxuron caused no significant effects on mortality, body weight or reproduction of Eisenia fetida in any of the test item concentrations. The results are summarized in Table 7.5.2.1/159.	
5.2.1.	LC_0	Not applicable	
5.2.2.	LC_{50}	Not applicable	
5.2.3.	LC_{100}	Not applicable	
5.2.4.	NOEC	5 mg/kg dry soil (equivalent to 3.75 kg ai/ha)	X
5.3. Conclusion		**In a 56-day reproduction study Flufenoxuron caused no adverse effects to earthworms (Eisenia foetida) up to the highest concentration tested. The NOEC was determined to be 5.0 mg a.s./kg dry soil (equivalent to 3.75 kg a.s./ha).**	X
5.3.1.	Other Conclusions	No	
5.3.2.	Reliability	1	X
5.3.3.	Deficiencies	No	

Section A7.5.2.1
BPD Annex Point IIIA, XIII.3.2

Reproduction study with non-target soil macro-organisms

7.5.2.1 Sub-lethal effect on earthworm (Flufenoxuron)

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	03/10/2005
Materials and Methods	Applicant's summary is acceptable with following amendments : - 2.1 Guideline study : Yes, BBA VI 2-2, *ISO 11268-2* - 2.3 Deviations : *Yes* - 3.2 Reference substance : Yes *(Derosal SC 360)* - 3.2.1 Method of analysis for reference substance : *No measurement* - 3.3.4 Test system : *Two* concentrations of the test item were mixed homogeneously into the soil before worms were placed on soil surface *in plastic boxes with perforated transparent lids*. 4 variants (2 item concentrations… - 3.3.5 Test conditions : Artificial soil according to OECD 207 amended with cow manure; *initial pH 6.7-6.8; final pH 6.2-6.3*; water content 55.5% - 62.8% (of water holding capacity); temperature: 18 – 21°C *(not measured on days 2, 3 and 4)*; photoperiod…
Results and discussion	Applicant's summary is acceptable with following amendments : - 4.1.4 Initial concentrations of test substance : Control, *1,05* and *5,27* mg a.s./kg *dry* soil - 4.1.9 Number/percentage of earthworms showing adverse effects : *None*
Conclusion	Applicant's version is acceptable.

Section A7.5.2.1 **BPD Annex Point IIIA, XIII.3.2**	**Reproduction study with non-target soil macro-organisms** 7.5.2.1 Sub-lethal effect on earthworm (Flufenoxuron)

Reliability	Two deviations were noticed by authors : - temperature was not measured on days 2, 3 and 4 - initial pH was 6.7-6.8 which is more than recommended by Guideline OECD 222 For both deviations, reason given by authors are considered as acceptable. One more deviation was noticed by competent authorities but not by authors : while glass boxes are recommended by Guideline OECD 222, test vessels were plastic boxes. It was not clarified by authors whether this plastic could be considered as chemically inert or not. Given that last deviation, this study is acceptable with restrictions but information should be given by applicant on nature of plastic used to know whether this plastic is chemically inert or not. Reliability index is 2.
Acceptability	Acceptable
Remarks	No other.

	COMMENTS FROM ... *(specify)*
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.5.2.1/159 Effect on earthworm (*Eisenia fetida*) exposed to Flufenoxuron in a 56 day reproduction study

Test item [mg a.s./kg soil dry weight]	**Control**	**1.0**	**5.0**
Adult mortality (day 28) [%]	0	0	0
Weight change [%] [1)]	35.4	34.6	33.3
Amount of food added [g] [1)]	25	25	25
Number of juveniles	282	307	292
Endpoints [mg a.s./kg soil dry weight]			
NOEC	≥ 5.0		**X**

1) results represent rounded values (% mean of 4 replicates)

Table 7.5.2.1/160: Validity criteria for acute earthworm test according to OECD 207

	Fulfilled	**Not fulfilled**
Mortality of control animals < 10%	**Yes**	

Section 7.5.2.2 **Terrestrial plant toxicity [Long term test]**

	JUSTIFICATION FOR NON-SUBMISSION OF DATA	**Official use only**
Other existing data [ ]	**Technically not feasible [ ] Scientifically unjustified [X]**	
Limited exposure [ ]	**Other justification [X]**	
Detailed justification:	Not required as used as a Wood Preservative, PT 8. Flufenoxuron is an insecticide and is used as a wood preservative PT8, class 1, 2 and 3. It is very unlikely that Flufenoxuron will present an acceptable risk to terrestrial plants. Therefore, these data are not required.	
Undertaking of intended data submission [ ]	Not applicable	

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	03/10/2005
Materials and methods	-
Conclusion	-
Reliability	Applicant's justification is not acceptable for the following reasons: it is not scientifically unjustified to test terrestrial plants because aim of tests IS to know if non target organisms could be affected or not by the substance Applicant should at least provide information available in PPP dossiers.
Acceptability	See above.
Remarks	A terrestrial plant toxicity test was provided in January 2006.
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*

Section 7.5.2.2 Terrestrial plant toxicity [Long term test]

Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section 7.5.3.1.1 **BPD Annex Point IIIA, XIII11.1**	**Acute oral toxicity on birds** 7.5.3.1.1 Bobwhite quail - Acute

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**1) XXXX** The acute oral toxicity (LD50) of WL 115110 to the bobwhite quail XXXX unpublished XXXX	
1.2.	**Data protection**	No	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	No data protection claimed	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Yes, EPA 71-1	X
2.2.	**GLP**	Yes (laboratory certified by the Department of Health of the Government of the United Kingdom as part of the UK GLP Compliance Programme)	
2.3.	**Deviations**	No	X
		3. MATERIALS AND METHODS	
3.1.	**Test material**		
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	As given in section 2	
3.1.3.	Purity	98% ± 1%	
3.1.4.	Composition of Product	Technical active substance	
3.1.5.	Further relevant properties	No	
3.1.6.	Method of analysis in the diet	Not applicable	
3.2.	**Administration of the test**	Oral gavage	

Section 7.5.3.1.1 **BPD Annex Point IIIA, XIII11.1**	**Acute oral toxicity on birds** 7.5.3.1.1 Bobwhite quail - Acute

	substance		
3.3.	**Reference substance**	None	
3.3.1.	Method of analysis for reference substance	Not applicable	
3.4.	**Testing procedure**		
3.4.1.	Test organisms	Bobwhite quail (*Colinus virginianus*), age: over 16 weeks: source: XXXX	X
3.4.2.	Test system	Birds treated once administering the test item with corn oil as vehicle by gavage (5 males/5 females per dose group). 14 days observation period.	
3.4.3.	Diet	Not appliccable	X
3.4.4.	Test conditions	Birds fasted overnight before administration of the test item, temperature 20 °C - 24 °C, relative humidity: about 82%, photoperiod 7 hours light, 17 hours dark during the test period.	X
3.4.5.	Duration of the test	14 days	
3.4.6.	Test parameter	LD_{50}, mortality, clinical signs, feed consumption, body weight (b.w.).	
3.4.7.	Examination / Observation	As described in EPA 71-1, see 3.4.2.	
3.4.8.	Statistics	Descriptive statistics	
		4. RESULTS	
4.1.	**Limit Test / Range finding test**	Not performed	
4.1.1.	Concentration	Not applicable	
4.1.2.	Number/ percentage of animals showing adverse effects	Not applicable	
4.1.3.	Nature of adverse effects	Not applicable	

Section 7.5.3.1.1 **BPD Annex Point IIIA, XIII11.1**	**Acute oral toxicity on birds** 7.5.3.1.1 Bobwhite quail - Acute

4.2.	**Results test substance**	
4.2.1.	Applied concentrations	Control, 500, 1000, and 2000 mg/kg body weight (nominal)
4.2.2.	Effect data (Mortality)	No mortality occurred
4.2.3.	Body weight	See 5.2
4.2.4.	Feed consumption	See 5.2
4.2.5.	Concentration / response curve	Not applicable, see 5.2
4.2.6.	Other effects	None
4.3.	**Results of controls**	
4.3.1.	Number/ percentage of animals showing adverse effects	None
4.3.2.	Nature of adverse effects	None
4.4.	**Test with reference substance**	Not performed
4.4.1.	Concentrations	Not applicable
4.4.2.	Results	Not applicable

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1.	**Materials and methods**	Flufenoxuron, as described under 3.1, was orally administrated to bobwhite quail as a single dose. The test procedure is detailed in 3.4

Section 7.5.3.1.1 **BPD Annex Point IIIA, XIII11.1**	**Acute oral toxicity on birds** 7.5.3.1.1 Bobwhite quail - Acute

5.2.	**Results and discussion**	Analytical measurements: The concentrations of the test item given to the birds by gavage were 102.5% - 106.3% of the nominal. Therefore the biological results are based on the nominal values. Biological results: The highest dose causing no mortality was 2000 mg/kg body weight for males and females. No toxic signs were observed in the control and in all test item concentrations. There was no compound-related impairment of mean feed uptake. At study termination (14 d) neither the mean body weight nor the development of body weight of female birds was statistically significant reduced, when compared to the control group. No compound-related macroscopic abnormalities were detected in the gross post-mortem examination. Table 7.5.3.1.1/161 summarizes the endpoint results.	

Table 7.5.3.1.1/161 Acute toxicity of Flufenoxuron to the bobwhite quail (*Colinus virginianus*)

Mortality **Dose [mg a.s./kg b.w.]**
LD_{50} (14 d) > 2000
NOEC 2000

5.2.1.	LD_{50}	> 2000 mg/kg b.w	
5.3.	**Conclusion**	In the acute toxicity test (single-dose oral application) of Flufenoxuron to the bobwhite quail the LD_{50} (14 d) was > 2000 mg a.s./kg b.w., the NOEC was 2000 mg a.s./kg b.w.	
5.3.1.	Reliability	1	X
5.3.2.	Deficiencies	No	

Section 7.5.3.1.1
BPD Annex Point IIIA, XIII11.1

Acute oral toxicity on birds

7.5.3.1.1 Bobwhite quail - Acute

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	03/15/2005
Materials and Methods	Applicant's summary is acceptable. Following deviations and lacking precisions were noticed : 2.1 Guideline study : Yes, EPA 71-1 *(newly OPPTS 850.2100)* 2.3 Deviations : *Yes* 3.4.1 Test organisms : Following precisions are lacking It is not precised whether test organisms have been acclimated or not. According to EPA Guideline OPPTS 850.2200 (formerly EPA 71-1), "Test birds should be acclimated to test facilities and basal diet for a minimum of 14 days. Acclimatation to test pens should be in the actual pens used in the test." 3.4.3 Diet : Text should be : *Not applicable* 3.4.4 Test conditions : According to EPA Guideline OPPTS 850.2200 (formerly EPA 71-1), photoperiod should be 8 hours light and 16 hours dark and relative humidity should be comprised between 45 and 70%.
Results and discussion	Applicant's summary is acceptable.
Conclusion	Applicant's summary is acceptable.
Reliability	See deviations above. Given those deviations, test can not be accepted without restriction and information on acclimatation is required to applicant. Reliability index is 2.
Acceptability	Acceptable.
Remarks	No other.
	COMMENTS FROM ... *(specify)*

Section 7.5.3.1.1 **BPD Annex Point IIIA, XIII11.1**	**Acute oral toxicity on birds** 7.5.3.1.1 Bobwhite quail - Acute

Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table A7.5.3.1.1/2: Validity criteria for avian acute oral toxicity test according to EPA OPPTS 850.2100

	Fulfilled	**Not fulfilled**
Mortality of control animals <10%	**Yes**	

Section 7.5.3.1.2 **BPD Annex Point IIIA, XIII.1.2**	**Short-term toxicity on birds** 7.5.3.1.2 Subacute

0.0 Justification of the key study

Two studies are submitted for the endpoint "Subacute dietary toxicity". and dedicated to the active substance Flufenoxuron.

In both studies, analyses were made on tested diet but only at the beginning of the study. Therefore, it was impossible to know if concentrations were maintained throughout the exposure period.

Given that, **no key study** was retained as both test had reliability index of 3.

Section 7.5.3.1.2 **BPD Annex Point IIIA, XIII.1.2**	**Short-term toxicity on birds** 7.5.3.1.2 Bobwhite quail – Subacute

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**2) XXXX** The subacute dietary toxicity (LC50) of WL 115110 to the bobwhite quail XXXX unpublished XXXX	X
1.2.	**Data protection**	No	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	No data protection claimed	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Yes, EPA 71-2	X
2.2.	**GLP**	Yes (laboratory certified by the Department of Health of the Government of the United Kingdom as part of the UK GLP Compliance Programme)	
2.3.	**Deviations**	No	X
		3. METHOD	
3.1.	**Test material**		
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	As given in section 2	
3.1.3.	Purity	98% ± 1%	
3.1.4.	Composition of Product	Not relevant	
3.1.5.	Further relevant properties	None	
3.1.6.	Method of analysis	HPLC-UV detection	
3.2.	**Administration of the test substance**	Diet	

Section 7.5.3.1.2 **BPD Annex Point IIIA, XIII.1.2**	**Short-term toxicity on birds** 7.5.3.1.2 Bobwhite quail – Subacute
3.3. Reference substance	No
3.3.1. Method of analysis for reference substance	Not applicable
3.4. Testing procedure	
3.4.1. Test organisms	Bobwhite quail (*Colinus virginianus*), chicks, age: 10 days; source: XXXX
3.4.2. Test system	Birds were administered different doses of the test item offered in the feed on 5 consecutive days; 10 birds per concentration; post-exposure period of 3 days.
3.4.3. Diet	See 3.4.2
3.4.4. Test conditions	Temperature: 26 °C - 28 °C; relative humidity 63%; photoperiod continuous artificial light.
3.4.5. Duration of the test	See 3.4.2
3.4.6. Test parameter	LC_{50} mortality, signs of toxicity, feed consumption, body weight
3.4.7. Examination / Observation	According to test guideline, see 3.4.2.
3.4.8. Statistics	Descriptive statistics
	4. RESULTS
Limit Test / Range finding test	Not performed
4.1.1. Concentration / dose	Not applicable
4.1.2. Number/ percentage of animals showing adverse effects	Not applicable
4.1.3. Nature of adverse effects	Not applicable
Results test substance	
4.1.4. Applied concentrations	Control 1, control 2, control 3, 500, 800, 1280, 2048, 3277 and 5243 mg a.s./kg feed

Section 7.5.3.1.2 **BPD Annex Point IIIA, XIII.1.2**		**Short-term toxicity on birds** 7.5.3.1.2 Bobwhite quail – Subacute	
4.1.5.	Effect data (Mortality)	See Table 7.5.3.1.2/163.	
4.1.6.	Body weight	See Table 7.5.3.1.2/163.	
4.1.7.	Food consumption	See Table 7.5.3.1.2/163.	
4.1.8.	Concentration / response curve	Not applicable see Table 7.5.3.1.2/163.	
4.1.9.	Other effects	None	
Results of controls			
4.1.10.	Number/ percentage of animals showing adverse effects	See Table 7.5.3.1.2/163.	
4.1.11.	Nature of adverse effects	None	
Test with reference substance		Not performed	
4.1.12.	Concentrations	Not applicable	
4.1.13.	Results	Not applicable	
		5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1.	**Materials and methods**	Flufenoxuron, as described under 3.1 was administered through the diet to bobwhite quail. The test procedure is described under 3.5	
5.2.	**Results and discussion**	Analytical measurements: The concentrations of the test item given to the birds were 86% - 100% of the nominal. Therefore the biological results are based on nominal values. Biological results: No mortalities were observed in the control groups and in all the treatment groups. No compound-related clinical signs were detected. No test item-related differences in body weights were observed. Feed consumption was not reduced in the test item groups during the treatment period and no other treatment-related effects were observed. The results are summarized in Table 7.5.3.1.2/163.	X
5.2.1.	LC_0	Not reported	
5.2.2.	LC_{50}	>5243 ppm	
5.2.3.	LC_{100}	Not applicable	

Section 7.5.3.1.2 **BPD Annex Point IIIA, XIII.1.2**	**Short-term toxicity on birds** 7.5.3.1.2 Bobwhite quail – Subacute

5.3.	**Conclusion**	In an avian dietary test with the bobwhite quail, the LC_{50} of Flufenoxuron is greater than 5243 mg a.s./kg feed. The NOEC was determined to be 5243 mg a.s./kg feed.	
5.3.1.	Reliability	1	X
5.3.2.	Deficiencies	No	

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	03/15/2005
Materials and Methods	Applicant's summary is acceptable. Following amendments should be done : 2.1 Guideline study : Yes, EPA 71-2 *(newly OPPTS 850.2200)* 2.3 Deviations : *Yes*
Results and discussion	Applicant's summary is acceptable. Following amendment shoud be noticed : Analytical measurements: The concentrations of the test item given to the birds were 86% - *118%* of the nominal. Therefore the biological results are based on nominal values. Following deviation was noticed : 5.2 Results and discussion & Table A7.5.3.1.2/162: Validity criteria for short-term toxicity test according to OECD 205 According to EPA Guideline OPPTS 850.2200 and OECD 205, one of three test acceptability criteria is "There must be evidence that the concentration of the substance being tested has been satisfactorily maintained in the diet (it should be at least 80 percent of the nominal concentration) throughout the first 5 days of the test period." Concentrations were analysed in the test. Study report give measured concentrations to be 86 – 118% of nominal values. However, it is not precised exactly when samples where taken but they were taken at the beginning of exposure period. Given that, it is not possible to know if concentrations of the substance being tested was "maintained in the diet throughout the first 5 days of the test period" and this criteria is considered as "*Not fulfilled*".
Conclusion	Applicant's summary is acceptable.
Reliability	See deviation above.

Section 7.5.3.1.2 **BPD Annex Point IIIA, XIII.1.2**	**Short-term toxicity on birds** 7.5.3.1.2 Bobwhite quail – Subacute
	Reliability index is 3.
Acceptability	See above.
Remarks	Reference is incorrect : "**1) Roberts N.L, Fairley C. 1987"** instead of **"2) Roberts N.L, Fairley C. 1987"**

Section 7.5.3.1.2
BPD Annex Point IIIA, XIII.1.2

Short-term toxicity on birds

7.5.3.1.2 Bobwhite quail - Subacute

	COMMENTS FROM ... *(specify)*
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.5.3.1.2/163 Avian dietary toxicity of Flufenoxuron to the bobwhite quail (*Colinus virginianus*)

Group [mg a.s./kg feed]	**Control 1 Control 2 Control 3**	**500**	**800**	**1280**	**2048**	**3277**	**5243**
Mortality [%]	0 0 0	0	0	0	0	0	0
Feed consumption [g/bird/day] [1)]	4.6 4.4 3.8	4.1	4.1	4.3	4.7	4.1	4.8
Body weight [g] [2)]	34.3 30.4 30.2	31.1	31.1	30.5	30.7	31.7	31.5
Symptoms	none	none	none	none	none	none	none
	Endpoints [mg a.s./kg feed]						
LC_{50}	> 5243						
NOEC	5243						

1) Mean of days 1 - 5 exposure period;2) Mean body weight at day 8

Table A7.5.3.1.2/164: Validity criteria for short-term toxicity test according to OECD 205

	Fulfilled	Not fulfilled
Mortality of control animals <10%	**Yes**	
Test substance concentration > 80 % of nominal concentration throughout the dosing period	**Yes**	
Lowest treatment level causing no compound-related mortality or other observable toxic effects	**Yes**	

Section 7.5.3.1.2 **Short-term toxicity on birds**
BPD Annex Point IIIA, XIII.1.2 7.5.3.1.2 Mallard duck - Subacute

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**2) XXXX** The subacute dietary toxicity (LC50) of WL 115110 to the mallard duck XXXX unpublished XXXX	
1.2.	**Data protection**	No	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	No data protection claimed	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Yes, EPA 71-2	X
2.2.	**GLP**	Yes, (Laboratory certified by the Department of Health of the Government of the United Kingdom as part of the UK GLP Compliance Programme)	
2.3.	**Deviations**	No	X
		3. METHOD	
3.1.	**Test material**		
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	As given in section 2	

Section 7.5.3.1.2 **BPD Annex Point IIIA, XIII.1.2**	**Short-term toxicity on birds** 7.5.3.1.2 Mallard duck - Subacute

3.1.3.	Purity	98% ± 1%
3.1.4.	Composition of Product	Not relevant
3.1.5.	Further relevant properties	None
3.1.6.	Method of analysis	HPLC-UV detection
3.2.	**Administration of the test substance**	Diet
3.3.	**Reference substance**	No
3.3.1.	Method of analysis for reference substance	Not applicable
3.4.	**Testing procedure**	
3.4.1.	Test organisms	Mallard duck (*Anas platyrhynchos*), chicks, animals visually indistinguishable from wild birds, age: 4 days; source: XXXX
3.4.2.	Test system	Birds were administered different doses for 5 consecutive days, post-exposure period of 3 days.
3.4.3.	Diet	According to test guideline, see 3.4.2.
3.4.4.	Test conditions	Temperature: 27 °C - 29 °C, relative humidity 47%, continuous artificial light
3.4.5.	Duration of the test	See 3.4.2
3.4.6.	Test parameter	LC_{50} mortality, signs of toxicity, feed consumption, body weight
3.4.7.	Examination / Observation	According to test guideline, see 3.4.2.
3.4.8.	Statistics	Descriptive statistics

4. RESULTS

Limit Test / Range finding test		Not performed
4.1.1.	Concentration / dose	Not applicable

Section 7.5.3.1.2 **BPD Annex Point IIIA, XIII.1.2**	**Short-term toxicity on birds** 7.5.3.1.2 Mallard duck - Subacute

4.1.2.	Number/ percentage of animals showing adverse effects	Not applicable	
4.1.3.	Nature of adverse effects	Not applicable	
Results test substance			
4.1.4.	Applied concentrations	Control, control, control, 500, 800, 1280, 2048, 3277 and 5243 mg a.s./kg feed	
4.1.5.	Effect data (Mortality)	See Table 7.5.3.1.2/165.	
4.1.6.	Body weight	See Table 7.5.3.1.2/165.	
4.1.7.	Food consumption	See Table 7.5.3.1.2/165.	
4.1.8.	Concentration / response curve	Not applicable see Table 7.5.3.1.2/165.	
4.1.9.	Other effects	None	
Results of controls			
4.1.10.	Number/ percentage of animals showing adverse effects	See Table 7.5.3.1.2/165.	
4.1.11.	Nature of adverse effects	None	
Test with reference substance		Not performed	
4.1.12.	Concentrations	Not applicable	
4.1.13.	Results	Not applicable	
		5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1.	**Materials and methods**	Flufenoxuron, as described under 3.1 was administered through the diet to Mallard duck. The test procedure is described under 3.5	
5.2.	**Results and discussion**	Analytical measurements: The concentrations of the test item given to the birds were 97% - 110% of the nominal. Therefore biological results are based on nominal values. Biological results: No mortality occurred in any of the treatment	X

Section 7.5.3.1.2 **BPD Annex Point IIIA, XIII.1.2**	**Short-term toxicity on birds** 7.5.3.1.2 Mallard duck - Subacute

		and control groups. No clinical signs of toxicity were observed in any bird. Body weight showed no test-item related differences compared to the control. Feed consumption was not affected up to the highest test item group during the treatment period. No compound-related findings were noted. The results are summarized in Table 7.5.3.1.2/165.	
5.2.1.	LC_0	Not reported	
5.2.2.	LC_{50}	>5243 ppm	
5.2.3.	LC_{100}	Not applicable	
5.3.	**Conclusion**	In an avian dietary test with the mallard duck, the LC_{50} of Flufenoxuron is greater than 5243 mg a.s./kg feed. The NOEC was determined to be 5243 mg a.s./kg feed.	
5.3.1.	Reliability	1	X
5.3.2.	Deficiencies	No	

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	03/15/2005
Materials and Methods	Applicant's summary is acceptable. Following amendments should be done : 2.1 Guideline study : Yes, EPA 71-2 *(newly OPPTS 850.2200)* 2.3 Deviations : *Yes*

Section 7.5.3.1.2 **BPD Annex Point IIIA, XIII.1.2**	**Short-term toxicity on birds** 7.5.3.1.2 Mallard duck - Subacute

Results and discussion	Applicant's summary is acceptable. Following amendment shoud be noticed : Analytical measurements: The concentrations of the test item given to the birds were 97% - *110%* of the nominal. Therefore the biological results are based on nominal values. Following deviation was noticed : 5.2 Results and discussion & Table A7.5.3.1.2/4: Validity criteria for short-term toxicity test according to OECD 205 According to EPA Guideline OPPTS 850.2200 and OECD 205, one of three test acceptability criteria is "There must be evidence that the concentration of the substance being tested has been satisfactorily maintained in the diet (it should be at least 80 percent of the nominal concentration) throughout the first 5 days of the test period." Concentrations were analysed in the test. Study report give measured oncentrations to be 86 – 118% of nominal values. However, it is not precised exactly when samples where taken but they were taken at the beginning of exposure period. Given that, it is not possible to know if concentrations of the substance being tested was "maintained in the diet throughout the first 5 days of the test period" and this criteria is considered as "*Not fulfilled*".
Conclusion	Applicant's summary is acceptable.
Reliability	See deviation above. Reliability index is 3.
Acceptability	See above.
Remarks	No other

Section 7.5.3.1.2 **BPD Annex Point IIIA, XIII.1.2**	**Short-term toxicity on birds** 7.5.3.1.2 Mallard duck - Subacute

	COMMENTS FROM ... *(specify)*
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.5.3.1.2/165 Avian dietary toxicity of Flufenoxuron to the mallard (*Anas platyrhynchos*)

Test item nominal [mg a.s./kg feed]	**Control 1 Control 2 Control 3**	**500**	**800**	**1280**	**2048**	**3277**	**5243**
Mortality [%]	0 0 0	0	0	0	0	0	0
Feed consumption [g/bird/days] [1)]	22.7 23.6 25.1*	25.2	27.4	25.8	24.7	25.6	26.5
Body weight [g] [2)]	207.3 213.9 231.3	213.4	228.4	216.4	196.0	221.3	217.9
Symptoms	none	none	none	none	none	none	none
	Endpoints [mg a.s./kg feed]						
LC_{50}	> 5243						
NOEC	5243						

1) mean of days 1-5 exposure period for all test item concentrations and controls; 2) mean body weight at day 8;* excluding day 4

Table A7.5.3.1.2/166: Validity criteria for short-term toxicity test according to OECD 205

	Fulfilled	**Not fulfilled**
Mortality of control animals <10%	**Yes**	
Test substance concentration > 80 % of nominal concentration throughout the dosing period	**Yes**	
Lowest treatment level causing no compound-related mortality or other observable toxic effects	**Yes**	

Section 7.5.3.1.3 Effects on reproduction of birds
BPD Annex Point IIIA, XIII.1.3

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**1) XXXX** WL 115110: The effects of dietary inclusion on reproduction and tissue residues in the bobwhite quail XXXX unpublished XXXX **2) XXXX** WL 115110 = Flufenoxuron new statistical evaluation of a 1-generation reproduction study on the bobwhite quail (Colinus virginianus) XXXX. unpublished XXXX	
1.2.	**Data protection**	No	
1.2.1.	Data owner	Give name of company	
1.2.2.			
1.2.3.	Criteria for data protection	No data protection claimed	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Yes, EPA 71-4	X
2.2.	**GLP**	Yes, (Laboratory certified by Department of Health of the Government of the United Kingdom, United Kingdom)	
2.3.	**Deviations**	No	
		3. METHOD	
3.1.	**Test material**		
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	As given in section 2	
3.1.3.	Purity	Purity: 97.4% ± 0.7%	
3.1.4.	Composition of Product	Not applicable	
3.1.5.	Further relevant properties	Not relevant	
3.1.6.	Method of analysis	The test item concentrations were analyzed using HPLC with UV-detection	
3.2.	**Administration of the test substance**	Diet	

Section 7.5.3.1.3 BPD Annex Point IIIA, XIII.1.3 Effects on reproduction of birds

3.3.	**Testing procedure**	
3.3.1.	Test organisms	Bobwhite quail *(Colinus virginianus)*, age: 11 months, the birds were indistinguishable from wild birds; weight: 166 g - 244 g; source: XXXX.
3.3.2.	Test system	Bobwhite quails approaching their first breeding season were kept in groups of 1 male and 1 female per replicate with 26 replicates per treatment in total. After a pre-treatment period of 1 week, a pre-egg production period of 12 weeks and an egg-laying period of 12 weeks followed during which the birds were offered the feed with test item ad libitum.
3.3.3.	Diet	According to test guideline recommendations
3.3.4.	Test conditions	Adult bobwhite study room: temperature 16 °C - 18 °C, relative humidity: 70%, photoperiod: 7 hours light (week 1 to week 8), at the end of week 8, the photoperiod was 16 hours light. Eggs were placed in a commercial incubator for about 21 days before being transferred to the hatcher. Incubator temperature: generally approx. 37.5 °C, relative humidity generally approx. 55%. Hatcher temperature 37.5 °C.
3.3.5.	Duration of the test	See 3.3.4
3.3.6.	Test parameter	Mortality, clinical signs, feed consumption, development of body weight.
3.3.7.	Examination / Observation	According to the test guideline recommendations
3.3.8.	Statistics	Descriptive statistics, ANOVA followed by Dunnett-test for body weight and food consumption of adult birds, egg data and chicks body weight; Wilcoxon-test for egg data, no. of dead-in-shell and no. of hatched chicks ($\alpha = 0.05$; $\alpha = 0.01$).

4. RESULTS

Limit Test / Range finding test		Not performed
Results test substance		
4.1.1.	Applied concentrations	Control, 1, 10 and 100 mg a.s./kg feed (nominal).
4.1.2.	Effect data (Mortality and reproductivity)	Table 7.5.3.1.3/167

Section 7.5.3.1.3 Effects on reproduction of birds
BPD Annex Point IIIA, XIII.1.3

4.1.3.	Body weight	Table 7.5.3.1.3/167	
4.1.4.	Food consumption	Table 7.5.3.1.3/167	
4.1.5.	Results of residue analysis	See 5.2	
4.1.6.	Other effects	See 5.2	
Results of controls			
4.1.7.	Number/ percentage of animals showing adverse effects	Table 7.5.3.1.3/167	
4.1.8.	Nature of adverse effects	Not applicable	
		5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1.	**Materials and methods**	Flufenoxuron, as described under 3.1 was administered through the diet to bobwhite quail. The test procedure is described under 3.3	
5.2.	**Results and discussion**	Analytical measurements: The results of the analytical concentration controls of the test item in the feed were within a range of 80.5% to 93.8% of the nominal concentrations. Hence the biological results are based on the nominal values. Biological results: A reduction in bodyweights of adult females at study termination related to increasing dose level was observed. Control values were higher than those of the treated groups for adult food consumption, total numbers of eggs laid and numbers laid per female, number and proportion of damaged eggs, number of 14-day survivors per female and initial chick bodyweights. Differences between control and treated groups were not considered to be of any biological significance. The overall NOEC in this study was 100 mg a.s./kg feed, the highest dietary concentration tested. The results are summarized in Table 7.5.3.1.3/167.	
5.2.1.	NOEC	100 mg/kg a.s/day	X
5.3.	**Conclusion**	The NOEL for bobwhite quail exposed to Flufenoxuron in the feed during this 22 week study was 100 mg a.s./kg feed, the highest concentration tested	
5.3.1.	Reliability	1	
5.3.2.	Deficiencies	No	

Section 7.5.3.1.3 BPD Annex Point IIIA, XIII.1.3 Effects on reproduction of birds

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	03/24/2005
Materials and Methods	Applicant's summary is acceptable with the following amendments : 2.1 Guideline study : Yes, EPA 71-4 *(Newly OPPTS 850.2300)*
Results and discussion	Applicant's summary is acceptable.
Conclusion	Applicant's summary is acceptable. 5.2.1 NOEC : 100 mg a.s./kg b.w. corresponding to 9.76 mg a.s./kg/day
Reliability	Reliability Index is 1.
Acceptability	Acceptable.
Remarks	No other.

Section 7.5.3.1.3 Effects on reproduction of birds

BPD Annex Point IIIA, XIII.1.3

	COMMENTS FROM ... *(specify)*
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.5.3.1.3/167 Effects of Flufenoxuron on the reproduction of the bobwhite quail (*Colinus virginianus*)

	Experimental group (mg a.s./kg diet)			
	Control	**1**	**10**	**100**
Number of replicates	16	16	16	16
Treatment-related mortality of adult birds	0	0	0	0
Adult body weight [g] (male/female) end of egg laying period	202 229	207 234	206 224	208 216
No. of eggs laid/group	1243	1146	1209	1031
No. of cracked and broken eggs/group	82	50	64	59
Mean egg weight (g)	10.5	10.0	10.1	10.3
Mean egg shell thickness (mm)	0.19	0.20	0.20	0.20
No. of eggs set [1)]/group	1082	1007	1072	913
No. of fertile eggs/group	918	884	940	840
No. of "dead-in-shell"/group	96	97	80	91
No. of chicks hatched/group	784	754	820	715
No. of 14-day surviving chicks/group	711	642	681	624
No. of eggs laid/female bird	55.6	51.2	55.1	48.2
No. of 14-day surviving chicks/female bird/week	31.7	28.7	31.1	29.2
Mean body weight of chicks at hatching [g]	7.3	6.7	6.8	7.0
Mean body weight of chicks14-d after hatching [g]	22	22	21	21
viable embryos of eggs set [1)] [%]	85	88	88	92
14-day survivors of chicks hatched [%]	91	85	83	87
cracked and broken eggs of eggs laid [%]	7	4	5	6

1) Incubated

Table 7.5.3.1.3/168 Validity criteria for bird reproduction test according to OECD 206

	Fulfilled	**Not fulfilled**
Mortality of control animals <10%	**Yes**	
Average number of 14-day-old survivors per hen in controls ≥ 14, 12 and 24 for mallard duck, bobwhite quail and Japanese quail	**Yes**	
Average eggshell thickness for the control group ≥ 0.34, 0.19 and 0.19 mm for mallard duck, bobwhite quail and Japanese quail	**Yes**	
Concentration of the test substance in the diet ≥ 80 % of the nominal concentration throughout the test period	**Yes**	

Section A7.5.4.1	**Effects on honeybees**
BPD Annex Point IIIA, XIII.3.1	7.5.4.1 Acute toxicity to honeybees

			Official use only
		1. REFERENCE	
1.1.	**Reference**	**1) XXXX** Effects of Flufenoxuron technical (AC 811678) (Acute contact and oral LD50) on honey bees (Apis mellifers L.) (Hymenoptera, Apidae) in the laboratory XXXX. unpublished XXXX	
1.2.	**Data protection**	Yes	
1.2.1.	Data owner	BASF	
1.2.2.	Companies with letter of access	XXXX	
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I.	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	Yes, OECD 213, OECD 214, ICPBR, EPPO Bulletin 22 (1992) No. 170	
2.2.	**GLP**	Yes (laboratory certified by Hessisches Ministerium fuer Umwelt, Landwirtschaft und Forsten, Wiesbaden)	
2.3.	**Deviations**	No	
		3. MATERIALS AND METHODS	
3.1.	**Test material**		
3.1.1.	Lot/Batch number	XXXX	
3.1.2.	Specification	As described in section 2	
3.1.3.	Purity	94.9%	
3.1.4.	Composition of Product	Not applicable, as test material = technical active substance	
3.1.5.	Further relevant properties	Not applicable	
3.1.6.	Method of analysis	Not required	
3.2.	**Reference substance**	Yes	X

Section A7.5.4.1	**Effects on honeybees**
BPD Annex Point IIIA, XIII.3.1	7.5.4.1 Acute toxicity to honeybees

3.2.1.	Method of analysis for reference substance	Not required	
3.3.	**Testing procedure**		
3.3.1.	Test organism	Honeybee (*Apis mellifera* L.), adult worker bees, colonies kept in-house; origin of bees: XXXX	X
3.3.2.	Test system	Limit-test, acute oral and contact toxicity test, duration 48 h; 5 replicates; each consisting of 10 bees in one cage, assessment of mortality and behavior after 4 h, 24 h and 48 h	
3.3.3.	Application of TS	See 3.3.2	
3.3.4.	Test conditions	Oral test: temperature: 25 °C - 26 °C, relative humidity 52% - 65% during the test. Contact test: temperature: 25 °C, relative humidity 43% - 52% during the test	
3.3.5.	Test parameter	Mortality, behavior of honeybees	
3.3.6.	Analytical parameter	See 3.3.5	
3.3.7.	Duration of the test	48 h	
3.3.8.	Sampling	Not relevant	
3.3.9.	Monitoring of TS concentration	Not relevant	
3.3.10.	Controls	Control without test substance	
3.3.11.	Statistics	Descriptive statistics	
		4. RESULTS	
Range finding test		Not performed	
4.1.1.	Concentration	Not applicable	
4.1.2.	Effect data	Not applicable	

Results test substance

Section A7.5.4.1	**Effects on honeybees**
BPD Annex Point IIIA, XIII.3.1	7.5.4.1 Acute toxicity to honeybees

4.1.3.	Initial concentrations of test substance	Control, contact test: 100 µg a.s./L; oral test: 109.1 µg a.s./bee. The reference item was applied at: oral test: 0.04, 0.08, 0.16 and 0.31 µg a.s./bee; contact test: 0.14, 0.16, 0.18 and 0.20 µg a.s./bee
4.1.4.	Actual concentrations of test substance	No measurement
4.1.5.	Effect data	See in Table 7.5.4.1/169.
4.1.6.	Other observed effects	See in Table 7.5.4.1/169.

Results of controls

Test with reference substance		Performed
4.1.7.	Concentrations	Dimethoat 400 g/L nominal: 0.14-0.2 µg a.s./bee.(contact) and 0.04-0.31 µg a.s./bee (oral)
4.1.8.	Results	The 24 h and 48 h contact LD_{50} values for the reference item Dimethoat were 0.15 and 0.14 µg a.s./bee. The 24 h and 48 h oral LD_{50} values for the reference item Dimethoat were 0.25 and 0.24 µg a.s./bee.

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1.	**Materials and methods**	Flufenoxuron, as described under 3.1, was applied to honeybees as procedure detailed in 3.3.2
5.2.	**Results and discussion**	At termination of the oral test (48 hours), the average mortality for the test item concentration was 2%. In the control, no mortality was observed after 48 hours in the oral test. At test termination, no affected bees were observed in any of the controls and the test item. At termination of the contact test (48 hours), the average mortality for the test item treatment was 2%. In the control, no mortality was observed after 48 hours. In the oral test, the test item caused a mortality of 2% after 48 hours, compared with 0% in the control. In the contact toxicity test, no mortality was observed at 100 µg a.s./bee after 48 hours, compared with 2% in the control. The results are summarized in Table 7.5.4.1/169.
5.2.1.	LC50 contact	LD_{50} (48 h) > 100 µg a.s. per bee
5.2.2.	LC50 oral	LD_{50} (48 h) > 109.1 µg a.s. per bee

Section A7.5.4.1	**Effects on honeybees**
BPD Annex Point IIIA, XIII.3.1	7.5.4.1 Acute toxicity to honeybees

5.3.	**Conclusion**	Toxicity of Flufenoxuron was tested in both, an acute oral and contact toxicity test on honeybees. The LD_{50} (48 h) was > 109.1 µg a.s. per bee in the oral toxicity test. In the contact toxicity test the LD_{50} (48 h) was > 100 µg a.s. per bee.
5.3.1.	Reliability	1
5.3.2.	Deficiencies	No

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	03/24/2005

Section A7.5.4.1	**Effects on honeybees**
BPD Annex Point IIIA, XIII.3.1	7.5.4.1 Acute toxicity to honeybees

Materials and Methods	Applicant's summary is acceptable with the following amendment : 3.2 Reference substance : Yes *(Dimethoate)* 3.3.1 Test organism: Honeybee (*Apis mellifera* L.), adult worker bees, colonies kept in-house; origin of bees: IBACON, Rossdorf, Germany; *collectec on the morning of use.*
Results and discussion	Applicant's summary is acceptable.
Conclusion	Applicant's summary is acceptable.
Reliability	Reliability index is 1.
Acceptability	Acceptable.
Remarks	It should be noticed that in Document IV A, validity criteria concerning mortality of controls is said to be "control mortality should not exceed 15%" while Guideline OECD 213 and 214 indicate "control mortality should not exceed 10%". However, no deviation was noticed as actual control mortalities in both studies (contact and oral toxicities) were far below 10%.
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 7.5.4.1/169 Toxicity of Flufenoxuron to honeybees (*Apis mellifera* L.) in oral and contact tests

Treatment nominal [µg a.s./bee]	**Uptake of test item [µg a.s./bee]**	**Mortality [%]**			
		Oral test		**Contact test**	
		24 h	**48 h**	**24 h**	**48 h**

Table 7.5.4.1/169 Toxicity of Flufenoxuron to honeybees (*Apis mellifera* L.) in oral and contact tests

Treatment nominal [µg a.s./bee]	**Uptake of test item [µg a.s./bee]**	**Mortality [%]**			
		Oral test		**Contact test**	
		24 h	**48 h**	**24 h**	**48 h**
Control	0	0	0	2	2
100	109.1	2	2	0	0
		Endpoints [µg a.s./bee]			
LD_{50}		> 109.1		> 100	

Section A7.5.4.1	**Effects on honeybees**
BPD Annex Point IIIA, XIII.3.1	7.5.4.1 Acute toxicity to Other Beneficial arthropods

	JUSTIFICATION FOR NON-SUBMISSION OF DATA	**Official use only**
Other existing data [ ]	**Technically not feasible [ ] Scientifically unjustified []**	
Limited exposure [ ]	**Other justification [X]**	
Detailed justification:	Not required as used as a Wood Preservative, PT8.	
Undertaking of intended data submission [ ]	Not applicable	

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	22/03/2007
Evaluation of applicant's justification	Applicant's version is acceptable.
Conclusion	Applicant's version is acceptable.
Remarks	

Section A7.5.4.1	**Effects on honeybees**
BPD Annex Point IIIA, XIII.3.1	7.5.4.1 Acute toxicity to Other Beneficial arthropods

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A7.5.5 **Bioconcentration in terrestrial organisms**
BPD Annex Point IIIA, XIII.7.5

Official use only

		1. REFERENCE
1.1.	**Reference**	XXXX Bioaccumulation study with BAS 307 I in earthworms XXXX unpublished XXXX
1.2.	**Data protection**	Yes
1.2.1.	Data owner	BASF
1.2.2.	Companies with letter of access	XXXX
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I.
		2. GUIDELINES AND QUALITY ASSURANCE
2.1.	**Guideline study**	No
2.2.	**GLP**	Yes (laboratory certified by Landesamt fuer Umweltschutz und Gewerbeaufsicht, Mainz, Germany)
2.3.	**Deviations**	No
		3. METHOD
3.1.	**Test material**	14C-labeled Flufenoxuron
3.1.1.	Lot/Batch number	XXXX
3.1.2.	Specification	See 3.1.3.
3.1.3.	Purity	99.9%
3.1.4.	Composition of Product	Not applicable
3.1.5.	Further relevant properties	None
3.1.6.	Method of analysis	Combustion samples were generated from soil or earthworms using the scintillator Oxysolve C-400 (Zinsser Analytic GmbH, Germany) for determination of generated radioactive carbon dioxide. The liquid samples were counted by a LSC apparatus, type Wallac 1409 (Perkin Elmer Wallac GmbH). Solutions of the test item were mixed with the scintillator Lumasafe (Lumac LSC B.V., Netherlands) for determination of radioactivity.
3.2.	**Reference**	No

Section A7.5.5 Bioconcentration in terrestrial organisms
BPD Annex Point IIIA, XIII.7.5

	substance		
3.2.1.	Method of analysis for reference substance	**Not applicable**	
3.3.	**Testing procedure**		
3.3.1.	Preparation of the test substance	None	
3.3.2.	Application of the test substance	The test item was mixed into the wet soil.	
3.3.3.	Test organisms	The test species (Eisenia fetida) was supplied by the ecotoxicology group of the test facility at XXXX (in-house culture). Before using the test animals for the test, they were kept in boxes and fed with horse manure. For the test adult animals with clitellum and a weight from 300 to 650 mg were chosen. The age of the worms ranged from 2 - 12 months.	
3.3.4.	Test system	Five earthworms were kept in approx. 500 g soil filled into a glass jar of 1000 mL with lid. A synthetic net was spanned on top of the glass containers and the lid was kept slightly open in order to enable continous gas exchange. One glass container was prepared for each sampling time point, including controls without test item and additional containers for reserve in case needed. After 14 days of the uptake phase horse manure was added on top of the soil surface in order to guarantee adequate feed supply. At the end of the uptake phase, all remaining earthworms were collected and transferred into soil of the same type as before, but without test item. The sampling time points of the elimination phase are described at point 3.3.9.	
3.3.5.	Test conditions	average temperature 20.7°C; continuous electric light was given throughout the experiment.	X
3.3.6.	Test duration	Uptake phase: 28 days Depuration phase: 28 days	
3.3.7.	Test parameter	BCF	
3.3.8.	Examination	See 3.3.9	
3.3.9.	Monitoring of test substance concentration	Earthworms were sampled on days 1, 2, 4, 8, 12, 16, 20, 24 and 28 of the uptake phase. During the elimination phase worms were sampled on days 1, 2, 3, 4, 8, 12, 16, 21, 24 and 28. Additional soil containers set up with test substance and worms were kept as a reserve during the uptake phase and were used for	

Section A7.5.5 BPD Annex Point IIIA, XIII.7.5 **Bioconcentration in terrestrial organisms**

		a prolonged uptake phase by sampling the worms at days 32, 36 and 40.
3.3.10.	Statistics	non-linear regression analysis applying the ModelMaker software version 4.0.1 from Cherwell Scientific Publishing Ltd., Oxford, UK.
		4. RESULTS TEST SUBSTANCE
4.1.1.	Initial concentrations of test substance	0.04 mg/kg dry soil.
4.1.2.	Actual concentrations of test substance	Concentration of test item in humid soil: mean value 0.033 mg/kg Concentration of test item in dry soil: mean value 0.041 mg/kg
4.1.3.	Kinetic parameters after Modelling	See 5.2
		5. APPLICANT'S SUMMARY AND CONCLUSION
5.1.	**Materials and methods**	In order to determine a bioaccumulation potential of BAS 307 I in earthworms, the worms were kept in soil containing radiolabeled test item at a concentration of 0.04 mg/kg dry soil for 28 days. The uptake phase was followed by an elimination phase of another 28 days.
5.2.	**Results and discussion**	The plateau levels were reached after 16 days. The calculation of the initial elimination rate constant α resulted in 0.592 day-1 and the terminal elimination rate constant β was 0.033 day-1. The absorption rate constant k12 was calculated from α and β to be 1.348 day-1. The kinetic micro constants k21, k23, and k32 were calculated at 0.552 day-1 0.038 day-1 and 0.035 day-1, respectively. The initial and terminal half-life time of elimination t α and tβ resulted in 1.170 and 21.249 days, respectively. The bioconcentration factor (BCF) was estimated at 5.12 (humid soil) and **4.22** (dry soil).
5.3.	**Conclusion**	For 28 days earthworms (Eisenia fetida) were exposed to ^{14}C-BAS 307 I distributed in soil followed by an elimination phase of 28 days. The bioconcentration factor (BCF) was estimated at **4.22** (dry soil).
5.3.1.	Other Conclusions	None
5.3.2.	Reliability	1
5.3.3.	Deficiencies	No

Section A7.5.5
BPD Annex Point IIIA, XIII.7.5

Bioconcentration in terrestrial organisms

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	23/08/2010
Materials and Methods	Applicant summary is acceptable *3.3.5 Test conditions* soil humidity = 70% max.
Results and discussion	Applicant summary is acceptable
Conclusion	Applicant summary is acceptable
Reliability	1
Acceptability	acceptable
Remarks	
	COMMENTS FROM ... *(specify)*
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section 7.5.6 **Effects on other terrestrial non-target organisms**

Annex Point IIIA, VII 7.5

Official use only

	1. REFERENCE	
1.1.	**Reference**	Klein S. 2003 Effects of Flufenoxuron 100 g/L DC (BAS 307 QA I) on reproduction of the collembola *Folsomia candida* in artificial soil XXXX. unpublished XXXX
1.2.	**Data protection**	YES
1.2.1.	Data owner	BASF
1.2.2.	Companies with letter of access	XXXX
1.2.3.	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s./b.p. for the purpose of its entry into Annex I.
	2. GUIDELINES AND QUALITY ASSURANCE	
2.1.	**Guideline study**	ISO 11267 (1999)
2.2.	**GLP**	YES (laboratory certified by Hessisches Ministerium fuer Umwelt, Landwirtschaft und Forsten, Wiesbaden, Germany)
2.3.	**Deviations**	None
	3. METHOD	
3.1.	**Test material**	Flufenoxuron
3.1.1.	Lot/Batch number	XXXX
3.1.2.	Specification	Active substance prepared as 100 g/l dispersible concentrate (supported product under Directive 91/414/EEC review program).
3.1.3.	Purity	103 g/L (measured)
3.1.4.	Composition of Product	Formulation containing 100 g Flufenoxuron /L (nominal)
3.1.5.	Further relevant properties	Not applicable
3.1.6.	Method of analysis	Not relevant
3.2.	**Reference substance**	Betosip (Phenmedipham, 157 g/L nominal)
3.2.1.	Method of	Not relevant

	analysis for reference substance	
3.3.	**Testing procedure**	
3.3.1.	Preparation of the test substance	Dilution in deionised water
3.3.2.	Application of the test substance	1.18, 2.06, 3.60, 6.31, and 11.0 mg product/kg (actual concentration), respectively, were added to vessels containing artificial soil according to OECD 207 (10% peat) and mixed homogenously.
3.3.3.	Test organisms	Collembola: *Folsomia candida* WILLEM 1902
3.3.4.	Test system	Dose-response test, effects on reproduction; 5 treatment groups with 5 replicates, each replicate consisted of a vessel containing 10 adult collembolas; Food: about 2 mg dry yeast at the beginning of the test for each test vessel and additional feeding on day 14.
3.3.5.	Test conditions	Artificial soil according to OECD 207 (10% peat): pH 6.5 at start, pH 5.6-5.8 at end; water content: 29-31 % (52-56% of max. WHC); maximum water holding capacity: 56.48% of dry weight; Light regime: 16 h light: 8 h dark, light intensity: 490-750 lux, temperature: 19-20°C.
3.3.6.	Test duration	28 days
3.3.7.	Test parameter	Mortality, behaviour, reproduction
3.3.8.	Examination	assessment of mortality, behaviour and reproduction after 28 d
3.3.9.	Monitoring of test substance concentration	Not relevant
3.3.10.	Statistics	Mortality data were statistically analysed using Fisher Exact Test, a distribution free test. Reproduction data were tested for normal distribution and homoscedasticity using Kolmogoroff-Smirnov-test and Cochran-test ($\alpha = 0.05$). Further statistical evaluation was performed using Dunnett Test (multiple comparison, $\alpha = 0.05$, one-sided smaller). The determination of the NOEC and LOEC values was based on the results of the statistical evaluation. The LC50 was calculated by Probit analysis; the EC50 was calculated by Logit analysis. The software used to perform the statistical analysis was SYSTAT Version 9.0, ©1999 SPSS Inc. (Fisher Exact Test) and Tox Rat Pro 2.07, ©2001-2002 SpiRiT Solutions (Dunnett Test, Probit and Logit analysis).

4. RESULTS

4.1.1.	Mortality	A statistically significant mortality of *Folsomia candida* was observed at concentrations of 6.29 and 11.0 mg product/kg (Fisher Exact Test, $\alpha = 0.05$, two-sided). Mortality values ranged from 4% at 1.17 mg product/kg to 56% at 11.0 mg product/kg. The No Observed Effect Concentration (NOEC) was 3.59 mg product/kg artificial soil (dry weight) and the Lowest Observed Effect Concentration (LOEC) was 6.29 mg product/kg artificial soil dry weight. The LC50 was calculated to be 10.2 mg product/kg with lower 95% confidence limit of 7.6 mg and upper 95 % confidence limit of 13.8 mg product/kg (Probit analysis).
4.1.2.	Behaviour	No abnormal behaviour or conditions were observed with the surviving adult collembola. Juvenile collembola in the test item treated groups were generally smaller compared to the control.
4.1.3.	Reproduction	Statistically significant effects on reproduction of *Folsomia candida* occurred at 2.05 mg product/kg and higher (Dunnett Test, $\alpha = 0.05$, one-sided smaller). The No Observed Effect Concentration (NOEC) was 1.17 mg product/kg artificial soil (dry weight) and the Lowest Observed Effect Concentration (LOEC) was 2.05 mg product/kg artificial soil dry weight. The EC50 was calculated to be 3.3 mg product/kg with lower 95 % confidence limit of 3.2 mg product/kg and upper 95 % confidence limit of 3.4 mg product/kg (Logit analysis).
4.1.4.		The toxic standard test showed statistically significant effects on reproduction at concentrations of ≥ 50 mg Betosip/kg artificial soil dry weight; the EC50 for reproduction was calculated as 135 mg Betosip/kg soil dry weight. Mortality was statistically significantly higher than the control at 400 mg Betosip/kg artificial soil dry weight, the LC50 for mortality was calculated as 285.1 mg Betosip/kg soil dry weight.

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1.	**Materials and methods**	For 28 days collembolas (*F. candida*) were exposed to flufenoxuron (BAS 307 QA I) mixed into artificial soil (OECD 207) containing 10 % peat. Mortality, behaviour and reproduction were assessed on day 28.
5.2.	**Results and discussion**	BAS 307 10 I (BAS 307 QA I) caused no adverse effects on the survival of adult *F. candida* at concentrations up to 3.59 mg/kg soil. In the two highest test item concentrations of 6.29 and 11.0 mg/kg soil statistically significant effects on mortality were observed (Fishers-exact-test, $\alpha = 0.05$). The reproduction in the control reached 521 juveniles at test termination. At concentrations of 2.05 mg/kg soil and higher a statistically significant reduction of reproduction was observed.
5.3.	**Conclusion**	In a 28 day reproduction study with BAS 307 QA I

		(BAS 307 Q10 I) on Collembola (*F. candida*) the LC_{50} was determined to be 10.2 mg BAS 307 QA I/kg soil dry weight and the EC_{50} was 3.3 mg/kg. The NOEC (mortality) was determined to be 3.59 mg/kg and the NOEC (reproduction) was 1.17 mg BAS 307 QA I/kg soil dry weight
5.3.1.	Other Conclusions	None
5.3.2.	Reliability	1
5.3.3.	Deficiencies	No

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	*23/08/2010*
Materials and Methods	Applicant summary is acceptable.
Results and discussion	Applicant summary is acceptable.
Conclusion	Applicant summary is acceptable without modifications.
Reliability	1
Acceptability	acceptable
Remarks	
	COMMENTS FROM ... *(specify)*
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A7.6

BPD Annex Point IIA, VI.7.8; IIIA, XII.4, XIII.5

Summary of ecotoxicology effects and fate & behaviour in the environment

Section A7.6

BPD Annex Point IIA, VI.7.8; IIIA, XII.4, XIII.5

Summary of ecotoxicology effects and fate & behaviour in the environment

TABLE OF CONTENT

Official use only

Section A7.6

BPD Annex Point IIA, VI.7.8; IIIA, XII.4, XIII.5

Summary of ecotoxicology effects and fate & behaviour in the environment

1.1 Reference ---- 1

1.2 Data protection ---- 1
1.2.1 Data owner ---- 1
1.2.2 Companies with letter of access ---- 1
1.2.3 Criteria for data protection ---- 1

2.1 Guideline study ---- 1

2.2 GLP ---- 1

2.3 Deviations ---- 1

3.1 Test material ---- 1
3.1.1 Lot/Batch number ---- 1
3.1.2 Specification ---- 2
3.1.3 Purity ---- 2
3.1.4 Further relevant properties ---- 2

3.2 Reference substance ---- 2
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3.4 Testing procedure ---- 2
3.4.1 Test system ---- 2
3.4.2 Temperature ---- 2
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5.1 Materials and methods ---- 3

5.2 Results and discussion ---- 3
5.2.1 k_H ---- 3
5.2.2 DT_{50} ---- 3
5.2.3 A^2 ---- 3

5.3 Conclusion ---- 3
5.3.1 Reliability ---- 3
5.3.2 Deficiencies ---- 3

5.4 Fate and distribution in the environment

Summary of the study results on flufenoxuron fate and distribution in the environment are given in **Appendix 1** including the following tables:

Table 6	- Sludge activity, Biotic degradation
Table 7	- Hydrolysis
Table 8	- Photolysis in water
Table 9	- Photolysis in Soil
Table 10	- Photochemical degradation in air
Table 11	- Laboratory degradation in soil
Table 12	- Water/Sediment degradation
Table 13	- Summary of degradation rates of Flufenoxuron in laboratory soil studies
Table 14	- Summary of degradation rates of "urea" metabolite (CL 932338) in laboratory soil studies
Table 15	- Adsorption data for [14C]-Flufenoxuron on different soils
Table 16	- Adsorption data ^{for} 14C-"urea" metabolite (CL 932338) on different soils
Table 17	- Desorption data for $^{14C\text{-}"urea"}$ metabolite (CL 932338) on different soils

Appendix 2 contains the document XXXX: Recalculation Recalculation of aquatic endpoints for the flufenoxuron (BAS 307 I) Annex I, PT8 biocide dossier

Hereafter find an overall assessment of those results.

5.4.1 Water

The behaviour of Flufenoxuron in aquatic systems is mostly characterised by its very low water solubility (sorption to sediment), no readily biodegradability and UV-instability.

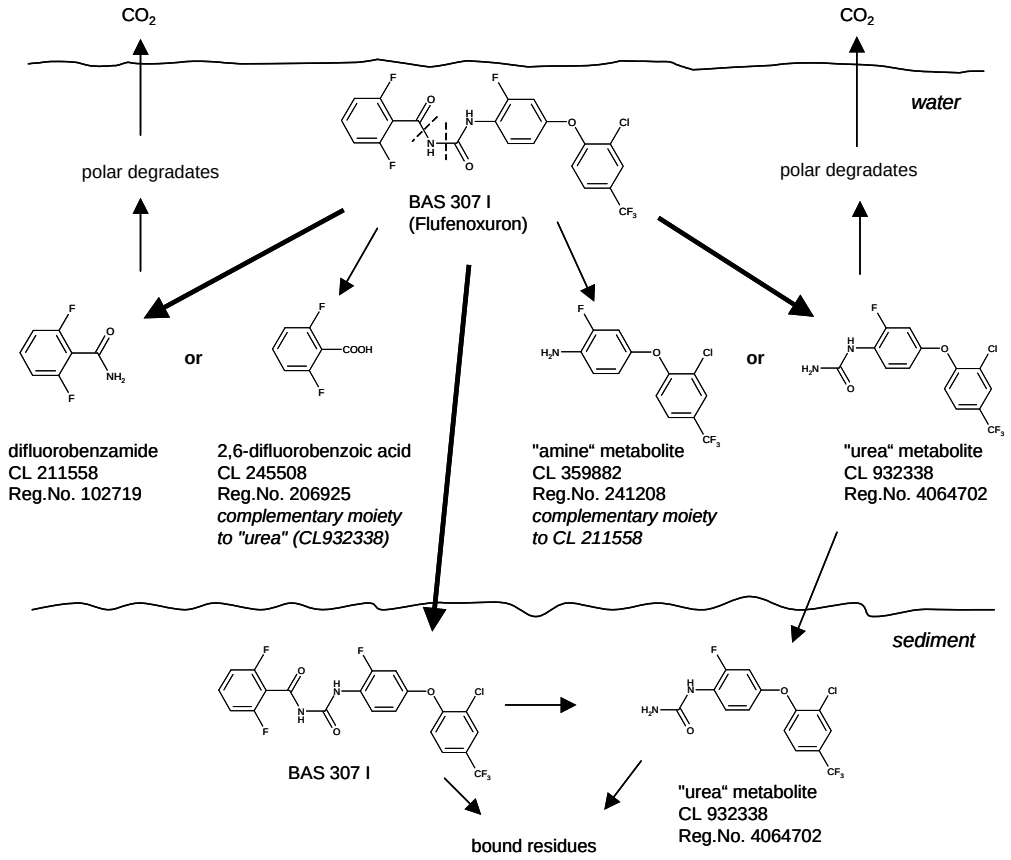
In all photolysis and water/sediment studies, the cleavage of the molecule is the first degradation step. The split can occur at two alternative locations within the molecule. In the aqueous photolysis studies the formation of 2,6-difluorobenzamide (CL 211558, Reg. No. 102719) is preferred with up to 88% total applied radioactivity (TAR). In the water/sediment systems also the alternative split leading to formation of the "urea"-metabolite (and theoretically 2,6-difluorobenzoic acid as counterpart, CL 245508, Reg. No. 206925) can occur. Furthermore, in the water/sediment studies the sorption of Flufenoxuron to the sediment leads to an even faster elimination from the water phase.

The 2,6-difluorobenzamide never exceeded 4.1% TAR in the dark water/sediment study and could not be detected in the irradiated water/sediment study. It was fast degraded to further polar compounds (all <5% TAR). The final degradation products were bound residues in the sediment and formation of CO_2.

The corresponding fluoroaniline moiety, which could not be detected in the photolysis study, was represented in the water/sediment studies exclusively by the "urea" metabolite (CL 932338, Reg.No. 4064702) appearing in both, water and sediment. It hardly reached 10% TAR in the water phase and a maximum amount of 19% TAR in the sediment. This metabolite was also further degraded forming finally bound residues in the sediment or mineralizing to CO_2. The proposed route of degradation is given in Figure 1.

Overall, the experimental results showed that Flufenoxuron disappears rapidly fromthe aquatic environment with half-lives of 0.3 days in water (at 12°C) and between 87 and 123 days (at 12°C) in sediment.

Figure 1 Proposed route of degradation of Flufenoxuron in the aquatic environment

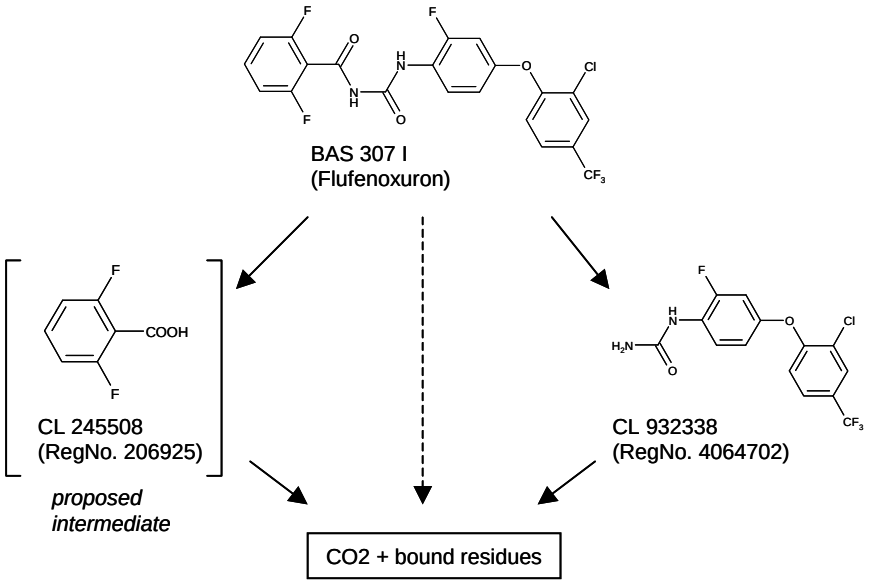


5.4.2 Soil

The metabolism of Flufenoxuron in soil is characterised by a splitting of the molecule into two halves. The fluoroaniline moiety forms the "urea" metabolite (CL 932338, Reg.No. 4064702), which is degraded further to form non-extractable residues and finally CO_2. With the benzamide-moiety, no distinct metabolite could be detected in soil, indicating that the degradation rate of the possibly formed difluorobenzoic acid is faster than the formation out of Flufenoxuron.

A proposed route of degradation is given in in Figure 2.

Figure 2 Proposed route of degradation of Flufenoxuron in soil



The transformation rates of Flufenoxuron and its metabolite CL 932338 were estimated using the program ModelMaker, vs 3.0.4. The kinetic parameters were optimized using the MARQUARDT method (option least squares). A three-compartment model was established for the degradation of Flufenoxuron. The model consists of the parent compartment, a compartment for the "urea" metabolite (CL 932338, Reg No. 4064702) and an elimination compartment which represents all degradation processes like formation of non-extractable residues and mineralization. To calculate the half-life of the metabolite, a simple two-compartment model was established consisting of the metabolite compartment and an elimination compartment. From these calculations, good estimation for the parent and metabolite half-life were obtained in all four tested soils. The half-lives of Flufenoxuron and metabolite were recalculated to a reference temperature of 12°C. All half-lives are shown in (Table 13 and Table 14).

The results of the soil experiments with Flufenoxuron under anaerobic and under irradiated conditions showed that in both cases no significant degradation could be observed. According to *Arrhenius equation*, an estimated value for DT50 at 10°C range between 252-267 and 103-129 days for flufenoxuron and its main soil degradates, Reg No. 4064702. It can therefore be concluded that soil photolysis and anaerobic conditions do not contribute to considerable extent to the degradation of Flufenxuron in soil**.**

In a new field soil dissipation study conducted in Southern Europe, a fast to moderate dissipation of Flufenoxuron was observed with DT_{50} values ranging from 6 days in Spain to 67 days in France and DT_{90} values between 20 and 222 days. Its "urea" metabolite CL 932338 (Reg.No. 4064702) was not detected in significant amounts under field conditions.

Flufenoxuron is strongly binding to soil independently of soil pH (Table 14)

Each of the desorption steps resulted in less than 5% of the adsorbed Flufenoxuron being released, except for two higher values (about 8% to 9%) found for the lowest concentration. These values confirm the strong adsorption of Flufenoxuron to the soil matrix.

Its "urea" metabolite (CL 932338, Reg 4064702) also strongly binds to soil (Table 16). Within the five soils tested, a slight dependence of the adsorption behaviour from the soil pH could be observed with the most acidic soil (Borgeby, pH = 5.6) showing the strongest adsorption. The desorption data are given in Table 17.

Based on the fact that Flufenoxuron as well as its "urea"-metabolite (WL 129183, CL 932338, Reg.No. 4064702) have very low water solubility and show very high adsorption values (Koc) in soil and that there was no indication of any leaching processes in field trials, it can be concluded that there is no risk of leaching into deeper soil layers or groundwater after Flufenoxuron application under outdoor conditions.

5.4.3 Air

Flufenoxuron has a very low volatilisation potential (vapor pressure 6.52 x 10^{-12} Pa at 20°C). Based on Atkinson calculation, Flufenoxuron would be fast degraded by photochemical processes when reaching the troposphere (DT_{50} < 27 h). Therefore, it can be concluded that there is no risk of short or long-range transport of Flufenoxuron via air.

5.4.4 Definition of the residue

Water

According to the presented results, the parent compound Flufenoxuron is the only relevant residue for quantitation in water.

In the hydrolysis study at pH 9, the major degradation product was the 2,6-difluorobenzoic acid (CL 245508, Reg.No. 206925) formed by cleavage of Flufenoxuron. At all other pH's, Flufenoxuron was stable. Under photolytic conditions the major degradation product with up to 89% was 2,6-difluorobenzamide (CL 211558, Reg.No. 102719), indicating an alternative cleavage location in the molecule.

In the water/sediment studies (in the dark and under sunlight) representing more realistic environmental conditions, only two metabolites could be detected in water and sediment.

The 2,6-difluorobenzamide (CL 211558, Reg.No. 102719) appeared in the water phase at maximum 4.1% and was not detected in sediment. The "urea" metabolite (CL 932338, Reg.No. 4064702) was formed up to 9.3% in the water phase and up to 19% in the sediment. The appearance of these two metabolites leads to the conclusion that under realistic environmental conditions, cleavage at both alternative molecule positions can occur simultaneously.

In exotoxicity studies, it was shown that the "urea" metabolite had only at the highest concentrations any effect on fish and daphnia, and no effect on algae. The 2,6-difluorobenzamide had no effect on fish, daphnia and algae even at the highest concentrations tested. Also the 2,6-difluorobenzamide proved to be not biologically active.

Therefore, the parent Flufenoxuron is proposed as the only relevant residue in water.

Valid data on sediment dwelling organisms exist only for the parent compound as the proposed study with urea metabolite was considered not reliable by the RMS. However, this metabolite, the only one detected in the sediment compartment, was proved to be a least 100 times less toxic than the parent molecule on fishes and daphnia. The half-life of urea metabolite in the sediment was also shorter than the parent compound half-life. For all these reasons, Flufenoxuron can be proposed as the only relevant residues in the sediment.

Soil

According to the presented results, the parent compound Flufenoxuron is the only relevant residue for quantitation in soil. Although the "urea" metabolite (CL 932338, Reg.No. 4064702) (cleavage product) was formed above 10% in several aerobic soils (maximum 16%) in the laboratory studies, the results of the field dissipation study showed that this metabolite was detected if at all only in trace amounts close to the determination limit. Ecotoxicity studies showed that the metabolite does not have any effect on earthworms or on the microbial activity in soil (See 4.3). Furthermore, this metabolite is not biologically active.

Under anaerobic conditions, no significant degradation of Flufenoxuron took place. No metabolites are formed under these conditions. Also during soil photolysis, no significant degradation of Flufenoxuron could be observed.

Since the adsorption to soil is very strong for Flufenoxuron (Koc > 88000) and also the "urea" metabolite (Koc > 3700), no risk for groundwater after application of Flufenoxuron exists.

Therefore, the parent Flufenoxuron is the only relevant residue in soil.

Air

Not relevant because very likely to present no risk of short or long-range transport of Flufenoxuron via air.

5.5 Effects on environmental organisms

For ease of reference, BASF code names for Flufenoxuron degradates are used hereafter. A chemical glossary with details is given in chapter 6 (pp 46-47).

5.5.1 Aquatic compartment

The effects of Flufenoxuron and its degradates are on aquatic organisms are summarized in Table 1.

Table 1 Summary of results of Flufenoxuron and its degradates on aquatic organisms

Test species	Test system	Result [µg a.s./L]		Reference
		LC_{50}/EC_{50}	NOEC	
Onchorynchus mykiss 9)	Flow-through - 96 h	> 4.9	n.d.	XXXX
Danio rerio 9)	Semi-static – 96 h	> 5.19	5.19	XXXX
Cyprinus carpio 8)	Static - 96 h	> 10 000	n.d.	XXXX
Pimephales promelas ELS 9)	Flow-through - 34 d	n.d.	≥ 0.82 11)	XXXX
Danio rerio 9)	static - (full life-cycle)- 143d with sediment	n.d.	≥ 1.199 11)	Shaefers XXXX
Daphnia magna 8)	Static - 48 h	0.0429	0.01	Funk XXXX XXXX
Daphnia magna 9)	Static - 48 h	test 1: 0.04 test 2: 0.083 11)	n.d.	Croucher XXXX
Daphnia carinata 8)	Static - 48 h	test 1:< 500 test 2: 1.4	n.d.	Shumei XXXX
Gammarus pulex 9) *Lymnaea stagnalis* *Tubifex tubifex* *Chironomus lugubris*	Semi-static - 96 h Semi-static - 96 h Semi-static - 96 h Semi-static - 48 h	> 1.2 > 1.2 > 0.4 > 0.6	n.d.	Pearson, Girling XXXX
Daphnia magna 8)	Static - 48 h	n.d.	10	Pearson, Girling XXXX
Daphnia magna 9)	Semi-static - 21 d	n.d.	0.00449 11)	Pearson, Girling XXXX
Pseudokirchneriella subcapitata 9)	Static - 96 h	19 228 1) 11)	600 3)	Kubitza XXXX
Pseudokirchneriella subcapitata 9)	Static - 96 h	> 2.975 11)	n.d.	Croucher XXXX
Chironomus riparius spiked-water 10)	Static - 28 d	0.131	0.05 4) 11) 0.1 5)	Mattock XXXX
Chironomus riparius spiked sediment 10)	Static – 32 d	n.d.	79 µg/kg	Toy, XXXX
Chironomus riparius spiked-sediment 8)	Static – 28 d	142.7 µg/kg dry sediment	80 µg/kg dry sediment	Weltje and Pupp, XXXX
Lumbriculus variegatus spiked-sediment 10)	Static – 28 d	n.d.	≥ 306 µg/kg dry sediment	Egeler and Seck, XXXX
Zooplankton community incl. *Daphnia* 10)	Static mesocosm – 63 d	--	NOEAEC 0.13 – 0.16 11)	Harrison (FX XXXX
"urea", Reg. No. 4064702				
Onchorynchus mykiss 8)	Static - 96 h	570 8) 520 9)	200 8) 230 9)	XXXX
Daphnia magna 8)	Static - 48 h	1030	500 2)	Jatzek XXXX
Pseudokirchneriella subcapitata 8)	Static - 72 h	90	E_bC_{10} : 66 E_rC_{10} : 70	Jatzek XXXX
Chironomus riparius 8)	Static - 28 d	1200 4) 4610 5)	800 4) 1600 5)	Funk XXXX

Test species	Test system	Result [µg a.s./L]		Reference
		LC_{50}/EC_{50}	NOEC	
Reg. No. 4108386				
Onchorynchus mykiss [9]	Semi-static - 96 h	2096 [11]	n.d.	XXXX
Daphnia magna [9]	Static - 48 h	3361 [6) 11)] 9700 [7)]	n.d.	Girling XXXX Ede XXXX (amendment 1
Reg. No. 4064703				
Onchorynchus mykiss [9]	Semi-static – 96 h	462 [11]	n.d.	XXXX
Daphnia magna [9]	Static - 48 h	5.45 [11]	n.d.	Girling XXXX
Pseudokirchneriella subcapitata [8]	Static - 72 h	600 [1]	100	Hanstveit, Oldersma XXXX
Reg. No. 102 719				
Onchorynchus mykiss [8]	Static - 96 h	> 100 000	100 000	XXXX
Daphnia magna [8]	Static - 48 h	> 100 000	25 000 [2]	Jatzek XXXX
Pseudokirchneriella subcapitata [8]	Static - 72 h	> 100 000 [1]	77 700 [3]	Jatzek XXXX
Reg. No. 241 208				
Daphnia magna [8]	Static - 48 h	654	500 [2]	Jatzek XXXX
Reg. No. 206 925				
Daphnia magna [8]	Static - 48 h	> 100	100 [2]	Jatzek XXXX

1) biomass; 2)$EC_{0;}$ 3) $E_bC_{10;}$ 4) based on emergency; 5) based on development ; 6) based on freshly prepared test item solutions; 7) based on aged (48 h) test item solutions 8) results based on nominal concentrations; 9) results based on measured concentrations; 10) results based on initial measured concentrations; 11) recalculated in XXXX, see IIIA 7.6 Appendix 2;

5.5.2 Soil Micro-organisms

The toxicity of Flufenoxuron in soil had been tested on physiological functions of soil micro-organisms (laboratory studies). The results are summarized Table 2.

Table 2 Summary of effects of Flufenoxuron and metabolites on soil micro-organisms

Test system/ Soil type	Application rate		Result	Reference
	[mg/kg]	[kg/ha]	[%] deviation from control [1)]	
C-transformation				
Flufenoxuron, tested as 100 g a.s./L DC				
Loamy sand (28 d)	0.17	0.128	-0.858	Koelzer, XXXX
	1.7	1.28	-3.66	
"urea", Reg. No. 4064702				
Loamy sand (28 d)	0.00761	0.0057	+5.18	Koelzer, XXXX
	0.0761	0.057	-1.01	
N-transformation				
Flufenoxuron, tested as 100 g a.s./L DC				
Loamy sand (28 d)	0.17	0.128	+12.6	Koelzer, XXXX
	1.7	1.28	+6.92	

Table 2 Summary of effects of Flufenoxuron and metabolites on soil micro-organisms

Test system/ Soil type	Application rate		Result	Reference
	[mg/kg]	[kg/ha]	[%] deviation from control [1)]	
„urea“, Reg. No. 4064702 [6)]				
Loamy sand (28 d)	0.00761	0.0057	-17.2	Koelzer, XXXX
	0.0761	0.057	-17.2	

1) - = inhibition; + = stimulation 2) analysis of nitrification levels at day 28 3) analysis of nitrification levels at day 91
4) amended with ammonia, 5) amended with Lucerne 6) 1x metabolite: 20% transformation from 0.04 kg a.s./ha

5.5.3 Soil Macro-organisms (earthworms)

Flufenoxuron and its soil “urea” metabolite Ref No. 4064702 [previously CL 932 338] has been tested on earthworms in 14-day toxicity studies up to 1000 mg a.s./kg substrate: Furthermore, the active substance was tested in a chronic toxicity and reproduction test up to 5.0 mg a.s./kg soil dry weight. The results are summarized in Table 3.

Table 3 Summary of effects of Flufenoxuron on earthworms

Test species	Test system	Toxicity [mg/kg soil dry weight]		Reference
		LC_{50}	NOEC	
Flufenoxuron				
E. fetida	14-d toxicity test	> 1000	> 1000	Hillaby, XXXX
E. fetida	56-d repro test	n.d.	5.0	Luehrs, XXXX
“urea”, Reg. No. 4640702				
E. fetida	14-d toxicity test	> 1000	316	Staebler, XXXX

n.d. = not determined

5.5.4 Terrestrial Plants (primary producers)

Flufenoxuron has been tested on six different plant species in a 15-day vegetative vigour test at rates of 40 g a.s./ha and 80 g a.s./ha, corresponding to 55 µg a.s./kg and 110 µg a.s./kg soil, respectively. Endpoints of the study were effects on plant weight and plant health. The results are summarized in Table 4.

Table 4 Summary of effects of Flufenoxuron on plants

Test species	Test system	Toxicity [mg/kg soil]		Reference
		LC_{50}	NOEC	
Flufenoxuron				
Avena sativa *Allium cepa* *Brassica oleracea* *Pisum sativum* *Daucus carota* *Helianthus annuus*	15-d vegetative vigour test	≥ 0.110	≥ 0.110	Sack XXXX

5.5.5 Birds

For the assessment of effects of Flufenoxuron on birds, tests with bobwhite quails (*Colinus virginianus*) and mallard ducks (*Anas platyrhynchos*) have been conducted. The results are summarized in Table 5.

In the single dose acute toxicity study with bobwhite no significant reduction in the mean feed uptake was observed compared to the control up to the highest dose group. The mean body weight and the development of body weight of female birds were not statistically significant reduced when compared to the control group. No compound-related macroscopic abnormalities were detected in the gross post-mortem examination.

In the short-term dietary study with bobwhite and mallard no test item related mortality, clinical signs, reduction of feed consumption or reduction of body weight were observed.

In the sub-chronic toxicity and reproduction studies with bobwhite no mortality was observed. No compound-related symptoms occurred. Feed consumption and body weight were within the normal limits in all groups.

Table 5 Summary of effects of Flufenoxuron on birds

Test species	Test system	Results	Reference
Colinus virginianus	Acute oral toxicity	LD_{50} > 2000 mg a.s./kg b.w. NOEL = 2000 mg a.s./kg b.w.	XXXX
Colinus virginianus	Short-term dietary toxicity	LD_{50} > 5243 mg a.s./kg b.w. NOEC = 5243 mg a.s./kg b.w.	XXXX
Anas platyrhynchos	Short-term dietary toxicity	LD_{50} > 5243 mg a.s./kg b.w. NOEC = 5243 mg a.s./kg b.w.	XXXX
Colinus virginianus	Sub-chronic toxicity and reproduction	NOEL = 100 mg a.s./kg feed corresponding to 9.76 mg a.s./kg b.w.	XXXX

5.5.6 Non compartment specific effects relevant to the food chain (secondary poisoning)

Under use recommendations, flufenoxuron is unlikely to present a risk to top predators. For detailed calculations of secondary poisoning please refer to Doc II A and II B.

APPENDIX 1 OVERALL STUDY RESULTS FOR FLUFENXORUON BIOTIC AND ABIOTIC DEGRADATION IN ENVIRONMENT COMPARTIMENT

Table 6 - Sludge activity, Biotic degradation

Guideline / Test method	Test type[1]	Test para-meter	Inoculum Type	Test substance concentr.	Degradation Incub. period	Degradation Degree [%]	Reference
OECD 301B	R	%ThOD	Sewage Sludge	3 mg/L	28 days	≤4%	Turner SJ, Watkinson RJ (1986) XXXX
OECD 301D	R	$\%ThCO_2$	Sewage Sludge	20 mg/L	28 days	≤4%	

[1] Test on *inherent (I)* or *ready (R)* biodegradability according to OECD criteria

Table 7 - Hydrolysis

Guideline / Test method	pH	Temp. [°C]	Initial TS concentration, C_0 [µg.mL]	Half-life, DT_{50} [days]		Reference
none	5, 7, 9, 12, and 14	25, 40, 60, 70 and 80ºC	0.002	At 25ºC, pH 5 - 205 d pH 7 - 267 d pH 9 - 36.7 d pH 12 - 2.68 d pH 14 – 0.11 d		Langner EJ, Camilleri P (1987) *XXXX*
EC Method C7		50ºC and 25ºC		25ºC	50ºC	Hassink J
US EPA N 161-1	4		1.0	434	66	(2003)
	5		1.0	682	99	*XXXX*
	7		0.8	234	36	
	9		1.8	88.0, 94.4	1.5, 1.0	
	9		Reg. No. 206935	59.3	--	
			Reg. No. 102719	--	3.0	

Table 8 - Photolysis in water

Guideline / Test method	Initial molar TS concen-tration	Photolysis rate constant (k^c_p)	Reaction quantum yield (ϕ^c_E)	Half-life ($t_{1/2E}$)	Reference
None	4.5x 10^{-9} mole/L	Not determined	Not determined	at Latitude 51º 20'N under June sunlight, the $t_{1/2}$ was about 11 days.	Camilleri P, Langner E J (1987) XXXX
SETAC (1995) OECD/GD (97)21	1.975 µg/L	0.14645 $days^{-1}$	4.76 x 10^{-6}	Summer – 12 days Winter – 24 to 72 days	Burgener A (2001) XXXX
Commission Directive 94/37/EEC amending Council Directive 91/414/EEC	1.6, 1.7 nM	0.15068 $days^{-1}$ 2,6-difluorobenzamide - 0.04951 $days^{-1}$	1.75 x 10^{-3}	39.2 days in April to 21.7 days in June.	Hassink J (XXXX
JAMFF Guideline, 9 Nohsan 5089: 16, 1997	0.0021 µg/ml	Distilled water – 0.0976 $days^{-1}$ Pond water – 0.1024 $days^{-1}$	Not determined	Spring 35ºN Distilled water – 17.7 days Pond water – 17.0 days	Mamouni A and van der Gaauw A (2001) XXXX

Table 9 - Photolysis in Soil

Guideline / Test method	Test Conditions	Half-life ($t_{1/2E}$)	Metabolites Identified	Reference
SETAC Europe March 1995	Samples were irradiated continuously by xenon lamp for up to 16 days at 20 ± 3ºC.	under bright summer sunlight in Harrowgate, UK (ca. 54ºN): 147 and 166 days	2,6-diflourobenzamide maximum of <3% TAR	Lewis CJ, Gross R (2001) XXXX

Table 10 - Photochemical degradation in air

Guideline / Test method	Test Conditions	k	$T_{1/2, OH}$	Reference
Council Directive 94/37/EC of July 22, 1994	The rate constant for reactions with OH radicals in the atmosphere was estimated using Atkinson's method. The half-life was calculated using the weighted global average OH radical concentration in the troposphere.	14.2568 x 10^{-12} cm^3 $molecule^{-1}$ s^{-1}.	0.7 days	Hassink J (2003) XXXX

According to the TGD, assuming a 24hrs – day and an OH concentration of 5.0 x 10^5 cm^{-1} this gives a half-life of 1.12 days or 27 hours.

Table 11 - Laboratory degradation in soil

Guideline / Test method	Reference	Test Temp. - Duration	Soil Type/ Source	DT_{50}	Metabolites Identified
None cited.	Richardson (1987) XXXX	22 ± 2ºC 90 days	Clay Loam, UK	~140 days	
None cited.	Richardson (1990/91) XXXX	21 ± 2ºC 152 days	Silty clay loam, UK	Aerobic: ~120 days Anaerobic: >>150 days (86%remaining at end of study)	WL 129183: Max. 16% at 90 days WL 115096: <1%
BBA Guideline, Part IV, 4-1 (Dec. 1986)	Standen & Hill (1993) XXXX	22 ± 2ºC 150 days	Clay Loam , UK	Aerobic: 90 days Anaerobic: >>150 days (77% remaining at 150 days)	WL 129183: Max. 7.3% at 60 days WL 115096: <1% Bound residues were ca. 46% of TAR at 150 days and were characterized as fulvic acids (ca. 5% TAR), humic acids (ca. 20% TAR), and humins (ca. 20% TAR).
SETAC 1995 OECD 307	Goodyear & Gross (2001) XXXX	20 ± 2ºC 120 days	Clay Loam , UK (3)	124 days 36 days 64 days	None Bound residues were 20-25% of TAR at 150 days and were characterized as fulvic acids (5-10% TAR), humic acids (2-8% TAR), and humins (8-13% TAR).
SETAC 1995 OECD 307	Stephan & Ebert (2003) XXXX	20 ± 2ºC 120 days	Silty sand , Germany (2 for flufenoxuron, 4 for CL932338)	Flufenoxuron: 122, 115 days CL932338: 57, 56, 59, 47 days	No

Table 12 - Water/Sediment degradation

Guideline / Test method	Reference	Water/Sediment source	Analyte	Compartment	DT_{50} (days)	DT_{90} (days)
BBA, Part IV, 5-1 US-EPA N, 162-4 SETAC Europe • OECD 308	Ebert D (2003) *XXXX*	Kellmetschweiher (20°C)	Flufenoxuron	whole system water sediment	61 0.3 65	203 0.9 216
			CL932338	sediment	21	71
		Berghäuser Altrhein (20°C)	Flufenoxuron	whole system water sediment	45 0.4 46	150 1.2 152
			CL932338	sediment	10	32
•		Kellmetschweiher (12°C)	Flufenoxuron	whole system water sediment	116 0.3 123	385 0.9 410
			CL932338	sediment	40	135
		Berghäuser Altrhein (12°C)	Flufenoxuron	whole system water sediment	85 0.4 87	285 1.2 288
			CL932338	sediment	19	61
• OECD Guideline, Draft Aug 2001 • This study was carried out under natural light in outdoor conditions	Fent G (2003) *XXXX*	Kellmetschweiher	Flufenoxuron	whole system water sediment	42.9 4.7 46.1	142.5 15.5 153.0

Table 13 - Summary of degradation rates of Flufenoxuron in laboratory soil studies

Study Reg.Doc.#	**Soil**	**Study duration [days]**	**Temp. [°C]**	**Moisture [%MWC]**	**Estimation**	**DT50 [days]**	**DT90 [days]**	**r^2**
aerobic degradation								
Richardson 1987 XXXX	Hoath, UK	90	22	42	graphical extrapolation	~ 140	n.c.	-
Richardson 1990/91 XXXX	Woodstock, UK	152	21	40	graphical extrapolation	~ 120	n.c.	-
			12	40	recalculation from 21°C result	~ 267	n.c.	-
Standen & Hill 1993 XXXX	Woodstock, UK aniline label toluyl label	150	22	40	 graphical estimation	 ~ 90 ~ 90	 n.c. n.c.	 - -
			12	40	recalculation from 22°C result	~ 200	n.c.	-
Goodyear & Gross 2001 XXXX	Chapel Hill F., UK Newhaven C., UK Baylam, UK	120	20	45	ModelMaker 4.0	124 36 64	432 191 449	0.998 0.997 0.997
	Chapel Hill F., UK Newhaven C., UK Baylam, UK	120	12	45	recalculation from 20°C result	235 68 121	819 362 852	- - -
Stephan & Ebert 2003 XXXX	Bruch West, FRG Li35b, FRG	119	20	40	ModelMaker 3.0.4 first order	122 115	407* 381*	0.95 0.98
	Bruch West, FRG Li35b, FRG	119	12	40	recalculation from 20°C result	231 218	772* 381*	- -
anaerobic degradation								
Richardson 1990/91 XXXX	Woodstock, UK	152	21	flooded	no significant degradation under anaerobic conditions			
Standen & Hill 1993 XXXX	Woodstock, UK	150	22	flooded				
soil photolysis								
Lewis & Gross 2001 XXXX	Newhaven C., UK	16	20	air dry	no significant degradation			

* value not reliable (too far extrapolated); MWC = maximum water holding capacity

Table 14 - Summary of degradation rates of "urea" metabolite (CL 932338) in laboratory soil studies

Study Reg.Doc.#	Soil	Study duration [days]	Temp. [°C]	Moisture [%MWC]	Estimation	DT50 [days]	DT90 [days]	r^2
aerobic degradation								
Stephan & Ebert 2003 XXXX	Bruch West, FRG	119	20	40	ModelMaker 3.0.4 first order	57	190	0.97
	Li35b, FRG					56	186	0.99
	Lufa 2.2, FRG					59	196	0.99
	Lufa 3A, FRG					47	156	0.99
	Bruch West, FRG	119	12	40	recalculation from 20°C result	108	360	-
	Li35b, FRG					106	353	-
	Lufa 2.2, FRG					112	372	-
	Lufa 3A, FRG					89	296	-

MWC = maximum water holding capacity

Table 15 - Adsorption data for [^{14}C]-Flufenoxuron on different soils

Soil	pH ($CaCl_2$)	K_d (ml/g)	K_{OC} (ml/g)
***Hill & Standen* 1993**			
Godstone	6.1	1738	289747
Elm Farm	6.5	3206	178093
Woodstock	6.1	4250	137104
***Rosenwald* 2002**			
Chelmorton	6.1	2756 ± 1282	95030 ± 44220
Kenslow Farm	5.7	3441 ± 1782	88240 ± 45700

Table 16- Adsorption data for ^{14}C-"urea" metabolite (CL 932338) on different soils

Soil	pH ($CaCl_2$)	K_F (ml/g)	1/n	K_{FOC} (ml/g)	K_d* (ml/g)	K_{OC}* (ml/g)
Borgeby	5.6	118.5	0.978	8467	145.2	10371
Birnbaum	6.1	37.52	0.922	4690	68.50	8563
2.2 F222002	6.3	101.7	0.918	3928	199.0	7681
Sora Bevern H9	6.5	63.09	0.895	3711	145.1	8536
Stetten	7.5	52.37	0.968	5237	67.56	6756

*determined at one concentration level (mean of two experiments). $K_d = C_{soil} / C_{water}$

Table 17 - Desorption data for ^{14}C-"urea" metabolite (CL 932338) on different soils

Soil	K_{FdesI} (ml/g)	1/n	$K_{FOCdesI}$ (ml/g)
Borgeby	134.8	0.951	9625
Birnbaum	42.71	0.882	5339
2.2 F222002	60.69	0.819	2343
Sora Bevern H9	129.3	0.935	7604
Stetten	33.19	0.853	3319

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
5.6	**EVALUATION BY RAPPORTEUR MEMBER STATE**
Date	May 2007 – September 2010
Materials and methods	
Conclusion	
Reliability	
Acceptability	For the corrected version of the summary by RMS, please refer to Document IIA – Section 4. Several corrections have been carried out in the document and underlined.
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

APPENDIX 2 RECALCULATION OF AQUATIC ENDPOINTS FOR THE FLUFENOXURON (BAS 307 I) ANNEX I, PT8 BIOCIDE DOSSIER

XXXX, January 20, 2006

XXXX

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INTRODUCTION

This document contains calculations on aquatic ecotoxicological data, which have been generated for the European registration of flufenoxuron (BAS 307 I) as a plant protection product. The evaluation of these studies and the accompanying risk assessment were therefore conducted according to the GUIDANCE DOCUMENT ON AQUATIC TOXICOLOGY (Sanco/3268/2001 rev.4, page 9), which advises for static tests to express endpoints on a nominal basis or based on initially measured concentrations. However, by request of INERIS, the Competent Authority (Rapporteur Member State France) the endpoints of these studies (*e.g.* LC_{50}, EC_{50} or NOECs) have been recalculated based on measured values, according to the recommendations of the relevant OECD guidelines.

DATA EVALUATION AND RECALCULATIONS

According to the OECD guidelines for fish, daphnid and algal studies, endpoints should be expressed based on mean-measured values. For *Chironomus* studies (XXXX), the OECD guidelines recommend to base the NOEC on the initial measured concentrations. The values are provided in Table 1.

A recalculation of the mesocosm study (XXXX) endpoint into mean-measured values is not appropriate for this type of study design. This is mainly related to the fact that in this long-lasting higher-tier study animals have no means to escape from exposure, and secondly, that recovery is to be assessed in a previously exposed community, which is critical in such a study to derive a no observed ecologically adverse effect concentration (NOEAEC).

The EC_{50} and LC_{50} values were determined with probit, logit and log-log models, after which the model with the lowest lack of fit was selected, since this describes the data best. The calculations were conducted on a PC using the commercial software package TOXSTAT, Version 3.5 (Western Ecosystems Technology, Inc., 2003 Central Avenue, Cheyenne, WY 82001, USA), which was previously validated against literature data. Toxstat can handle up to 10 treatment groups and for this reason some groups had to be excluded from analysis in the *Daphnia* studies XXXX and XXXX (see below). These groups were selected at the higher and lower end of the concentration-response curve, but only when multiple groups were available with 0% or 100% immobility, respectively. These exclusions have no influence on the outcome of the EC_{50} calculation. Full details of the calculations are provided at the end of this document.

TABLE 1. RECALCULATED ENDPOINTS FOR THE FLUFENOXURON BIOCIDE DOSSIER

Doc. III-A Section No.	**Study DocID**	**Endpoint**	**Old (µg/L)**	**New (µg/L)**
7.4.1.1. Rainbow trout acute	XXXX	LC_{50} (96 h)	2400	2096[1]
7.4.1.1. Rainbow trout acute	XXXX	LC_{50} (96 h)	460	462[2]
7.4.1.2. *Daphnia magna* acute	XXXX	EC_{50} (48 h)	0.09	0.083[3]
7.4.1.2. *Daphnia magna* acute	XXXX	EC_{50} (48 h)	6200	3361[4]
7.4.1.2. *Daphnia magna* acute	XXXX	EC_{50} (48 h)	5.9	5.45[5]
7.4.1.3. Algal growth	XXXX	E_bC_{50} (96 h) E_rC_{50} (96 h)	24 600 > 100 000	19 228[6] 71 940[6]
7.4.1.3. Algal growth	XXXX	EC_{50} (96 h)	> 4.0	> 2.975[7]
7.4.3.1. Fish early life stage	XXXX	NOEC (34 d)	≥ 0.82	≥ 0.82[8]
7.4.3.2. Fish full life cycle	XXXX	NOEC (148 d)	≥ 4.5	≥ 1.199[9]
7.4.3.4. *Daphnia magna* chronic	XXXX	NOEC (21 d)	0.010	0.0065[10]
7.4.3.4. Zooplankton experimental ponds	XXXX	$NOEC_{community}$ (63 d) NOEAEC (63 d)	0.030 - 0.040 -	- 0.13 - 0.16[11]
7.4.3.5.1. *Chironomus riparius*	XXXX	NOEC (28 d)	0.050	0.050[12]
7.4.3.5.1. *Chironomus riparius*	XXXX	NOEC (32 d)		79 µg/kg[12]
7.5.1.3. Terrestrial plants	XXXX	NOEC (15 d)		≥ 110 µg/kg[13]

[1] based on mean-measured concentrations, detailed calculation provided below.

[2] based on mean-measured concentrations, detailed calculation provided below.

[3] mean-measured values available for 4 concentrations. Other concentrations recalculated into mean-measured concentrations based on average recovery of the measured groups (73.6%). The highest treatment group was excluded from statistical analysis, since Toxstat can handle maximal 10 treatment groups. Detailed calculation provided below.

[4] based on mean-measured concentrations, detailed calculation provided below.

[5] mean-measured values available for the 8 highest concentrations, due to analytical limitations (values below LoQ). Lower concentrations recalculated into mean-measured concentrations based on an average recovery of the measured groups of about 90%. The 4 highest treatment groups and the lowest treatment group were excluded from statistical analysis, since Toxstat can handle maximal 10 treatment groups. Detailed calculation provided below.

[6] based on mean-measured concentrations, detailed calculation provided below.

[7] Limit test. Value based on a mean-measured concentrations.

[8] request for recalculation is a misunderstanding – the study endpoint is already based on mean-measured values.

[9] Value based on a mean-measured concentrations.

[10] Due to its chemical properties flufenoxuron will adsorb to surfaces in a glass-water-algae system. This was tested in a preliminary experiment and lossess of about 50% from the water phase were measured. The recalculation of the NOEC (nominal 10 ng a.s./L) is based on the mean-measured concentrations in the water phase: 3.25 ng a.s./L, and a removal of 50% through centrifugation and adsorption to glass, hence a NOEC of 6.5 ng a.s./L is achieved. It should be noted that the dosing of the semi-static system was correctly performed since a mean recovery of 81.2% was measured for the added amount. The calculated NOEC value fits very well to the observations of the distribution of flufenoxuron in a water-algae-glass system: 85% of nominal added, total recovery 76% (= flufenoxuron in algae, water and on glass), which would result in a NOEC of 6.46 ng a.s./L.

[11] alternative study code: XXXX. The $NOEC_{community}$ derived from this study is based on maximum mean concentrations recorded in the first 24 h after application. However, an aspect overlooked by the evaluation of this study is the recovery of the zooplankton populations by latest DAT 63. This information allows for the derivation of a no observed ecologically adverse effect concentration or NOEAEC, which may be directly compared with the PEC (*i.e.* assessment factor of 1) and can be used in combination with all other endpoints in establishing an ecologically acceptable concentration or EAC, which is comparable to the PNEC (GUIDANCE DOCUMENT ON AQUATIC TOXICOLOGY, page 30-32 and further).

[12] spiked water study; NOEC based on measured concentrations of the on t = 0 added amount.

[13] application rate of 80 g a.s./ha was recalculated into a soil concentration by using 5 cm soil depth, the batch analysis which yielded 103 g a.s./L (nominal 100 g a.s./L) and an average soil densitiy of 1.5 g/cm^3.

Title: FX-570-001 Salmo gairdneri LC50 mean measured 96 h
File: SG_AFP . Transform: LOG 10 DOSE

Log-Log Analysis - not Using Smoothed Proportions

DOSE	NUMBER SUBJECTS	NUMBER OBSERVED	OBSERVED PROPORTION	PREDICTED PROPORTION
Control	10	10	1.0000	0.9999
0.25 mg/L	10	10	1.0000	0.9991
0.37 mg/L	10	10	1.0000	0.9969
0.69 mg/L	10	9	0.9000	0.9786
1.58 mg/L	10	9	0.9000	0.7505
2.92 mg/L	10	1	0.1000	0.1424
5.05 mg/L	10	0	0.0000	0.0000
11.05 mg/L	10	0	0.0000	0.0000

Est. Mu = 0.3725 Est. Sigma = 0.1392
sd = 0.0475 sd = 0.0412

Chi-Square lack of fit = 4.3277 Likelihood lack of fit = 3.2595
Table Chi-square = 16.8119 (alpha = 0.01, df = 6)
Table Chi-square = 12.5916 (alpha = 0.05, df = 6)

Log-Log EC Estimates

POINT	UNADJUSTED EST. END POINT	95% CONFIDENCE LIMITS	
EC 1	0.5395 mg/L	0.2260	1.2878
EC 5	0.9098 mg/L	0.5090	1.6261
EC10	1.1459 mg/L	0.7242	1.8131
EC20	1.4576 mg/L	1.0359	2.0509
EC25	1.5813 mg/L	1.1643	2.1475
EC30	1.6941 mg/L	1.2818	2.2389
EC40	1.9008 mg/L	1.4931	2.4199
EC50	**2.0962 mg/L**	1.6808	2.6143
EC60	2.2924 mg/L	1.8511	2.8389
EC70	2.5021 mg/L	2.0100	3.1147
EC75	2.6178 mg/L	2.0880	3.2820
EC80	2.7461 mg/L	2.1675	3.4792
EC90	3.0802 mg/L	2.3468	4.0429
EC95	3.3514 mg/L	2.4712	4.5450
EC99	3.8467 mg/L	2.6677	5.5468

Title: FX-570-002 Salmo gairdneri LC50 mean measured 96 h
File: WL1258_S. Transform: LOG 10 DOSE
Probit Analysis - not Using Smoothed Proportions

DOSE	NUMBER SUBJECTS	NUMBER OBSERVED	OBSERVED PROPORTION	PREDICTED PROPORTION
Control	10	10	1.0000	1.0000
0.06 mg/L	10	10	1.0000	1.0000
0.11 mg/L	10	10	1.0000	1.0000
0.20 mg/L	10	10	1.0000	0.9999
0.35 mg/L	10	9	0.9000	0.9008
0.61 mg/L	10	1	0.1000	0.0985
0.95 mg/L	10	0	0.0000	0.0004
1.77 mg/L	10	0	0.0000	0.0000

Est. Mu = -0.3355 Est. Sigma = 0.0936
sd = 0.0357 sd = 0.0271

Chi-Square lack of fit = 0.0050 Likelihood lack of fit = 0.0096
Table Chi-square = 16.8119 (alpha = 0.01, df = 6)
Table Chi-square = 12.5916 (alpha = 0.05, df = 6)

Probit EC Estimates

POINT	UNADJUSTED EST. END POINT	95% CONFIDENCE LIMITS	
EC 1	0.2797 mg/L	0.2013	0.3885
EC 5	0.3240 mg/L	0.2499	0.4199
EC10	0.3504 mg/L	0.2794	0.4394
EC20	0.3852 mg/L	0.3178	0.4670
EC25	0.3994 mg/L	0.3328	0.4792
EC30	0.4125 mg/L	0.3465	0.4911
EC40	0.4373 mg/L	0.3709	0.5156
EC50	**0.4619 mg/L**	0.3931	0.5427
EC60	0.4878 mg/L	0.4141	0.5746
EC70	0.5172 mg/L	0.4352	0.6146
EC75	0.5342 mg/L	0.4462	0.6395
EC80	0.5538 mg/L	0.4580	0.6696
EC90	0.6089 mg/L	0.4872	0.7610
EC95	0.6585 mg/L	0.5099	0.8504
EC99	0.7627 mg/L	0.5514	1.0552

Title: FX-511-001 Daphnia magna EC50 mean measured 48 h
File: DAPH115 . Transform: LOG 10
DOSE

Log-Log Analysis - not Using Smoothed Proportions

DOSE	NUMBER SUBJECTS	NUMBER OBSERVED	OBSERVED PROPORTION	PREDICTED PROPORTION
Control	30	30	1.0000	0.9971
4.20 ng/L	30	30	1.0000	0.9913
7.36 ng/L	30	30	1.0000	0.9804
15.00 ng/L	30	28	0.9333	0.9451
37.00 ng/L	30	23	0.7667	0.8087
74.00 ng/L	30	16	0.5333	0.5557
147.00 ng/L	30	7	0.2333	0.2001
380.00 ng/L	30	0	0.0000	0.0015
740.00 ng/L	30	0	0.0000	0.0000
1470.00 ng/L	30	0	0.0000	0.0000

Est. Mu = 2.0266 Est. Sigma = 0.2959
sd = 0.0462 sd = 0.0396

Chi-Square lack of fit = 1.6875 Likelihood lack of fit = 2.6401
Table Chi-square = 20.0902 (alpha = 0.01, df = 8)
Table Chi-square = 15.5073 (alpha = 0.05, df = 8)

Log-Log EC Estimates

POINT	UNADJUSTED EST. END POINT	95% CONFIDENCE LIMITS	
EC 1	4.6301 ng/L	2.0787	10.3132
EC 5	14.0553 ng/L	8.3184	23.7489
EC10	22.9517 ng/L	15.2458	34.5523
EC20	38.2684 ng/L	28.3421	51.6713
EC25	45.4991 ng/L	34.7799	59.5221
EC30	52.6751 ng/L	41.2171	67.3182
EC40	67.2793 ng/L	54.2065	83.5048
EC50	**82.8294 ng/L**	67.5329	101.5905
EC60	100.1747 ng/L	81.5487	123.0550
EC70	120.6547 ng/L	96.9718	150.1215
EC75	132.8201 ng/L	105.6420	166.9901
EC80	147.0354 ng/L	115.3908	187.3582
EC90	187.6662 ng/L	141.5091	248.8786
EC95	224.5149 ng/L	163.5675	308.1721
EC99	300.9299 ng/L	206.0386	439.5234

Title: FX-570-001 Daphnia magna EC50 mean measured 48 h
File: DM_AFP . Transform: LOG 10
DOSE

Probit Analysis - not Using Smoothed Proportions

DOSE	NUMBER SUBJECTS	NUMBER OBSERVED	OBSERVED PROPORTION	PREDICTED PROPORTION
Control	20	20	1.0000	1.0000
0.31 mg/L	20	20	1.0000	1.0000
0.49 mg/L	20	20	1.0000	0.9995
1.06 mg/L	20	20	1.0000	0.9755
1.50 mg/L	20	17	0.8500	0.9156
3.11 mg/L	20	12	0.6000	0.5527
6.52 mg/L	20	3	0.1500	0.1292
11.57 mg/L	20	0	0.0000	0.0175

Est. Mu = 0.5265 Est. Sigma = 0.2546
sd = 0.0451 sd = 0.0391

Chi-Square lack of fit = 2.2427 Likelihood lack of fit = 2.8996
Table Chi-square = 16.8119 (alpha = 0.01, df = 6)
Table Chi-square = 12.5916 (alpha = 0.05, df = 6)

Probit EC Estimates

POINT	UNADJUSTED EST. END POINT	95% CONFIDENCE LIMITS	
EC 1	0.8595 mg/L	0.5527	1.3366
EC 5	1.2815 mg/L	0.9127	1.7995
EC10	1.5857 mg/L	1.1858	2.1205
EC20	2.0522 mg/L	1.6123	2.6123
EC25	2.2635 mg/L	1.8043	2.8395
EC30	2.4717 mg/L	1.9911	3.0683
EC40	2.8973 mg/L	2.3610	3.5555
EC50	**3.3612 mg/L**	2.7417	4.1207
EC60	3.8993 mg/L	3.1533	4.8218
EC70	4.5709 mg/L	3.6282	5.7584
EC75	4.9913 mg/L	3.9079	6.3749
EC80	5.5050 mg/L	4.2350	7.1560
EC90	7.1246 mg/L	5.1884	9.7833
EC95	8.8156 mg/L	6.0977	12.7449
EC99	13.1448 mg/L	8.1867	21.1055

Title: FX-570-002 Daphnia magna EC50 mean measured 48 h
File: WL2 . Transform: LOG 10
DOSE

Probit Analysis - not Using Smoothed Proportions

DOSE	NUMBER SUBJECTS	NUMBER OBSERVED	OBSERVED PROPORTION	PREDICTED PROPORTION
Control	20	20	1.0000	0.9999
0.03 µg/L	20	20	1.0000	0.9995
0.09 µg/L	20	20	1.0000	0.9946
0.27 µg/L	20	20	1.0000	0.9692
0.90 µg/L	20	17	0.8500	0.8686
2.70 µg/L	20	12	0.6000	0.6689
10.00 µg/L	20	6	0.3000	0.3529
25.00 µg/L	20	5	0.2500	0.1717
95.00 µg/L	20	1	0.0500	0.0377
250.00 µg/L	20	0	0.0000	0.0087

Est. Mu = 0.7364 Est. Sigma = 0.6983
sd = 0.0981 sd = 0.0914

Chi-Square lack of fit = 2.6098 Likelihood lack of fit = 3.4190
Table Chi-square = 20.0902 (alpha = 0.01, df = 8)
Table Chi-square = 15.5073 (alpha = 0.05, df = 8)

Probit EC Estimates

POINT	UNADJUSTED EST. END POINT	95% CONFIDENCE LIMITS	
EC 1	0.1294 µg/L	0.0446	0.3755
EC 5	0.3870 µg/L	0.1708	0.8772
EC10	0.6941 µg/L	0.3458	1.3936
EC20	1.4082 µg/L	0.7975	2.4865
EC25	1.8424 µg/L	1.0866	3.1239
EC30	2.3453 µg/L	1.4268	3.8550
EC40	3.6264 µg/L	2.2960	5.7278
EC50	**5.4501 µg/L**	3.5008	8.4848
EC60	8.1908 µg/L	5.2094	12.8785
EC70	12.6652 µg/L	7.7721	20.6391
EC75	16.1223 µg/L	9.6086	27.0516
EC80	21.0931 µg/L	12.0918	36.7951
EC90	42.7920 µg/L	21.6390	84.6226
EC95	76.7486 µg/L	34.4245	171.1093
EC99	229.6071 µg/L	80.5330	654.6316

Title: 2003/1004462 P. subcapitata biomass mean measured 96 h
File: PKS_B .TXT Transform: LOG 10 DOSE
Log-Log Analysis - not Using Smoothed Proportions

DOSE	NUMBER SUBJECTS	NUMBER OBSERVED	OBSERVED PROPORTION	PREDICTED PROPORTION
Control	1000	0	0.0000	0.0457
0.18 mg/L	1000	17	0.0170	0.0607
0.51 mg/L	1000	268	0.2680	0.1015
1.29 mg/L	1000	211	0.2110	0.1585
3.48 mg/L	1000	147	0.1470	0.2499
10.37 mg/L	1000	511	0.5110	0.3961
26.04 mg/L	1000	272	0.2720	0.5553
80.37 mg/L	1000	894	0.8940	0.7648

Est. Mu = 1.5932 Est. Sigma = 0.8437
sd = 0.0220 sd = 0.0203

Chi-Square lack of fit = 935.4301 Likelihood lack of fit = 935.7212
Table Chi-square = 16.8119 (alpha = 0.01, df = 6)
Table Chi-square = 12.5916 (alpha = 0.05, df = 6)

Log-Log LC Estimates

POINT	UNADJUSTED EST. END POINT	95% CONFIDENCE LIMITS	
LC 1	0.0052 mg/L	0.0035	0.0075
LC 5	0.1222 mg/L	0.0969	0.1541
LC10	0.4948 mg/L	0.4169	0.5874
LC20	2.1263 mg/L	1.8939	2.3872
LC25	3.4831 mg/L	3.1496	3.8520
LC30	5.2886 mg/L	4.8302	5.7906
LC40	10.6272 mg/L	9.7879	11.5384
LC50	**19.2282 mg/L**	17.6595	20.9362
LC60	33.0688 mg/L	30.0679	36.3692
LC70	56.2082 mg/L	50.3557	62.7409
LC75	73.9219 mg/L	65.6312	83.2599
LC80	98.7874 mg/L	86.8123	112.4145
LC90	198.1000 mg/L	169.4826	231.5495
LC95	330.3083 mg/L	276.7188	394.2760
LC99	761.5867 mg/L	615.6104	942.1775

Title: 2003/1004462 P. subcapitata growth rate mean-measured 96 h
File: PKS_GR .TXT Transform: LOG 10 DOSE

Log-Log Analysis - not Using Smoothed Proportions

DOSE	NUMBER SUBJECTS	NUMBER OBSERVED	OBSERVED PROPORTION	PREDICTED PROPORTION
Control	1000	0	0.0000	0.0013
0.18 mg/L	1000	2	0.0020	0.0022
0.51 mg/L	1000	55	0.0550	0.0061
1.29 mg/L	1000	38	0.0380	0.0147
3.48 mg/L	1000	5	0.0050	0.0374
10.37 mg/L	1000	111	0.1110	0.1029
26.04 mg/L	1000	36	0.0360	0.2305
80.37 mg/L	1000	659	0.6590	0.5373

Est. Mu = 2.0233 Est. Sigma = 0.4537
sd = 0.0218 sd = 0.0146

Chi-Square lack of fit = 739.9984 Likelihood lack of fit = 584.5179
Table Chi-square = 16.8119 (alpha = 0.01, df = 6)
Table Chi-square = 12.5916 (alpha = 0.05, df = 6)

Log-Log LC Estimates

POINT	UNADJUSTED EST. END POINT	95% CONFIDENCE LIMITS	
LC 1	0.8633 mg/L	0.6772	1.1004
LC 5	4.7388 mg/L	4.1060	5.4691
LC10	10.0521 mg/L	9.0551	11.1588
LC20	22.0154 mg/L	20.4239	23.7310
LC25	28.7069 mg/L	26.7575	30.7983
LC30	35.9351 mg/L	33.5295	38.5132
LC40	52.2987 mg/L	48.5768	56.3057
LC50	**71.9395 mg/L**	66.2140	78.1600
LC60	96.2924 mg/L	87.6293	105.8119
LC70	128.0781 mg/L	115.0514	142.5797
LC75	148.4057 mg/L	132.3508	166.4080
LC80	173.4467 mg/L	153.4574	196.0398
LC90	252.1499 mg/L	218.6655	290.7618
LC95	331.9355 mg/L	283.4746	388.6809
LC99	520.1662 mg/L	432.9055	625.0160

8 MEASURES NECESSARY TO PROTECT MAN, ANIMALS AND THE ENVIRONMENT

8.1 Recommended methods and precautions concerning handling, use storage, transport or fire

Wear personal protection according to the risk classification and the safety recommendations as given in annex point 10 when handling Flufenoxuron TC.

Store in original container, tightly closed in a dry and well-ventilated place. Avoid temperatures above 40 °C. Do not store with food or feeding-stuff. Keep out of reach of unauthorized persons.

On contact with eye: wash affected eyes immediately for at least 15 minutes under running water with eyelids held open, consult an eye specialist.

On ingestion: rinse mouth immediately and then drink plenty of water, get medical attention; but never induce vomiting or give anything by mouth if the victim is unconscious or having convulsions.

On skin contact: wash thoroughly with soap and water, seek medical attention.

If inhaled: keep patient calm, remove to fresh air and summon medical help.

In the case of combustion CO_2/CO, H_2O, N_2/NO_x, HF, fluorinated hydrocarbons and HCl will be generated.

Sprayed water, foam, CO_2, extinguishing powder or sand are suitable extinguishing media.
Fire fighters shall wear full protection including self-contained breathing apparatus. Fire fighting water is to be contained.

8.2 In case of fire, nature of reaction products, combustion gases, etc.

See 8.1

8.3 Emergency measures in case of an accident

See 8.4

8.4 Possibility of destruction or decontamination following release in or on the following: (a) air; (b) water, including drinking water and (c) soil

Unwanted amounts of flufenoxuron TC can be destroyed best by combustion in a licensed incinerator. Decontamination of equipment, packaging a.s.o. is achieved by washing with water plus detergent.

Possible procedures for the decontamination of water from Flufenoxuron
(Schenk W. 2001); BASF AG, Ludwigshafen/Rhein, Germany Fed.Rep.
unpublished; XXXX

Flufenoxuron is efficiently adsorbed onto activated carbon under neutral conditions.
In the case of spillage the contaminated solid is to be collected and incinerated.
In case of leakage or contamination of water, the aqueous phase is to be contained and to be treated for at least 6 hrs with activated carbon: 100 mg/l. The spent adsorbant is to be separated and incinerated. The treated water (pH 6.5-9) should be introduced slowly into a public sewer leading into a waste water treatment plant.

8.5 Procedures for waste management of the active substance for industry or professional users

Possibility of re-use or recycling: not applicable as not recommended

Possibility of neutralization of effects: see MSDS

Conditions for controlled discharge including leaching qualities on disposal: see MSDS

Conditions for controlled incineration : the halogen content of Flufenoxuron TC is below 60%. Approx. 1100 °C with a residence time of 2 seconds are advised as incineration temperature. Expected combustion products are CO_2/CO, H_2O, N_2/NO_x, HFand HCl.

Combustion in a licensed incinerator is the only disposal recommended, if flufenoxuron TC cannot be used according to its purpose, i.e. the production of insecticides.

8.6 Observations on undesirable or unintended side-effects

None currently reported incident or observations

Identification within the scope of list I or II of the Annex to Directive 80/68/EEC on the protection of ground water against pollution caused by certain dangerous substance

Not applicable

8.7 Identification of substances falling within the scope of list II of the Annex to Directive 80/68/EEC

None

9 CLASSIFICATION AND LABELLING

9.1 Classification proposal:

Indication of danger	dangerous to the (aquatic) environment
Risk phrase(s):	50, 53
Safety phrases(s)	02, 13, 20/21, 61

9.2 Labelling proposal:

Indication of danger	dangerous to the (aquatic) environment
Symbol	N
Risk phrase(s):	50, 53
Safety phrases(s)	02, 13, 20/21, 61

Based on toxicological and ecotoxicological investigations on the active substance.

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	03/04/2007
Materials and Methods	-
Results and discussion	-
Conclusion	According to the toxicological data, the following classification is proposed: Xn; R48 Repr. Cat.3; R63, R64 In view of the environmental classification, RMS also recommend the safety phrase S60.
Reliability	-
Acceptability	-
Remarks	-
	COMMENTS FROM ...

Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A10 **10 Summary and Evaluation of Sections 2 to 9**

BPD Annex Point IIA, IIIA, X

Official use only

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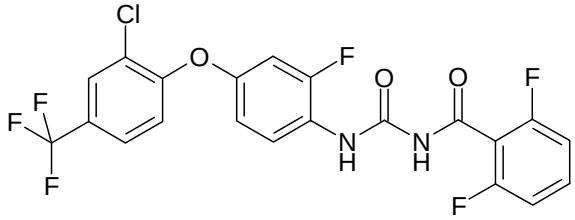
10.1 General substance information

10.1.1 Identification of the substance

CAS-No.	101463-69-8
EINECS-No.	Not available
Other No. (CIPAC, ELINCS	470
IUPAC Name	N-{4-[2-chloro-4-(trifluoromethyl)phenoxy]-2-fluorophenyl}-N'-(2,6-difluorobenzoyl)urea
Common name, synonyma	Flufenoxuron
Molecular formula	$C_{21}H_{11}Cl\ F_6N_2O_3$
Structural formula	
Molecular weight (g/mol)	488.8 g/mol

10.1.2 Purity/impurities, additives

	CAS-No.	Common name	Typical concentration or concentration range (% w/w)	Remarks
Purity of a.s.	95 % w/w			
Impurities	See Business Confidential Information			
Additives				

10.1.3 Physico-chemical properties

Flufenoxuron belongs to the chemical family of benzoylureas. The pure (PAI) and the technical grade (TGAI) active ingredient are white, crystalline solids, which melt at 169-172 °C under decomposition. The PAI and TGAI have a sourish to spicy odour. Flufenoxuron is poorly soluble in n-heptane (<0.001 mg/l) and in water (136 µg/l at pH 7) but of moderate to good solubility in some of the tested organic solvents, i.e. acetone (83 g/l) and ethyl acetate (55 g/l). Flufenoxuron has an octanol/water partition coefficient (log Pow) of 4.0.

Depending on pH and temperature, Flufenoxuron can be degraded to cleavage products in aqueous media. All three degradation products showed no to low potential to bioaccumulate and a low water solubility at 20 °C (3 – 11 mg/L).

10.2 Analytical methods for detection and identification

10.2.1 Analysis of active substance as manufactured

The content of Flufenoxuron in the technical (TC) is determined by dissolving the TC in THF and subsequent reversed phase HPLC using UV detection at 254 nm and external calibration.

No impurities of toxicological or ecotoxicological significance are present in Flufenoxuron.

Methods for impurities or by-products are based on HPLC with UV detection or high resolution GC procedure with internal standard calculation. This confidential information is included in Document BCI [Business Confidential Information].

10.2.2 Formulation analysis

See following documents prepared by *XXXX*

- Document IIB "Basiment Holzwurm, BV Konzentrat"
- Document IB "Basiment Holzwurm, BV U 1551"

10.2.3 Residue analysis

Methods for the determination of Flufenoxuron (the residue definition in soil, water, and air) and the Limit of Quantification (LOQ) in these matrices are summarised in Table IIA/1. Details are provided in Document IIIA 4.2.

Table 1 Summary of the methods for the determination of Flufenoxuron and limit of quantification in soil water and air

Matrix	**Method**	**LOQ**
Soil	HPLC-UV	0.01 mg/kg
Water	HPLC-MS/MS	0.01 µg/l
Air	LC-MS/MS	0.0001 µg/l
Plant or Product of animal origin	Not required as used as a wood preservative	
Animal fluid	Not required	

10.3 Classification and Labelling

10.3.1 Current classification

Classification according to Annex I of Council Directive 67/548/EEC is given hereafter.

Table 2 Current classification of a.s.

Classification	**as in Directive 67/548/EEC**
Class of danger	N
R phrases	R50, R53
S phrases	S02,S13, S20/21, S61

10.3.2 Proposed classification

See 1.5.1.

10.4 Effectiveness against target organisms

10.4.1 Function

Insecticides

10.4.2 Field of use envisaged

PT 8 – Wood preservatives

10.4.3 Effects on target organisms

It is a growth regulator that interferes in chitin production during cuticule development.

10.5 Human health effects assessment

10.5.1 Toxicokinetics, metabolism and distribution

After oral administration of ^{14}C-Flufenoxuron to male and female rats at dose levels of 3.5 mg/kg bw and 350 mg/kg bw the radioactivity was excreted with a half-life of ca. 200 – 400 h at the low dose level and 22 - 37 h at the high dose level. At the high dose level, excretion occurred mainly via feces (85% within 72 hours) while urinary excretion amounted to 0.5%. At the low dose level, excretion via feces amounted to 21 – 24 % of dose within 168 hours, urinary excretion accounted for 5 %. There were no significant sex-related differences regarding routes of excretion. Also, excretion patterns after single and multiple oral administration were similar.
In a bile-duct cannulation study in rats, small amounts of radioactivity (up to 20% in males, 7 % in females both at the low dose level of 3.5 mg/kg bw) were excreted via the bile. Based on the sum of urinary and biliary excretion as well as the amounts of radioactivity in carcass and organs, the bioavailability of Flufenoxuron was approximated to be 56 % (female) to 81 % (male).

After a 28-day treatment with ^{14}C-Flufenoxuron at 3.5 mg/kg bw an equilibrium concentration (plateau level) was close to being achieved for the majority of tissues. The radioactivity was well distributed throughout the carcass, with fat showing the highest concentrations of radioactivity (144 µg/g), and the lowest tissue residues were detected in the kidney (11 µg/g). Blood residues were 3 µg/g.
The fat residue was characterized as being unchanged ^{14}C-Flufenoxuron. The mean elimination half-life was 34 days, with liver having the highest half-life (48 days) and the carcass and fat the lowest (28 days).

After oral dosing, only small amounts of Flufenoxuron were metabolized in the rat. The metabolites found indicated that that the absorbed Flufenoxuron was metabolized by cleavage of the benzoyl urea linkage adjacent to the 2, 6-difluorobenzoyl moiety.

Metabolism and kinetic studies in male and female beagle dogs at dose levels of 3.5 mg/kg bw and 500 mg/kg bw indicated that kinetic and metabolic behavior of Flufenoxuron is comparable in dogs and rats.

10.5.2 Acute toxicity

The oral toxicity of Flufenoxuron in rats, tested in two studies using different vehicles, is low (LD_{50} above 5,000 mg/kg bw). No specific clinical symptoms were observed. In the acute oral toxicity study using DMSO as vehicle, unspecific symptoms were observed within the first two days after dose administration. One of 10 rats given 3,000 mg/kg bw Flufenoxuron suspended in DMSO died. No abnormalities were detected upon necroscopy examinations except for compacted powder in the stomach associated with mucosal hemorrhage in the rat that died. Taking both studies together, the overall LD_{50} is assessed to be above 5,000 mg/kg bw.

Flufenoxuron is of low toxicity to rats after dermal application, with an LD_{50} value above 2,000 mg/kg body weight causing neither mortality nor systemic toxicity. In addition, no local reaction was observed at the application site.

The inhalation toxicity (dust aerosol study) of Flufenoxuron in Sprague-Dawley rats is regarded to be low (LC_{50} > 5.1 mg/l/4h). No mortalities or other treatment-related adverse effects were observed in this study.

Results are summarized in Table 3.

10.5.3 Irritation and Corrosivity

Flufenoxuron is non-irritant in the skin irritation study in New Zealand White rabbits and is not irritating to the eye in the same rabbit strain according to EU classification criteria.

Results are summarized in Table 3.

10.5.4 Sensitisation

Flufenoxuron was not a skin sensitizer in the Guinea pig Magnusson & Kligman Maximisation Test.

Results are summarized in Table 3.

Table 3 Acute toxicity, irritancy and dermal sensitization of Flufenoxuron

Test facility / Reference	**Test substance Study type Species**	**Results**	**Comment**
XXXX	Flufenoxuron (in CMC) LD_{50} oral gavage Fischer 344 rat	> 5,000 mg/kg bw	No systemic toxicity
XXXX	Flufenoxuron (in DMSO) LD_{50} oral gavage Fischer 344 rat	> 3,000 mg/kg bw	1/10 rats administered 3,000 mg/kg bw died; unspecific clinical signs reversible within 2 days
XXXX	Flufenoxuron LD_{50} dermal Fischer 344 rat	> 2,000 mg/kg bw	No systemic toxicity, no local irritation
XXXX	Flufenoxuron LC_{50} 4-hour nose-only inhalation Albino (Sprague-Dawley) rat	> 5.1 mg/l (dust aerosol; MMAD 3.6 µm)	No systemic toxicity, no local irritation
XXXX	Flufenoxuron Primary skin irritation New Zealand White rabbit	Not a skin irritant	–
XXXX	Flufenoxuron Primary eye irritation New Zealand White rabbit	Not an eye irritant	–
XXXX	Flufenoxuron Skin sensitization (GPMT) Guinea pig	Not a skin sensitizer	Intradermal induction: 1% in corn oil Dermal induction: 50% in petroleum jelly Dermal challenge: 50% in petroleum jelly

10.5.5 Repeated dose toxicity

Short-term oral feed studies were conducted in rats, mice, and dogs.

28-day dietary exposure of Fischer 344 rats and $B6C3F_1$ mice to Flufenoxuron resulted in no adverse treatment-related effects, supporting NOAELs of 50,000 ppm, the highest concentration tested (equivalent to 5,147 mg/kg bw/d for the rat and 9,820 mg/kg bw/d for the mouse), for the respective studies.

A 90-day feeding study in Fischer 344 rats showed slight anemia in females, as evidenced by changes in erythrocyte parameters in association with evidence of compensatory hematopoiesis (increased reticulocyte counts, decreases in myeloid:erythroid ratios). Increases in spleen weights of females at 5,000 ppm and higher dietary concentrations were considered to be related to the hematological effects of flufenoxuron. No signs of anemia were seen in males, although evidence of compensatory hematopoiesis (decreased myeloid:erythroid ratio) was observed at the highest dose level of 50,000 ppm. This study supported a NOAEL of 50 ppm (equivalent to 3.5 mg/kg bw/d in males and 4.1

mg/kg bw/d in females), based on hematological changes in females at the LOAEL of 500 ppm (equivalent to 35 mg/kg bw/d in males and 41 mg/kg bw/d in females).

A mild anemia, as evidenced by decreases in erythrocyte parameters and increases in serum bilirubin, was also noted in the 90-day feeding study in $B6C3F_1$ mice. This 90-day dietary study in mice supported a NOAEL of 50 ppm (equivalent to 10.3 mg/kg bw/d).

Flufenoxuron-related anemia was also apparent in the 15-wk feeding study in Beagle dogs, as revealed by changes in erythrocyte parameters (first noted after 9 weeks of treatment), increased reticulocyte counts, bone marrow hyperplasia, increased hemosiderin deposition in bone marrow, in the Kupffer cells of the liver in the proximal tubules of the kidney, and in the spleen. Methemoglobin levels were elevated in males and females at all concentrations tested ($\geq$ 500 ppm). Furthermore, sulfhemoglobin levels were increased at 5,000 and 50,000 ppm in both sexes. Although a NOAEL could not be determined for this study, the available hematological data from the 90-day time point in the one-year dog study support a NOAEL for subchronic (90-day) treatment of 100 ppm (equivalent to 3.7 and 3.8 mg/kg bw/d in males and females, respectively, as calculated from body weight and food consumption data from the first 13 weeks of the 52-week study).

Findings similar to those observed in the 90-day dog study were also apparent in the 52-week dietary toxicity study conducted in Beagle dogs. The one-year feeding study in Beagle dogs supported a NOAEL of 100 ppm (equivalent to 3.5 mg/kg bw/d in males and 3.8 mg/kg bw/d in females), based on hematological and histopathological changes in both sexes at 500 ppm. These effects were indicative of a mild anemia and compensatory hematopoiesis. Histopathological changes that were related to the anemia were bone marrow hyperplasia and pigment deposition in the spleen, liver and kidney. Methemoglobinemia was increased over control levels at 50,000 ppm in both sexes at most time points of investigation and to a minimal degree also in females at 500 ppm. In addition to hematological findings, effects on the liver were observed. Increased liver weights were seen in males at and above a dietary concentration of 500 ppm and in females at 50,000 ppm. At the highest concentration of 50,000 ppm, this increase in liver weights was accompanied by increased incidences of hepatocellular fatty vacuolation.

In conclusion, the main effect exerted by Flufenoxuron in short-term toxicity study with rats, mice and dogs is anemia, which is characterised by decreases in red blood cell parameters with compensatory hematopoiesis and hemosiderin/pigment deposition in bone marrow, liver, kidney and spleen. In addition to anemia, dogs showed methemoglobinemia at and above 500 ppm and displayed slight effects on the liver at higher dose levels (increased liver weights and fatty vacuolation of hepatocytes). The results of short-term toxicity studies are summarised in Table 4 below:

Table 4 Summary of short-term toxicity studies

Test facility / Reference	**Study period/ test substance administration / Species**	**Dose levels**	**Results**	**NOAEL**
XXXX	28-d oral feed Fischer 344 rat	0; 50; 500; 5,000; 10,000 and 50,000 ppm	No adverse effects.	50,000 ppm Males **= 5,147 mg/kg bw/d** Females = 5,432 mg/kg bw/d
XXXX	28-d oral feed range-finding	0; 50; 500; 5,000; 10,000	No adverse effects.	50,000 ppm

Table 4 Summary of short-term toxicity studies

	$B6C3F_1$ mouse	and 50,000 ppm		Males **= 9,820 mg/kg bw/d** Females = 12,157 mg/kg bw/d
XXXX XXXX XXXX	90-d oral feed Fischer 344 rat	0; 50; 500; 5,000; 10,000 and 50,000 ppm	**≧ 500 ppm:** Females: altered RBC parameters indicative of mild anemia with evidence of compensatory erythropoiesis; slightly increased cholesterol (no dose-dependence) **≧ 5,000 ppm:** Females: increased spleen wt. **50,000 ppm:** Males: evidence of mild compensatory erythropoiesis without signs of anemia; marginally increased ALAT and ASAT levels	50 ppm Males **= 3.5 mg/kg bw/d** Females = 4.1 mg/kg bw/d
XXXX	90-d oral feed $B6C3F_1$ mouse	0; 50; 500; 5,000; 10,000 and 50,000 ppm	**≧ 500 ppm:** Both sexes: increased serum bilirubin; **≧ 10,000 ppm:** Females: decreased blood urea nitrogen	50 ppm Males **= 10.3 mg/kg bw/d** Females = 11.7 mg/kg bw/d
XXXX			**50,000 ppm:** Males: slightly decreased bw; altered RBC parameters indicative of mild anemia Both sexes: decreased blood urea nitrogen	
XXXX	15-wk oral feed Beagle dog	0; 500; 5,000; 50,000 ppm	**≧ 500 ppm:** both sexes: transient signs of anemia (wk 9), evidence of compensatory hematopoeisis females: increased methemoglobin and Kupffer cell pigmentation	< 500 ppm Males **< 18 mg/kg bw/d** Females < 21 mg/kg bw/d

Table 4 Summary of short-term toxicity studies

XXXX			≥ **5,000 ppm:** both sexes: slightly increased cholesterol; Kupffer cell pigmentation males: increased liver wt. females: Pigment deposition in bone marrow	
XXXX			**50,000 ppm:** both sexes: pigment deposition in bone marrow and spleen males: persistent signs of anemia; pigment deposition in renal proximal tubules	
XXXX	52-wk oral feed Beagle dog	0; 10; 100; 500; 50,000 ppm	≥ **500 ppm:** both sexes: evidence of anemia with compensatory hematopoeisis and increased methemoglobin; hemosiderin deposition in Kupffer cells of the liver males: increased platelets; increased liver wt. females: pigment deposition in bone marrow and renal proximal tubular cells **50,000 ppm:** both sexes: increased liver wt., fatty vacuolation of hepatocytes; pigment deposition in bone marrow, renal proximal tubular cells and spleen.	100 ppm Males **= 3.5 mg/kg bw/d** Females = 3.7 mg/kg bw/d (13-wk data: 100 ppm Males **= 3.7 mg/kg bw/d** Females = 3.8 mg/kg bw/d)

The effects of chronic administration of Flufenoxuron were investigated in mice and rats. The results are summarized in Table 4.

The chronic toxicity and oncogenicity of Flufenoxuron was investigated in two separate rat studies. In a 24 month chronic toxicity study administration of Flufenoxuron to Fischer 344 rats at dietary dose levels of 0; 1; 5; 50; 500; 5,000 and 50,000 ppm resulted in decreased body weight gain and slightly higher food consumption in males and females at ≥ 5,000 ppm. A slight anemia characterized by lower red blood cell counts, hemoglobin concentrations, hematocrit and slightly increased reticulocyte counts was observed at the two highest dose levels. Macro- and micropathological changes at higher dose levels were largely related to a general reduction of age-related pathology. There were no adverse treatment-related histopathological changes. There were no treatment-related increases in the incidence of any neoplastic lesion for males or females.

In the oncogenicity study Flufenoxuron was administered to Fischer 344 rats at dietary dose levels of 0; 500; 5,000 and 50,000 ppm and resulted in increased survival of treated groups. This was especially obvious at 50,000 ppm with 57% and 35% higher survival than in control males and females, respectively. The higher survival rate was thought to be due to the slightly to moderately lower body weights of rats at the high dose level. The few statistically significant organ weight changes were not accompanied by any treatment-related histopathological findings. These changes were therefore of questionable toxicological relevance. No treatment-related effects on the incidence of non-neoplastic lesions was observed in treated males or females.
There was no evidence for an oncogenic effect of Flufenoxuron in rats at dose levels up to 50,000 ppm. On the contrary, there was a significant decrease of multiple primary benign tumors in males and females and of malignant primary tumors in males at 50,000 ppm.

In absence of any treatment-related changes in the incidence of neoplastic findings, the NOEL for oncogenicity was 50,000 ppm, the highest concentration tested, which is equivalent to a mean daily dose of about 2,290 mg/kg bw in males and 2,900 mg/kg bw in females. The NOAEL for systemic toxicity in this study was 500 ppm (21.57 mg/kg in males and 25.91 mg/kg in females) based mainly on body weight effects observed at 5,000 ppm.

The oncogenic effect of Flufenoxuron in mice was investigated in two separate studies employing B3C6F1 mice. In the first study, dietary administration of Flufenoxuron to mice at dose levels of 0; 500; 5,000 and 50,000 ppm resulted in impaired body weight development at 50,000 ppm. The liver, stomach and spleen were identified as target organs. The livers of top dose mice displayed higher absolute and relative weights as well as an increased incidence of single cell necrosis, hepatocellular hypertrophy and aggregation of Kupffer cells. The incidence of the latter finding was also increased in mid dose females. Like in the liver, an aggregation of Kupffer cells was observed in the spleen of high dose males and females. An increased incidence of inflammation was observed in the glandular stomach of high dose males.

The combined incidence of benign and malignant hepatocellular tumors was comparable between treated and control groups. An increased incidence of hepatocellular carcinoma was observed in all treated male groups and in low dose females. This increase of hepatocellular carcinoma was paralleled by a decrease of hepatocellular adenoma. The incidence of hepatocellular carcinoma in treated groups was within the US National Toxicology Program (NTP) historical control range for this type of tumor whereas the incidence in control males was below the historical control range. The apparent increase in the incidence of hepatocellular carcinoma in treated male mice is therefore considered to be associated with the unusually low incidence of these tumors recorded in the control males and is not considered to be directly related to treatment. This view is supported by the results of the second carcinogenicity study in B6C3F1 mice which was conducted some years later [see below]. In this study the incidence of hepatocellular adenoma and carcinoma as well as the combined incidence of hepatocellular tumors was comparable between controls and treated groups.

For female mice at 50,000 ppm, the incidence of vascular tumors was statistically significantly increased. This increase reflected an increase in the incidence of hemangiosarcomas in the spleen. At lower treatment levels of Flufenoxuron (5,000 ppm or less), no differences in the incidence of vascular tumors were observed among females. The 50,000 ppm treatment level, which is about 7.5-fold higher than the limit dose (7,000 ppm), elicited both excessive hepatocellular toxicity and body weight depression and exceeded the maximum tolerated dose for Flufenoxuron. Thus, the vascular tumors observed in the female mouse at 50,000 ppm should not be considered significant for human risk assessment. In male mice, no statistically significant increased incidence of vascular tumors was observed at any treatment level.

Based on the histopathological findings in the liver (Kupffer cell aggregation) as well as the effects on body weight in female mice at 5,000 ppm, the NOAEL for systemic toxicity was 500 ppm. This is equivalent to a mean daily dose of 56 mg/kg bw in males and 73 mg/kg bw in females. Due to the equivocal nature of the oncogenicity results no NOAEL for oncogenic activity is proposed for this study.

In the second mouse oncogenicity study administration of Flufenoxuron at dietary dose levels up to 10,000 ppm for up to 2 years did not result in any adverse findings. This second mouse oncogenicity study in B3C6F1 mice did not reveal any carcinogenic potential of Flufenoxuron at dose levels well exceeding the limit dose of 1,000 mg/kg bw/day. The incidence of hepatocellular adenoma and carcinoma in male rats was comparable to the control incidence. The overall incidence of hepatocellular tumors was well within the historical control range and thus indicate that the increased incidence of hepatocellular carcinoma in all treated male groups observed in the first study was purely incidental. Likewise, in the second oncogenicity study there was no increase in the number of splenic vascular tumors in female mice at the high dose level of 10,000 ppm (1,890 mg/kg bw/day). The increased incidence of vascular tumors in the first mouse oncogenicity was probably due to the exaggerated dose (7,780 mg/kg bw/day) and thus is not considered relevant for human risk assessment. As a conclusion Flufenoxuron is considered to be devoid of a relevant oncogenic potential.

Table 5 Summary of long-term toxicity and carcinogenicity studies

Test facility / Reference	**Study period/ test substance administration / Species**	**Dose levels**	**Results**	**NOAEL**
XXXX	Chronic toxicity study in rats (Fisher 344)	0; 1; 5 ; 50; 500; 5,000; 50,000 ppm	**≥ 5,000 ppm**: impairment of body weight development, slight anemia, decreased spleen weights (without corroborative histopathology) **50,000 ppm**: changes of bilirubin, calcium and triglyceride levels. No treatment-related effects on tumor incidence	NOAEL systemic toxicity: 500 ppm (equivalent to 22.0 mg/kg bw/day in males and 28.3 mg/kg bw/day in females)
XXXX	Carcinogenicity study in rats (Fisher 344)	0; 500; 5,000; 50,000 ppm	**≥ 5,000 ppm**: higher survival rate; impairment of body weight development; marginal increase of food consumption; decreased spleen weights in males, increased adrenal weights in females (both without corroborative histopathology findings)	NOAEL systemic toxicity: 500 ppm (equivalent to 21.6 mg/kg bw/day in males and 25.9 mg/kg bw/day in females) NOAEL oncogenicity: 50,000 ppm (equivalent to 2,290 mg/kg bw/day in males and 2,900 mg/kg bw/day in females).

Table 5 Summary of long-term toxicity and carcinogenicity studies

Test facility / Reference	**Study period/ test substance administration / Species**	**Dose levels**	**Results**	**NOAEL**
XXXX	Oncogenicity study in mice (B6C3F1)	0; 500; 5,000; 50,000 ppm	**≥ 5,000 ppm**: Kupffer cell aggregates in the liver **50,000 ppm**: impaired body weight development; single cell necrosis, hepatocellular hypertrophy and inflammation of the liver; Kupffer cell aggregates in the spleen; inflammation of the glandular stomach in males; increased incidence of hepatocellular carcinoma in treated males (overall incidence of hepatocellular tumors not affected, absence of a dose-response relationship); increased incidence of vascular tumors in high dose females	NOAEL systemic toxicity: 500 ppm (equivalent to 56 mg/kg bw/day in males and 73 mg/kg bw/day in females).
XXXX	Oncogenicity study in mice (B6C3F1)	0; 100; 1,000; 10,000 ppm	no adverse effects	NOAEL systemic toxicity 10,000 ppm (equivalent to 1,592 mg/kg bw/day in males and 1,890 mg/kg bw/day in females) NOAEL oncogenicity 10,000 ppm (equivalent to 1,592 mg/kg bw/day in males and 1,890 mg/kg bw/day in females)

10.5.6 Genotoxicity

Flufenoxuron was tested in an extensive battery of in vitro and in vivo assays measuring several different endpoints of potential genotoxicity such as gene mutation, chromosomal aberration and DNA damage/repair. Results from mutagenicity studies indicated that Flufenoxuron did not induce base pair substitution or frame-shift mutation in any of the bacterial tester strains, or gene mutation in mammalian cells in culture. A positive response was noted in the chromosomal aberration test with CHO cells in the presence of an exogenous metabolic activation system (S-9 mix). This response was not expressed in the absence of S-9 mix. Moreover, the positive response with S-9 mix was totally

abolished by conducting a similar test with CHO cells in the presence of physiological concentrations of glutathione, a peptide naturally present in mammalian tissues. It has been reported in the literature that S-9 metabolic activation, utilized to increase the detection of potential positive effects, often does not contain adequate cofactors for activating detoxifying mechanisms that are present in the whole animal system [see Ashby, J.: "The Unique Role of Rodents in the Detection of Possible Human Carcinogens and Mutagens", Mutation Res. 115, 117-123, (1983); Galloway, S. M.: "Chromosome Aberrations Induced In Vitro: Mechanisms, Delayed Expression, and Intriguing Questions", Environ. Mol. Mutagen. 23/24, 44-53 (1994)].

No potential for clastogenicity was observed in two other in vitro chromosomal aberration assays using either rat liver cells or human lymphocytes. Importantly, Flufenoxuron did not induce chromosomal damage in vivo in the rat bone marrow chromosomal aberration assay or the mouse micronucleus assay. Furthermore, Flufenoxuron also did not induce unscheduled DNA synthesis in rat hepatocytes following in vivo administration.

In conclusion, using an overall weight-of-evidence approach, the negative results (non-clastogenicity) – observed in vitro in rat liver epitheloid cells and in human peripheral lymphocytes, as well as in vivo in the rat bone marrow chromosomal aberration assay and the mouse micronucleus assay – should override the positive response noted in the in vitro chromosomal aberration assay in CHO cells. Hence, the available data on Flufenoxuron does not suggest genotoxic concern.

Table 6 Summary of genotoxicity studies

Institute / Reference	Study/strains/species	Test conditions	Results
XXXX Brooks T. M, Wiggins D. E.; 1986]	Bacterial mutation assay S. typhimurium TA98, TA100, TA1535, TA1537, TA1538; E. coli WP2 uvrA pKM101	Without S–9 mix With S–9 mix	Negative Negative
XXXX Clare M. G., Wiggins D. E.; 1986]	In vitro mammalian cell HGPRT gene mutation test Chinese hamster V79 cells	Without S–9 mix With S–9 mix	Negative Negative
XXXX Meyer A. L.; 1987] [XXXX Meyer A. L; 1991(b)]	In vitro chromosome aberration assay CHO cells	Without S–9 mix With S–9 mix	Negative Positive
XXXX Meyer A. L.; 1988(a)] [XXXX; Meyer A. L.; 1991(a)]	In vitro chromosome aberration assay with glutathione (GSH) CHO cell	With S–9 mix but without GSH supplement With S–9 mix and GSH supplement	Positive Negative
XXXX); Meyer A. L.; 1988(b)] [XXXX); Meyer A. L.; 1991(c)]	In vitro chromosome aberration assay Rat liver epitheloid cell line (RL4)	Without S–9 mix With S–9 mix	Negative Negative
XXXX); McEnaney S. 1992]	In vitro chromosome aberration assay Peripheral human lymphocytes	Without S–9 mix With S–9 mix	Negative Negative
XXXX); Brooks T. M., Wiggins D. E.; 1986]	In vitro Saccharomyces Gene Conversion Assay Yeast S. cerevisiae JD1	Without S–9 mix With S–9 mix	Negative Negative
XXXX	In vivo Chromosome Aberration Assay Bone marrow cells from male and female Sprague-Dawley rats	4,000 mg/kg bw	Negative
XXXX	In vivo Micronucleus Assay Polychromatic erythrocytes obtained from ICR male mice	500; 1,000; 2,000 mg/kg bw/d, 2 days	Negative
XXXX	In vivo / in vitro UDS Assay Primary hepatocytes prepared from orally gavaged male F344 rats	188; 375; 750 and 1,500 mg/kg bw	Negative

10.5.7 Carcinogenicity

See 3.5

10.5.8 Reproductive toxicity

The data on reproductive and developmental toxicity studies on Flufenoxuron are summarized in Table 7.

The effects of Flufenoxuron on reproductive parameters were investigated in a 2-generation study in rats employing 2 matings per generation. In this study Flufenoxuron was fed to five groups of Sprague-Dawley rats at dietary concentrations of 0; 50; 190; 710 or 10,000 ppm throughout the entire study. The F_1 parental generation was selected from F_{1b} offspring. Treatment resulted in a decreased parental and pup body weight gain at dose levels ≥ 190 ppm as well as minor, but statistically significant changes of absolute or terminal body weight adjusted organ weights in parental and offspring rats. A remarkable feature of the above findings was that in most cases a clear dose-response of the effects was missing.
The ability to induce and maintain gestation as well as the ability to give birth to offspring was not affected by treatment. During lactation an increased incidence of full litter losses was observed at dose levels ≥ 710 ppm. In addition an increase of post cull pup losses was noted at ≥ 190 ppm. The latter was evident by a statistically significant decrease of litter size at 10,000 ppm. A slightly low lactation index was noted at 190 and 710 ppm whereas a more pronounced effect on the lactation index was observed at 10,000 ppm. No effects on pre- and post-weaning development of parental F1b rats were observed.

Based on the results of this study the NOAEL for systemic effects was 50 ppm for both parental animals and offspring. This is equivalent to a mean daily dose of 4.3 mg/kg bw. The NOAEL for fertility was at least 10,000 ppm (≈ 875 mg/kg bw/day). The reproductive performance NOAEL for males was likewise 10,000 ppm. Based on the effects on pup survival the NOAEL for female reproductive performance was 50 ppm (4.3 mg/kg bw/day). The developmental NOAEL was determined to be 50 ppm (4.3 mg/kg bw/day).

In a preliminary study to the cross fostering study, a group of 15 (presumably) pregnant Sprague-Dawley rats was administered Flufenoxuron at a dietary level of 20,000 ppm from day 3 of gestation until weaning. The life birth index (no. live pups/no. pups born x 100), the viability index (pups alive day 4/pups alive at birth x 100) and the lactation index (pups alive day 21/pups alive day 4 x 100) were 98.2, 98.2 and 98.8%, respectively and thus not considered to be affected by treatment.

In a cross-fostering study a group of 50 females was administered Flufenoxuron at a dietary level of 20,000 ppm during a 10 week pre-mating period, during mating and subsequent gestation. During lactation previously treated dams received control diet in order to avoid a direct exposure of the offspring. A control group of 50 females was likewise mated after a 10 week pre-mating period. As soon as possible after parturition, the young were counted, individually identified, sexed, weighed and examined for external abnormalities. Thereafter, the litters were culled to a standard litter size of 8 pups consisting - wherever possible - of 4 male and 4 female pups. A reciprocal cross-fostering of 26 litters was performed between control and treated dams, i.e. control dams (CD) reared treated pups (TP) from treated dams (TD) and vice versa.
Treatment at a dietary level of 20,000 ppm resulted in a slight impairment of maternal body weight development. No effects on fertility were observed. The survival of control pups reared by treated dams and of 'treated' pups reared by control dams was essentially identical. The determination of Flufenoxuron levels in fat and milk revealed a rapid decrease upon cessation of treatment. The depletion half-life time was 7.6 and 2.3 days in fat and milk, respectively.

Neither the administration of Flufenoxuron during gestation and lactation alone nor the administration of Flufenoxuron starting 10 weeks prior to mating and continuing till parturition was sufficient to reproduce the adverse effects on pup survival observed in the 2-generation study. These findings

indicate that a continued exposure to Flufenoxuron is required to result in reduced pup survival. The results of the cross-fostering study indicate that the adverse effects on pup survival are not due to in-utero exposure.

Administration of Flufenoxuron by oral gavage during gestational days 6 to 15 did not cause any adverse effects in pregnant rats at dose levels up to 1,000 mg/kg bw/day. Neither embryo- or developmental toxicity nor teratogenicity was observed up to the highest dose tested. Accordingly, the maternal and developmental NOAELs for Flufenoxuron in the rat are 1,000 mg/kg bw/day (highest dose tested), which corresponds to the limit dose for this type of mammalian toxicity study.

Administration of Flufenoxuron to New Zealand White rabbits at dose levels of 0; 10; 100 and 1,000 mg/kg bw by oral gavage during gestational days 6 to 18 did not result in any maternal toxicity up to the highest dose tested. The slight effects on fetal weights (non significant decrease by 7% when compared to the control) were probably due to a slightly higher mean litter size at the high dose level. Secondary to the slightly lower fetal weights, delays of fetal ossification were observed at the high dose level. These observations are not considered to be of adverse nature.
Accordingly, the maternal NOEL was 1,000 mg/kg bw/day and the developmental NOAEL was 1,000 mg/kg bw/day.

Table 7 Summary of reproductive toxicity studies

Test facility / Reference	**Study period/ test substance administration/ Species**	**Dose levels**	**Results**	**NOAEL**
XXXX	2-Generation study in Sprague-Dawley rats; 2 litters per generation	0; 50; 190; 710 and 10,000 ppm	Parental generations **> 190 ppm:** F_1 males: decreased body weight gain (bwg) during premating and entire study duration; F_0 and F_1 females: decreased bwg during premating period (no dose-dependency) changes of mainly relative organ weights of brain, liver, kidney **10,000 ppm:** F_1 females: decreased bwg for lactational days 0 - 14 increased abs. adrenal weights No effects on fertility, gestation and parturition parameters Litter data **> 190 ppm:** lower body weights at day 21; not always statistically significant or strictly dose dependent, altered relative organ weights of brain, heart, liver and kidney; only effect in livers was consistently observed in all generations increased post cull pup losses as indicated by decreased lactation indices **> 710 ppm:** increased number of total litter losses (pre- and post cull) **> 10,000 ppm:** decreased mean litter size from day 8 onwards	Parental systemic toxicity: 50 ppm = 4.3 mg/kg bw/day Parental fertility and reproductive performance in males: 10,000 ppm = 875 mg/kg bw/day Reproductive performance in females: 50 ppm = 4.3 mg/kg bw/day Developmental toxicity: 50 ppm = 4.3 mg/kg bw/day
XXXX	Investigative Study in Sprague-Dawley rats	20,000 ppm	No effects on live-birth, viability or lactation indices	A determination of a meaningful NOAEL not possible
XXXX	Cross-fostering study in Sprague-Dawley rats	0; 20,000 ppm	**20,000 ppm:** slightly lower body weight gain no effects on fertility, ability to deliver and rear offspring	A determination of a meaningful NOAEL not possible
XXXX	Developmental toxicity in Sprague-Dawley rats	0; 10; 100; 1,000 mg/kg bw/ day	No adverse effects observed	Maternal toxicity: 1,000 mg/kg bw/day Developmental toxicity: 1,000 mg/kg bw/day

Table 7 Summary of reproductive toxicity studies

Test facility / Reference	**Study period/ test substance administration/ Species**	**Dose levels**	**Results**	**NOAEL**
XXXX	Developmental toxicity in New Zealand White rabbits	0; 10; 100; 1,000 mg/kg bw/ day	No adverse effects observed	Maternal toxicity: NOEL: 1,000 mg/kg bw/day Developmental toxicity: NOAEL: 1,000 mg/kg bw/day

10.5.9 Neurotoxicity

The potential neurotoxicity of Flufenoxuron was assessed in a 28-day oral feed neurotoxicity study in Wistar rats. Only weak indications of general toxicity were obtained at dose levels of 5,000 ppm and 20,000 ppm, whereas no signs of neurotoxicity were detected at any dose level. Thus, under the conditions of the present study the no observed adverse effect level (NOAEL) for neurotoxicity was 20,000 ppm in both sexes (1,775 mg/kg bw/d in males and 1,934 mg/kg bw/d in females).

Table 8 Summary of neurotoxicity studies with Flufenoxuron

Test facility **Reference**	**Study type** **Species/strain, route** **Dose levels**	**Findings**	**NOAEL (neurotoxicity):**
XXXX	28-d neurotoxicity, Wistar rat, oral feed 0–1,000–5,000–20,000 ppm	≧ 5,000 ppm: Reduced bw / bw gain (males only) No evidence of neurotoxicity at any dose level	20,000 ppm <u>Males</u> = 1,775 mg/kg bw/d <u>Females</u> = 1,934 mg/kg bw/d

10.5.10 Additional Toxicity Data

Toxicity of Flufenoxuron degradates

Reg. No. 4064702 is formed in soil via microbial Flufenoxuron degradation. The oral LD_{50} in CD-1 mice was found to be 433 mg/kg bw for males and 302 mg/kg bw for females. There was no evidence of mutagenicity in the Ames test for Reg. No. 4064702.

Table 9 Summary of studies conducted with Reg. No. 4064702

Study type Species	Reg. No.	Result	Reference Test facility
Acute oral toxicity, rat	4064702	LD_{50} = 433 mg/kg bw (m) = 302 mg/kg bw (f)	XXXX
Ames test	4064702	No evidence of mutagenicity with or without S9-mix	XXXX

XXXX

Reg. No. 241208 [4-(2-chloro-α, α, α,-trifluoro-p-toluyloxy)-2-fluoroaniline] has been identified at trace amounts (< 1% of administered dose) in excreta of dog and rats following Flufenoxuron treatment. Reg. No. 241208 may be formed via alkaline hydrolysis at high temperatures. Studies were conducted with Reg. No. 241208 or with its hydrochloric acid salt, **Reg. No. 4064703**.

The oral LD_{50} for males and females combined was found to be 2,372 mg/kg bw in mice (Reg. No. 241208) and 612 mg/kg bw in rats (Reg. No. 4064703). Cyanosis and pale skin were effects typically seen in the treated animals.

In a 28-day study, rats were administered Reg. No. 4064703 as a corn oil suspension at dose levels of 10; 30 or 100 mg/kg bw via oral gavage (treatment at 300 and 500 mg/kg bw/d was discontinued after 1 week to overt toxicity). Rats given 100 mg/kg bw/d were cyanotic throughout the study. No treatment-related clinical signs were observed at 10 or 30 mg/kg bw/d. Body weight and food intake were transiently reduced during week 1 at 30 and 100 mg/kg bw/d. Evidence of hemolytic anemia (reduced red blood cells, hemoglobin concentration, hematocrit, increased reticulocytes and normoblasts, increased bilirubin) was seen in females at all dose levels and in males at and above 30 mg/kg bw/d. Increased spleen weights, and splenic hemosiderosis and erythropoiesis were associated with the hematological findings. A dose-related increase in medullary mineralisation (very slight/slight) was established in kidneys of males at 10 and in females at 30 mg/kg bw/d. Effects on the liver were indicated by increased alkaline phosphatase activities at and above 30 mg/kg bw/d, decreased cholesterol in males at ≥ 10 mg/kg bw/d and slightly increased albumin and total serum protein at 100 mg/kg bw/d. Liver weights were marginally increased in females at the low dose level, and moderately increased at 30 and 100 mg/kg bw/d. Histopathology of the liver revealed an increased incidence of centrilobular hypertrophy and acidophilia (very slight/slight) in high-dose group males. A NOAEL could not be established in this study based on decreased erythrocyte parameters in females, increased female liver and spleen weights, increased hemosiderosis and erythropoiesis in the spleen of both sexes and increased medullary mineralisation of the kidney in males found at 10 mg/kg bw/d, the lowest dose tested.

In genotoxicity studies, both Reg. No. 241208 and Reg. No. 4064703 proved to be weak indirect acting mutagens when tested in the bacterial mutagenicity test using strains TA 98 and TA 100. No evidence of clastogenicity were established in two in-vitro cytogenicity tests with CHO cells. Furthermore, in an in-vivo micronucleus test, oral treatment of mice at up to 750 mg/kg bw showed that Reg. No. 4064703 has no chromosome-damaging (clastogenic) effect.

Table 10 Summary of studies conducted with Reg. No. 241208 and Reg. No. 4064703

Study type Species	Reg. No.	Result	Reference Test facility
Acute oral toxicity, mouse	241208	LD_{50} = 1,937 mg/kg bw (m) = 2,898 mg/kg bw (f) = 2,372 mg/kg bw (m&f)	XXXX
Acute oral toxicity, rat	4064703	LD_{50} = 667 mg/kg bw (m) = 621 mg/kg bw (f) = 621 mg/kg bw (m&f)	XXXX
Acute dermal toxicity, rat	4064703	LD_{50} = 2,000 mg/kg bw	XXXX
28-day oral gavage, rat	4064703	NOAEL: < 10 mg/kg bw/d Anemia with methemoglobinemia, liver and kidney toxicity	XXXX
Ames test	241208	No evidence of mutagenicity without S9-mix, weak mutagen with S9-mix in strains TA 98 and TA 100	XXXX
Ames test	4064703	No evidence of mutagenicity without S9-mix, weak mutagen with S9-mix in strains TA 98 and TA 100	XXXX
In-vitro cytogenicity in CHO cells	241208	Negative with and without S9-mix	XXXX
In-vitro cytogenicity in CHO cells	4064703	Negative with and without S9-mix	XXXX
In-vivo micronucleus test, mouse	4064703	Negative	XXXX

XXXX

Supplemental data

For assessment of methemoglobinemia induction by Flufenoxuron, it was found that apparently false-positive results are produced if the (indirect) CO-Oximeter method is used for detection of methemoglobin. The generation of false-positive findings is avoided by use of a specific methemoglobin detection method developed by Evelyn and Malloy.

In a pilot study, the binding of Flufenoxuron and Reg. No. 4064703 to hemoglobin were assessed in female rats. The formation of hemoglobin adducts was investigated 24 hours after single oral gavage treatment of female rats with either 3 mmol/kg bw Flufenoxuron or 0.3 mg/kg bw Reg. No. 4064703 (hydrochloric acid salt of Reg. No. 241208). It was found that the extent of Hb adducts formed depends on the formation of Reg. No. 241208. As expected, following treatment of rats with Flufenoxuron only little Hb binding was found as evidenced by a very low hemoglobin binding index (ratio of Hb adduct formation to administered dose) of about 0.00055. This is most probably due to the minimal formation of Reg. No. 241208 (based on rat metabolism data available for Flufenoxuron). In rats orally dosed with 0.3 mmol Reg. No. 4064703/kg bw, Hb adducts with Reg. No. 241208 were readily formed.

Flufenoxuron was tested in the in vivo replicative DNA synthesis (RDS) assay to assess its potential hepatocarcinogenic promoter activity. Groups of rats were killed up to 48 hours after single gavage administration of Flufenoxuron at 2,000 or 4,000 mg/kg bw. Hepatocytes prepared from the treated animals were exposed to radiolabelled thymidine for 4 hours. The percentage of nuclei in replicative

DNA synthesis (% RDS) was subsequently determined. The RDS incidence by test compound was found to be less than 1% in all groups. Thus, no induction of RDS was observed at 2,000 and 4,000 mg/kg bw, indicating a lack of hepatocarcinogenic promoter activity.

Table 11 Summary of supplemental information

Study type Species	Test substance	Result	Reference Test facility
Method for hemoglobin detection	Flufenoxuron	An alternative specific method for detection of methemoglobin is presented.	XXXX
Hemoglobin-binding pilot study, Rat	Flufenoxuron Reg. No. 4064703 Reg. No. 241208	Adduct of formation of Reg. No. 241208 to hemoglobin is observed after oral treatment of rats with Reg. No. 4064703. Hemoglobin adducts are formed to only a minimal degree following Flufenoxuron treatment at high dose levels.	XXXX
In-vivo replicative DNA synthesis (RDS) study, rats	Flufenoxuron	No evidence of RDS induction in hepatocytes of rats administered up to 4,000 mg/kg bw Flufenoxuron via single oral gavage	XXXX

10.5.11 Summary of mammalian toxicity and overall evaluation

Flufenoxuron is characterized by a low acute oral, dermal and inhalation toxicity in rats. It is not irritating to the skin and the eyes of rabbits and has no sensitizing effect to the skin of Guinea pigs when tested according to the method of Magnusson & Kligman.

Short-term oral feed studies were conducted in rats, mice, and dogs.

28-day dietary exposure of Fischer 344 rats and B6C3F_1 mice to Flufenoxuron resulted in no adverse treatment-related effects, supporting NOAELs of 50,000 ppm, the highest concentration tested (equivalent to 5,147 mg/kg bw/d for the rat and 9,820 mg/kg bw/d for the mouse), for the respective studies.

A 90-day feeding study in Fischer 344 rats showed slight anemia in females, as evidenced by changes in erythrocyte parameters in association with evidence of compensatory hematopoiesis (increased reticulocyte counts, decreases in myeloid:erythroid ratios). Increases in spleen weights of females at 5,000 ppm and higher dietary concentrations were considered to be related to the hematological effects of Flufenoxuron. No signs of anemia were seen in males, although evidence of compensatory hematopoiesis (decreased myeloid:erythroid ratio) was observed at the highest dose level of 50,000 ppm. This study supported a NOAEL of 50 ppm (equivalent to 3.5 mg/kg bw/d in males and 4.1 mg/kg bw/d in females), based on hematological changes in females at the LOAEL of 500 ppm (equivalent to 35 mg/kg bw/d in males and 41 mg/kg bw/d in females).

A mild anemia, as evidenced by decreases in erythrocyte parameters and increases in serum bilirubin, was also noted in the 90-day feeding study in B6C3F_1 mice. This 90-day dietary study in mice supported a NOAEL of 50 ppm (equivalent to 10.3 mg/kg bw/d).

Flufenoxuron-related anemia was also apparent in the 15-wk feeding study in Beagle dogs, as revealed by changes in erythrocyte parameters (first noted after 9 weeks of treatment), increased reticulocyte counts, bone marrow hyperplasia, increased hemosiderin deposition in bone marrow, in the Kupffer cells of the liver, in the proximal tubules of the kidney, and in the spleen. Methemoglobin levels were elevated in males and females at all concentrations tested (≥ 500 ppm). Furthermore, sulfhemoglobin levels were increased at 5,000 and 50,000 ppm in both sexes. Although a NOAEL could not be determined for this study, the available hematological data from the 90-day time point in the one-year dog study support a NOAEL for subchronic (90-day) treatment of 100 ppm (equivalent to 3.7 and 3.8 mg/kg bw/d in males and females, respectively, as calculated from body weight and food consumption data from the first 13 weeks of the 52-week study).

Findings similar to those observed in the 90-day dog study were also apparent in the 52-week dietary toxicity study conducted in Beagle dogs. The one-year feeding study in Beagle dogs supported a NOAEL of 100 ppm (equivalent to 3.5 mg/kg bw/d in males and 3.8 mg/kg bw/d in females), based on hematological and histopathological changes in both sexes at 500 ppm. These effects were indicative of a mild anemia and compensatory hematopoiesis. Histopathological changes that were related to the anemia were bone marrow hyperplasia and pigment deposition in the spleen, liver and kidney. Methemoglobinemia was increased over control levels at 50,000 ppm in both sexes at most time points of investigation and to a minimal degree also in females at 500 ppm. In addition to hematological findings, effects on the liver were observed. Increased liver weights were seen in males at and above a dietary concentration of 500 ppm and in females at 50,000 ppm. At the highest concentration of 50,000 ppm, this increase in liver weights was accompanied by increased incidences of hepatocellular fatty vacuolation.

In conclusion, the main effect exerted by Flufenoxuron in short-term toxicity study with rats, mice and dogs is anemia, which is characterised by decreases in red blood cell parameters with compensatory hematopoiesis and hemosiderin/pigment deposition in bone marrow, liver, kidney and spleen. In addition to anemia, dogs showed methemoglobinemia at and above 500 ppm and displayed slight effects on the liver at higher dose levels (increased liver weights and fatty vacuolation of hepatocytes). The NOAEL's of short-term toxicity studies are summarised in Table 12 below:

Table 12 NOAELs from short-term toxicity studies in different species (mg/kg bw/d)

Species	Study type Dose levels tested (NOAEL; LOAEL)	NOAEL (mg/kg bw/d)		LOAEL (mg/kg bw/d)	
		Males	Females	Males	Females
Rat	oral diet – 4 weeks 0–50–500–5,000–10,000–**50,000** ppm	5,147	5,432	–	–
	oral diet – 13 weeks 0–**50**–500–5,000–10,000–50,000 ppm	3.5	4.1	35	41
Mouse	oral diet – 4 weeks 0–50–500–5,000–10,000–**50,000** ppm	9,820	12,157	–	–
	oral diet – 13 weeks 0–**50**–500–5,000–10,000–50,000 ppm	10	12	103	124
Dog	oral diet – 15 weeks 0–500–5,000–50,000 ppm	< 18	< 21	18	21
	oral diet – 52 weeks, –13-wk interim hematology – 0–10–**100**–500–50,000 ppm	3.7	3.8	19	20
	– 52-wk overall assessment – 0–10–**100**–500–50,000 ppm	3.5	3.8	19	19

Flufenoxuron was tested in an extensive battery of *in vitro* and *in vivo* assays measuring several different endpoints of potential genotoxicity such as gene mutation, chromosomal aberration and DNA damage/repair. Results from mutagenicity studies indicated that Flufenoxuron did not induce base pair substitution or frame-shift mutation in any of the bacterial tester strains, or gene mutation in mammalian cells in culture (HGPRT test in V79 cells).

A positive response was noted in the chromosomal aberration test with CHO cells in the presence of an exogenous metabolic activation system (S-9 mix). This response was not expressed in the absence of S-9 mix. Moreover, the positive response with S-9 mix was totally abolished by conducting a similar test with CHO cells in the presence of physiological concentrations of glutathione, a peptide naturally present in mammalian tissues. No potential for clastogenicity was observed in two other *in vitro* chromosomal aberration assays using either rat liver cells or human lymphocytes. Importantly, Flufenoxuron did not induce chromosomal damage *in vivo* in the rat bone marrow chromosomal aberration assay or the mouse micronucleus assay. Finally, Flufenoxuron also did not induce unscheduled DNA synthesis in rat hepatocytes following *in vivo* administration.

In conclusion, using an overall weight-of-evidence approach, the negative results (non-clastogenicity) – observed *in vitro* in rat liver epitheloid cells and in human peripheral lymphocytes, as well as *in vivo* in the rat bone marrow chromosomal aberration assay and the mouse micronucleus assay – should override the positive response noted in the *in vitro* chromosomal aberration assay in CHO cells. Hence, the available data on Flufenoxuron does not suggest genotoxic concern.

The chronic toxicity and oncogenicity of Flufenoxuron was investigated in two separate rat studies. In the 24 month chronic toxicity study the administration of Flufenoxuron to Fischer 344 rats at dietary dose levels of 0; 1; 5; 50; 500; 5,000 and 50,000 ppm resulted in decreased body weight gain and slightly higher food consumption in males and females at ≥ 5,000 ppm. A slight anemia characterized by lower red blood cell counts, hemoglobin concentrations, hematocrit and slightly increased reticulocyte counts was observed at the two highest dose levels. Macro- and micropathological changes at higher dose levels were largely related to a general reduction of age-related pathology. There were no treatment-related adverse histopathological changes. The incidence of neoplastic lesion

was comparable between treated and control groups thus indicating the absence of an oncogenic effect in rats.

Based on the effects on body weight development as well as on hematology parameters the NOAEL for chronic toxicity was 500 ppm, which is equivalent to a mean daily dose of 22.0 mg/kg bw in males and 28.3 mg/kg bw in females.

In the oncogenicity study Flufenoxuron was administered to Fischer 344 rats at dietary dose levels of 0; 500; 5,000 and 50,000 ppm and resulted in increased survival of treated groups. This was especially obvious at 50,000 ppm with 57% and 35% higher survival than in control males and females, respectively. The higher survival rate was thought to be due to the slightly to moderately lower body weights of rats at the high dose level. The few statistically significant organ weight changes were not accompanied by any treatment-related histopathological findings. These changes were therefore of questionable toxicological relevance. No treatment-related effects on the incidence of non-neoplastic lesions was observed in treated males or females.
There was no evidence for an oncogenic effect of Flufenoxuron in rats at dose levels up to 50,000 ppm. On the contrary, there was a significant decrease of multiple primary benign tumors in males and females and of malignant primary tumors in males at 50,000 ppm.

In absence of any treatment-related changes in the incidence of neoplastic findings, the NOEL for oncogenicity was 50,000 ppm, the highest concentration tested, which is equivalent to a mean daily dose of about 2,290 mg/kg bw in males and 2,900 mg/kg bw in females. The NOAEL for systemic toxicity in this study was 500 ppm (21.6 mg/kg in males and 25.9 mg/kg in females) based mainly on body weight effects observed at 5,000 ppm.

The oncogenic potential of Flufenoxuron in mice was investigated in two separate studies employing B3C6F1 mice. In the first study, dietary administration of Flufenoxuron to mice at dose levels of 0; 500; 5,000 and 50,000 ppm resulted in impaired body weight development at 50,000 ppm. The liver, stomach and spleen were identified as target organs. The livers of top dose mice displayed higher absolute and relative weights as well as an increased incidence of single cell necrosis, hepatocellular hypertrophy and aggregation of Kupffer cells. The incidence of the latter finding was also increased in mid dose females. Like in the liver, an aggregation of Kupffer cells was observed in the spleen of high dose males and females. An increased incidence of inflammation was observed in the glandular stomach of high dose males.

The combined incidence of benign and malignant hepatocellular tumors was comparable between treated and control groups. An increased incidence of hepatocellular carcinoma was observed in all treated male groups and in low dose females. This increase of hepatocellular carcinoma was paralleled by a decrease of hepatocellular adenoma. The incidence of hepatocellular carcinoma in treated groups was within the US National Toxicology Program (NTP) historical control range for this type of tumor whereas the incidence in control males was below the historical control range. The apparent increase in the incidence of hepatocellular carcinoma in treated male mice is therefore considered to be associated with the unusually low incidence of these tumors recorded in the control males and is not considered to be directly related to treatment. This view is supported by the results of the second carcinogenicity study in B6C3F1 mice which was conducted some years later [see below]. In this second study the incidence of hepatocellular adenoma and carcinoma as well as the combined incidence of hepatocellular tumors was comparable between controls and treated groups.
For female mice at 50,000 ppm, the incidence of vascular tumors was statistically significantly increased. This increase reflected an increase in the incidence of hemangiosarcomas in the spleen. At lower treatment levels of Flufenoxuron (5,000 ppm or less), no differences in the incidence of vascular tumors were observed among females. The 50,000 ppm treatment level, which is about 7.5-fold higher than the limit dose (7,000 ppm), elicited both excessive hepatocellular toxicity and body weight

depression and exceeded the maximum tolerated dose for Flufenoxuron. Thus, the vascular tumors observed in the female mouse at 50,000 ppm should not be considered significant for human risk assessment. In male mice, no statistically significant increased incidence of vascular tumors was observed at any treatment level.

Based on the histopathological findings in the liver (Kupffer cell aggregation) as well as the effects on body weight in female mice at 5,000 ppm, the NOAEL for systemic toxicity was 500 ppm. This is equivalent to a mean daily dose of 56 mg/kg bw in males and 73 mg/kg bw in females. Due to the equivocal nature of the oncogenicity results no NOAEL for oncogenic activity is proposed for this study.

In the second mouse oncogenicity study, administration of Flufenoxuron at dietary dose levels up to 10,000 ppm for 2 years did not result in any adverse findings. This second mouse oncogenicity study in B3C6F1 mice did not reveal any carcinogenic potential of Flufenoxuron at dose levels well exceeding the limit dose of 1,000 mg/kg bw/day. The incidence of hepatocellular adenoma and carcinoma in male rats was comparable to the control incidence. The overall incidence of hepatocellular tumors was well within the historical control range and thus indicate that the increased incidence of hepatocellular carcinoma in all treated male groups observed in the first study was purely incidental. Likewise, in the second oncogenicity study there was no increase in the number of spleenic vascular tumors in female mice at the high dose level of 10,000 ppm (1,890 mg/kg bw/day). The increased incidence of vascular tumors in the first mouse oncogenicity was probably due to the exaggerated dose (7,780 mg/kg bw/day) and thus is not considered relevant for human risk assessment. As a conclusion Flufenoxuron is considered to be devoid of a relevant oncogenic potential.

The NOAEL's of long-term toxicity studies are summarised in Table 13 below:

Table 13 NOAELs from long-term / carcinogenicity studies in rat and mice (mg/kg bw/d)

Species	**Study type** **Dose levels tested (NOAEL; LOAEL)**	**NOAEL (mg/kg bw/d)**		**LOAEL (mg/kg bw/d)**	
		Males	**Females**	**Males**	**Females**
Rat	oral diet – 104 weeks, chronic toxicity study 0-1-5-50-**500**-5,000-50,000 ppm	22	28	233	301
	oral diet – 104 weeks, carcinogenicity study 0–**500**–5,000–50,000 ppm	22	26	218	276
Mouse	oral diet – 104 weeks, carcinogenicity study 0–**500**–5,000–50,000 ppm	56	73	559	739
	oral diet – 104 weeks, carcinogenicity study 0–100–1,000–**10,000** ppm	1,592	1,890	-	-

The effects of Flufenoxuron on reproductive parameters were investigated in a rat 2-generation study employing 2 matings per generation. In this study Flufenoxuron was fed to five groups of rats at dietary concentrations of 0; 50; 190; 710 or 10,000 ppm. Treatment resulted in a decreased parental and pup body weight gain at dose levels ≥ 190 ppm as well as minor, but statistically significant

changes of absolute or terminal body weight adjusted organ weights. A remarkable feature of the above findings was that in most cases a clear dose-response of the effects was missing.
The ability to induce pregnancy, to maintain gestation as well as the ability to give birth to offspring was not affected by treatment. A dose dependent decrease in the ability to rear offspring was observed at dose levels ≥ 190 ppm. This was indicated by an increased cumulative incidence of full litter losses at 710 and 10,000 ppm, by an increase of post cull pup losses at ≥ 190 ppm as well as by a significant decrease of litter sizes at 10,000 ppm. No effects on pre- and post-weaning development of parental F1(b) rats were observed.

In a preliminary study to a cross fostering study, a group of 15 (presumably) pregnant Crl: CD® (SD) BR VAF/Plus Sprague Dawley rats was administered Flufenoxuron at a dietary level of 20,000 ppm from day 3 of gestation until weaning. The life birth (no. live pups/no. pups born x 100), the viability (pups alive day 4/pups alive at birth x 100) and the lactation (pups alive day 21/pups alive day 4 x 100) indices were 98.2, 98.2 and 98.8%, respectively and thus not considered to be affected by treatment.

In a cross fostering study a group of 50 females was administered Flufenoxuron at a dietary level of 20,000 ppm during a 10 week pre-mating period, during mating and subsequent gestation. During lactation previously treated dams received control diet in order to avoid a direct exposure of the offspring. A control group of 50 females was likewise mated after a 10 week pre-mating period. As soon as possible after parturition, the young were counted, individually identified, sexed, weighed and examined for external abnormalities. Thereafter, the litters were culled to a standard litter size of 8 pups consisting - wherever possible - of 4 male and 4 female pups. A reciprocal cross-fostering of 26 litters was performed between control and treated dams, i.e. control dams (CD) reared treated pups (TP) from treated dams (TD) and vice versa.
Treatment at a dietary level of 20,000 ppm resulted in a slight impairment of maternal body weight development. No effects on fertility were observed. The survival of control pups reared by treated dams and of 'treated' pups reared by control dams was identical. The determination of Flufenoxuron levels in fat and milk revealed a rapid decrease upon cessation of treatment. The depletion half-life time was 7.6 and 2.3 days in fat and milk respectively.

Neither the administration of Flufenoxuron during gestation and lactation alone nor the administration of Flufenoxuron starting 10 week prior to mating and continuing till parturition was sufficient to reproduce the adverse effects on pup survival observed in the 2-generation study. These findings indicate that a continued exposure to Flufenoxuron is required to result in reduced pup survival. The results of the cross-fostering study indicate that the adverse effects on pup survival are not due to in-utero exposure.

Administration of Flufenoxuron by oral gavage during gestational days 6 to 15 did not cause any adverse effects in pregnant rats at dose levels up to 1,000 mg/kg bw/day. Neither embryo- or developmental toxicity nor teratogenicity was observed up to the highest dose tested. Accordingly, the maternal and developmental NOAELs for Flufenoxuron in the rat are 1,000 mg/kg bw/day (highest dose tested), which corresponds to the limit dose for this type of mammalian toxicity study.

Administration of Flufenoxuron to New Zealand White rabbits at dose levels of 0; 10; 100 and 1,000 mg/kg bw by oral gavage during gestational days 6 to 18 did not result in any maternal toxicity up to the highest dose tested. The slight effects on fetal weights (non significant decrease by 7% when compared to the control) were probably due to a slightly higher mean litter size at the high dose level. Secondary to the slightly lower fetal weights, delays of fetal ossification were observed at the high dose level. These observations are not considered to be of adverse nature.
Accordingly, the maternal NOEL was 1,000 mg/kg bw/day and the developmental NOAEL was 1,000 mg/kg bw/day.

Table 14 NOAELs from reproduction and developmental toxicity studies in rat and rabbits (mg/kg bw/d)

Species	**Study type** **Dose levels tested (NOAEL; LOAEL)**	**Parental/maternal toxicity**		**Reproductive/ developmental toxicity**	
		NOAEL mg/kg bw/d	**LOAEL** mg/kg bw/d	**NOAEL** mg/kg bw/d	**LOAEL** mg/kg bw/d
Rat	oral diet – 2-generation study 0-**50**-190-710-10,000 ppm	4.3	16.3	4.3	16.3
	oral gavage - prenatal developmental toxicity 0-10-100-**1,000** mg/kg bw/d	1,000	-	1,000	-
Rabbit	oral gavage - prenatal developmental toxicity 0-10-100-**1,000** mg/kg bw/d	1,000		1,000	

The potential neurotoxicity of Flufenoxuron was assessed in a 28-day oral feed neurotoxicity study in Wistar rats. Only weak indications of general toxicity were obtained at dose levels of 5,000 ppm and 20,000 ppm, whereas no signs of neurotoxicity were detected at any dose level. Thus, under the conditions of the present study the no observed adverse effect level (NOAEL) for neurotoxicity was 20,000 ppm in both sexes (1,775 mg/kg bw/d in males and 1,934 mg/kg bw/d in females).

Reg. No. 4064702 is formed in soil via microbial Flufenoxuron degradation. The oral LD_{50} in CD-1 mice was found to be 433 mg/kg bw for males and 302 mg/kg bw for females. There was no evidence of mutagenicity in the Ames test for Reg. No. 4064702.

Reg. No. 241208 [4-(2-chloro-α, α, α,-trifluoro-*p*-toluyloxy)-2-fluoroaniline] has been identified at trace amounts (< 1% of administered dose) in excreta of dog and rats following Flufenoxuron treatment. Studies were conducted with Reg. No. 241208 or with its hydrochloric acid salt (Reg. No. 4064703). The oral LD_{50} for males and females combined was found to be 2,372 mg/kg bw in mice (Reg. No. 241208) and 612 mg/kg bw in rats (Reg. No. 4064703). Cyanosis and pale skin were effects typically seen in the treated animals.

In a 28-day study, rats were administered Reg. No. 4064703 as a corn oil suspension at dose levels of 10; 30 or 100 mg/kg bw via oral gavage (treatment at 300 and 500 mg/kg bw/d was discontinued after 1 week due to overt toxicity and mortality). Rats given 100 mg/kg bw/d were cyanotic throughout the study. No treatment-related clinical signs were observed at 10 or 30 mg/kg bw/d. Body weight and food intake were transiently reduced during week 1 at 30 and 100 mg/kg bw/d. Evidence of hemolytic anemia (reduced red blood cells, hemoglobin concentration, hematocrit, increased reticulocytes and normoblasts, increased bilirubin) was seen in females at all dose levels and in males at and above 30 mg/kg bw/d. Increased spleen weights, and splenic hemosiderosis and erythropoiesis were associated with the hematological findings. A dose-related increase in medullary mineralisation (very slight/slight) was established in kidneys of males at 10 and in females at 30 mg/kg bw/d. Effects on the liver were indicated by increased alkaline phosphatase activities at and above 30 mg/kg bw/d, decreased cholesterol in males at ≥ 10 mg/kg bw/d and slightly increased albumin and total serum protein at 100 mg/kg bw/d. Liver weights were marginally increased in females at the low dose level,

and moderately increased at 30 and 100 mg/kg bw/d. Histopathology of the liver revealed an increased incidence of centrilobular hypertrophy and acidophilia (very slight/slight) in high-dose group males. A NOAEL could not be established in this study based on decreased erythrocyte parameters in females, increased female liver and spleen weights, increased hemosiderosis and erythropoiesis in the spleen of both sexes and increased medullary mineralisation of the kidney in males found at 10 mg/kg bw/d, the lowest dose tested.

In genotoxicity studies, both Reg. No. 241208 and Reg. No. 4064703 proved to be weak indirect acting mutagens when tested in the bacterial mutagenicity test using strains TA 98 and TA 100. No evidence of clastogenicity were established in two in-vitro cytogenicity tests with CHO cells. Furthermore, in an in-vivo micronucleus test, oral treatment of mice at up to 750 mg/kg bw showed that Reg. No. 4064703 has no chromosome-damaging (clastogenic) effect.
In a pilot study, the extent of Reg. No. 241208 binding to hemoglobin was determined following oral treatment of rats with either Flufenoxuron at approx 1,446 mg/kg bw or with Reg. No. 4064703 (= Reg. No. 241208 hydrochloric acid salt, 91.68 mg/kg bw). Only minimal binding of Reg. No. 241208 to hemoglobin was detectable after Flufenoxuron treatment, confirming that Flufenoxuron is hardly metabolised to Reg. No. 241208. Following treatment of rats with Reg. No. 4064703, a high level of Reg. No. 241208-hemoglobin adducts were formed, indicating that Reg. No. 241208 readily binds to hemoglobin.

Impact of Reg. No. 241208's toxicity on risk assessment of Flufenoxuron

Operators and consumers are potentially exposed to Reg. No. 241208 indirectly via exposure to Flufenoxuron, as evidenced by trace amounts of Reg. No. 241208 identified in excreta of rats and dogs administered Flufenoxuron. No other routes of exposure to Reg. No. 241208 are anticipated, based on the available data on the environmental fate and, on plant and animal residues of Flufenoxuron.

Critical endpoints of Reg. No. 241208's toxicity to consider in the hazard assessment of Flufenoxuron are the assumed mutagenicity and the hematological effects of Reg. No. 241208. Reg. No. 241208 can be considered to have been co-tested in all toxicological studies with Flufenoxuron, since it was identified as a minor metabolite of Flufenoxuron in both rat and dog metabolism studies (< 1% in rat and dog excreta).

The results of the genotoxicity studies with Flufenoxuron show that Flufenoxuron is neither mutagenic nor genotoxic. Furthermore, Flufenoxuron was tested at dose levels of up to 50,000 ppm in rats and mice in long-term carcinogenicity studies. No evidence of carcinogenicity was found in these studies. Thus, the weak mutagenic activity of Reg. No.241208 had no impact on genotoxicity or carcinogenicity potential of Flufenoxuron even when administered at extremely high feed concentrations of 50,000 ppm.

No adverse hematological findings were seen after 28-day dietary administration of Flufenoxuron when tested up to 50,000 ppm in rats and mice. After subchronic or chronic administration of Flufenoxuron, signs of anemia were seen in rats, mice and dogs and methemoglobinemia was additionally observed in dogs. Clear NOAEL's for Flufenoxuron's hematotoxicity were established for all species in these studies. Thus, even if Reg. No. 241208 contributed to the hematotoxicity that was observed in Flufenoxuron studies, the NOAEL's established for these studies already take account of the co-exposure to Reg. No. 241208.

In conclusion, Reg. No 241208 does not need to be considered in the risk assessment of Flufenoxuron, since Reg. No. 241208 was co-tested as Flufenoxuron metabolite in all relevant studies that were conducted with Flufenoxuron. No other sources of exposure of consumers or operators to Reg. No. 241208 are anticipated.

10.5.11.1 Effect assessment for operator, worker and bystander

The use pattern of Flufenoxuron containing wood preservatives is significantly different for professionals and non-professionals (Do-it-yourself). Whereas the former group may be exposed to Flufenoxuron for a considerable proportion of the year, the latter group is expected to be exposed for single days only

The predominant findings in short-term studies in rats, mice and dogs pertain hematology. In all species there were indications for an anemia with compensatory cellular responses in bone marrow as well as indications for an increased turnover of erythrocytes. There is a striking difference in respect to the NOAELs observed in sub-acute (28-day) and sub-chronic (90-day) studies. Whereas in 28-day studies the NOAELs were in the range of 5150 mg/kg bw/day to 10,000 mg/kg bw/day, the NOAELs in the 90-day studies were 1000 to 1500-fold lower, i.e. in the range of 3.5 to 10 mg/kg bw/day.

Given this, it would make sense to derive two AOELs (Acceptable Operator Exposure Levels):

- one for long(er)-term exposure of professional users and,
- one for short-term exposure of non-professionals.

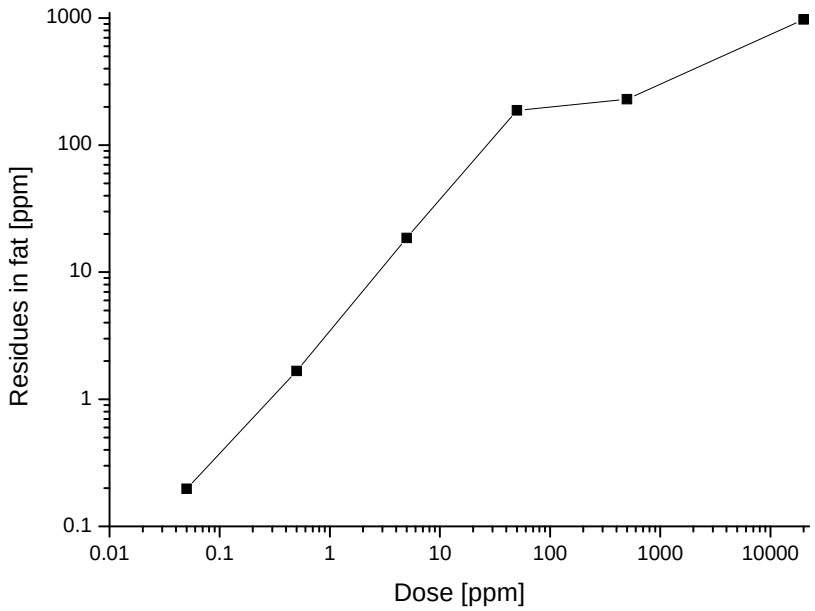
In a bile-duct cannulation study in rats, approx. 81% of a low Flufenoxuron dose (3.5 mg/kg bw) orally administered to males was recovered in urine, cage-wash, bile and carcass within 48 h of treatment (in females recovery was approx. 56%). Based on the relatively high absorption value obtained in males, it is not considered necessary to correct for reduced absorption when deriving the systemic AOEL from an oral route study.

A safety factor (SF) of 100 is appropriate for estimation of the AOEL, based on the absence of genotoxicity, and the absence of carcinogenic activity in the rat at concentrations up to 50,000 ppm (approx. 2,290 mg/kg bw/d) or in the mouse at concentrations up to 10,000 ppm (approx. 1,592 mg/kg bw/d). Additionally, results from the two-generation reproduction study in rats and the developmental toxicity studies in rats and rabbits show no increased sensitivity to developing offspring as compared to parental toxicity.

10.5.11.1.1 Short-term AOEL

Upon repeated oral administration there is a certain potential of Flufenoxuron to accumulate in animals. Different aspects of the Flufenoxuron kinetics were investigated in different species.

Figure 1: Flufenoxuron levels in fat after administration of Flufenoxuron to rats for 100 days



Administration of Flufenoxuron to rats at dietary dose levels of 0, 0.005, 0.05, 0.5, 5, 50, 500 ppm for 100 days resulted in a dose dependent increase of Flufenoxuron in fat at dose levels ≥ 0.05 ppm (see IIIA 6.2., XXXX (Cascade): Residues in the body fat of rats following ingestion in diet for 100 days, XXXX). This increase was linear at dose levels up to 50 ppm and a non linear at dose levels ≥ 500 ppm[1] (Figure 1).

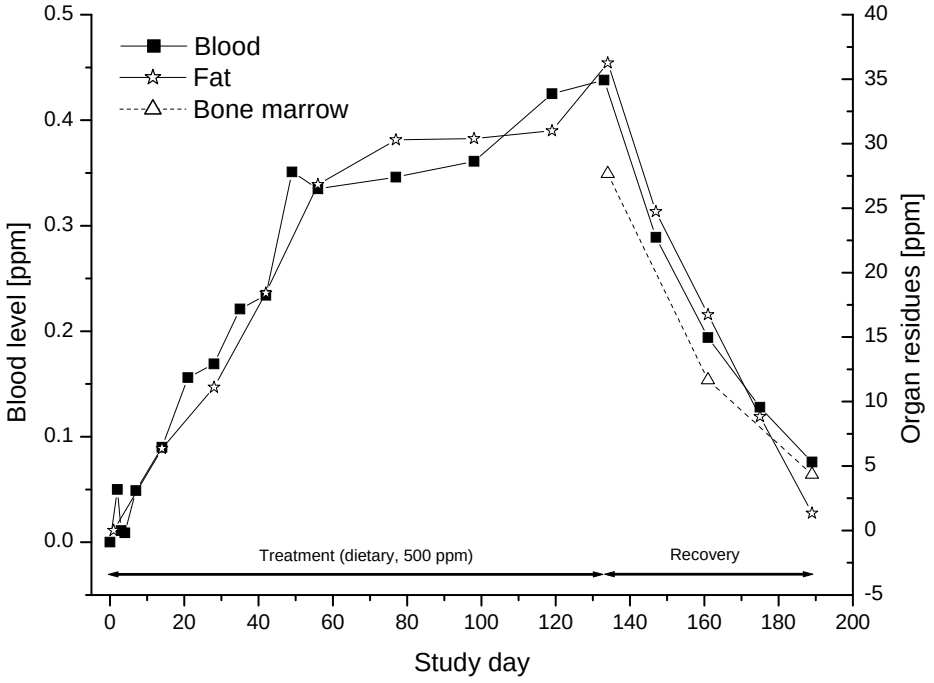
In a feeding study dogs were administered Flufenoxuron at a dietary dose level of 500 ppm (equivalent to a daily dose of 10.5 ± 1.4 mg/kg bw) for 19 weeks followed by a 8 week recovery (treatment free) period (see IIIA 6.2 XXXX - Kinetic accumulation/ elimination study in dogs, XXXX). Blood and fat samples were taken on a regular basis throughout the study period (fat was sampled by biopsy under local anaesthesia). Groups of dogs were sacrificed at study days 134 (end of administration), 161 and 189. At this occasions organ samples were taken (fat, blood, muscle, kidneys, liver and bone marrow). All samples were analyzed for Flufenoxuron content.

As evident from Figure 2, blood and fat residues displayed a parallel and linear increase for about 77 days and then reached some kind of plateau. Upon cessation of treatment residues in blood and fat decreased with a half-live of 33 and 28 days, respectively.

Residual Flufenoxuron levels in bone marrow paralleled that of blood and fat during the depletion phase. It therefore can be assumed, that Flufenoxuron levels in bone marrow during the treatment period developed comparable to the levels in blood and fat.

[1] The value for the 20000 ppm concentration was taken from the Flufenoxuron cross-fostering study (see IIIA 6.8.2, XXXX WL115110: A cross-fostering study, supplementary to a previous two generation rat reproduction study, XXXX). In this study (pregnant) rats were administered Flufenoxuron at a dietary dose level of 20000 ppm for approx. 16 weeks (112 days).

Figure 2: Flufenoxuron levels in blood, fat and bone-marrow of dog administered Flufenoxuron at a dietary dose level of 500 ppm for 19 weeks followed by a 8 week recovery period.



There is no principal difference in the toxicological response to Flufenoxuron treatment between rats, mice and dogs. In all species the most susceptible parameter was hematology as indicated by changes in RBC counts, hematocrit, hemoglobin concentration and reticulocyte counts. In addition cellular changes in the bone marrow (main hematopoietic organ) were observed. The NOAELs for hematological effects in subchronic (90-day) studies were comparable between all species (approx. 3.5 mg/kg bw/day in rats, 10.3 mg/kg bw/day in mice and 3.5 mg/kg bw/day in dogs). The fact that the NOAELs in the 28-day rat and mouse studies were about 1000 fold higher indicates that it takes some time before adverse effects on hematological parameters are observed. The most likely explanation for this is that a certain level of Flufenoxuron in blood and bone marrow is required to finally result in adverse hematological effects. Based on the kinetic data presented above, there is no reason to assume that the dog behaves different in this respect.

Based on the above, the 28-day studies in rats and mice are most suitable for the definition of a short-term AOEL since the relevant parameters for Flufenoxuron toxicity were measured in these studies. The lowest NOAEL in these studies was 5,147 mg/kg bw/day. This would result in a **short-term AOEL of 51 mg/kg bw/day** when a Safety Factor of 100 is used. Alternatively, as a more conservative approach, the NOAELs of the developmental toxicity studies (administration of Flufenoxuron for 11 and 13 days to rats and rabbits, respectively; NOAEL = 1000 mg/kg bw/day) may be used for the derivation of a short-term AOEL, thus resulting in a **short-term AOEL of 10 mg/kg**.

$$\mathrm{AOEL}_{\mathrm{short-term}} = \frac{\mathrm{NOAEL}}{\mathrm{SF}} = \frac{1000}{100}\ \mathrm{mg \cdot kg^{-1}} = 10\ \mathrm{mg \cdot kg^{-1}}$$

10.5.11.1.2 Long-term AOEL

The NOAEL values from repeated (sub-chronic) dietary studies to be used in the risk assessments are derived from a 1-year dog study, a 90-d oral rat study and a two-generation reproductive toxicity study in the rat:

Dog	1-year chronic toxicity study NOAEL = 100 ppm or approx. **3.5 mg/kg bw/d**, based on by hematological changes (decreased hemoglobin and erythrocyte count and increased reticulocyte count, methemoglobin and sulfhemoglobin) and histological changes (bone marrow hyperplasia and increased hemosiderin deposition in the proximal tubular cells of the kidney, and Kupffer cells of the liver) in males and/or females, and increased absolute liver weights and liver weights adjusted for terminal body weights in males, at 500 ppm (approx. 19 mg/kg bw/d), the next highest concentration tested.
Rat	90-day oral diet study NOAEL = 50 ppm or approx. **3.5 mg/kg bw/d**, based on hematological changes in females at the LOAEL of 500 ppm (equivalent to 35 mg/kg bw/d in males and 41 mg/kg bw/d in females)
Rat	Two-generation reproduction toxicity study NOAEL (parental toxicity) = 50 ppm or approx. **4.3 mg/kg bw/d**, based on reduced body weight gains for P and F_1 females during the pre-mating period and for F_1 males during the entire study period, and organ weight changes at 190 ppm (approx. 16.3 mg/kg bw/d), the next highest concentration tested NOAEL (offspring toxicity) = 50 ppm or approx. 4.3 mg/kg bw/d, based on decreased pup survival and decreased mean pup weights at 190 ppm NOAEL (fertility/reproductive function) = 10,000 ppm or approx. 875 mg/kg bw/d (highest dose level tested)

Thus, applying a safety factor of 100 to the NOAEL of 3.5 mg/kg bw/d (derived from the 90-day oral rat and the 1-year oral dog study) results in an **long-term AOEL of 0.035 mg/kg bw/d**.

$$AOEL_{long-term} = \frac{NOAEL}{SF} = \frac{3.5}{100}\ mg \cdot kg^{-1} = 0.035\ mg \cdot kg^{-1}$$

10.5.11.2 Effect assessment for consumer

10.5.11.2.1 Acceptable Daily Intake (ADI)

Results from the long-term dietary studies in the dog, rat and mouse, and the 2-generation reproduction study in the rat were evaluated in calculating the ADI for Flufenoxuron. An assessment of the toxicology database for Flufenoxuron supports the following NOAELs from the aforementioned studies conducted with this compound:

Dog	One-year chronic toxicity study NOAEL = 100 ppm or approx. 3.5 mg/kg bw/d, based on by hematological changes (decreased hemoglobin and erythrocyte count and increased reticulocyte count, methemoglobin and sulfhemoglobin) and histological changes (bone marrow hyperplasia and increased hemosiderin deposition in the proximal tubular cells of the kidney, and Kupffer cells of the liver) in males and/or females, and increased absolute liver weights and liver weights adjusted for terminal body weights in males, at 500 ppm (approx. 19 mg/kg bw/d), the next highest concentration tested.
Rat	Two-year chronic toxicity study NOAEL = 500 ppm or approx. 22 mg/kg bw/d, based on impairment of body weight development, slight anemia, decreased spleen weights in males, increased adrenal weights in females (both without histopathological correlate) at 5,000 ppm (approx. 233 mg/kg bw/d), the next highest concentration tested Two-generation reproduction toxicity study NOAEL (parental toxicity) = 50 ppm or approx. 4.3 mg/kg bw/d, based on reduced body weight gains for P and F_1 females during the pre-mating period and for F_1 males during the entire study period, and organ weight changes at 190 ppm (approx. 16.3 mg/kg bw/d), the next highest concentration tested NOAEL (offspring toxicity) = 50 ppm or approx. 4.3 mg/kg bw/d, based on decreased pup survival and decreased mean pup weights at 190 ppm NOAEL (fertility/reproductive function) = 10,000 ppm or approx. 875 mg/kg bw/d (highest dose level tested)
Mouse	Two-year chronic toxicity/carcinogenicity study I NOAEL = 500 ppm or approx. 56 mg/kg bw/d, based on increased incidence of Kupffer cell aggregates in the female liver at 5,000 ppm (approx. 556 mg/kg bw/d), the next higher dose level tested) Two-year chronic toxicity/carcinogenicity study II NOAEL = 10,000 ppm or approx. 1,592 mg/kg bw/d (the highest dose level tested)

Based on the above data, the NOAEL of 3.5 mg/kg bw/d from the 1-year dog study is the most appropriate NOAEL for estimation of the ADI of Flufenoxuron in humans.

A safety factor of 100 is appropriate for estimation of the ADI, based on the absence of genotoxicity, and the absence of carcinogenic activity in the rat at concentrations up to 50,000 ppm (approx. 2,290 mg/kg bw/d) or in the mouse at concentrations up to 10,000 ppm (approx. 1,592 mg/kg bw/d). Additionally, results from the two-generation reproduction study in rats and the developmental toxicity studies in rats and rabbits show no increased sensitivity to developing offspring as compared to parental toxicity.

Thus, applying a safety factor of 100 to the NOAEL of 3.5 mg/kg bw/d results in an **ADI of 0.035 mg/kg bw**:

$$\mathrm{ADI} = \frac{\mathrm{NOAEL}}{\mathrm{SF}} = \frac{3.5}{100}\ \mathrm{mg \cdot kg^{-1}} = 0.035\ \mathrm{mg \cdot kg^{-1}}$$

10.5.11.2.2 Acute Reference Dose (ARFD)

or the determination of the acute reference dose acute, short-term and developmental toxicity studies are considered to be most important.

The acute oral studies demonstrate the low toxicity of Flufenoxuron (LD_{50} > 5,000 mg/kg bw) which is also evident in 28-day oral toxicity studies in rats and mice, where no adverse effects were observable up to 50,000 ppm (NOAELs of > 5,147 and > 9,820 mg/kg bw/d in rats and mice, respectively). In the 28-day oral neurotoxicity study, the NOAEL for neurotoxicity was > 20,000 ppm, while the NOAEL for general toxicity was established at 1,000 ppm (88 mg/kg bw/d) based on slight effects on body weight at 5,000 ppm that were first noticed 2 weeks after start of treatment (i.e. no effects that resulted from single exposure). In oral prenatal toxicity studies with rats and rabbits, no adverse effects on dams or fetuses were observed up to the limit dose level of 1,000 mg/kg bw/d.

In conclusion, from the evaluation of the available toxicological database of Flufenoxuron, no critical endpoint could be identified that would be relevant to a single human exposure. Therefore, due to the low acute oral toxicity of Flufenoxuron, there is no need to establish an ARfD for Flufenoxuron.

10.5.11.2.3 Establishment of a Maximum Acceptable Concentration in drinking water (MAC)

The Maximum Acceptable Concentration (MAC) in drinking water has been based on the ADI derived from dietary studies. Taking into account that exposure through drinking water should not exceed 10% of the ADI and assuming that a 60 kg person consumes 2 litres of water per day, the MAC was calculated as follows:

$$\mathrm{MAC} = \frac{0.035\,\mathrm{mg \cdot kg^{-1} \cdot day^{-1}} \times 60\,\mathrm{kg}}{2\,\mathrm{L \cdot day^{-1}}} \times 0.1 = 0.105\,\frac{\mathrm{mg}}{\mathrm{L}}$$

10.6 Environmental effects assessment

10.6.1 Fate and distribution in the environment

Summary of the study results on flufenoxuron fate and distribution in the environment are given in Appendix 1 including the following tables:

Table 19	- Sludge activity, Biotic degradation
Table 20	- Hydrolysis
Table 21	- Photolysis in water
Table 22	- Photolysis in Soil
Table 23	- Photochemical degradation in air
Table 24	- Laboratory degradation in soil
Table 25	- Water/Sediment degradation

Table 26	- Summary of degradation rates of Flufenoxuron in laboratory soil studies
Table 27	- Summary of degradation rates of "urea" metabolite (CL 932338) in laboratory soil studies
Table 28	- Adsorption data for [14C]-Flufenoxuron on different soils
Table 29	- Adsorption data for $^{14C\text{-}"urea"}$ metabolite (CL 932338) on different soils
Table 30	- Desorption data for $^{14C\text{-}"urea"}$ metabolite (CL 932338) on different soils

Hereafter find an overall assessment of those results.

10.6.1.1 Water

The behaviour of Flufenoxuron in aquatic systems is mostly characterised by its very low water solubility (sorption to sediment)m no readily biodegradability and UV-instability.

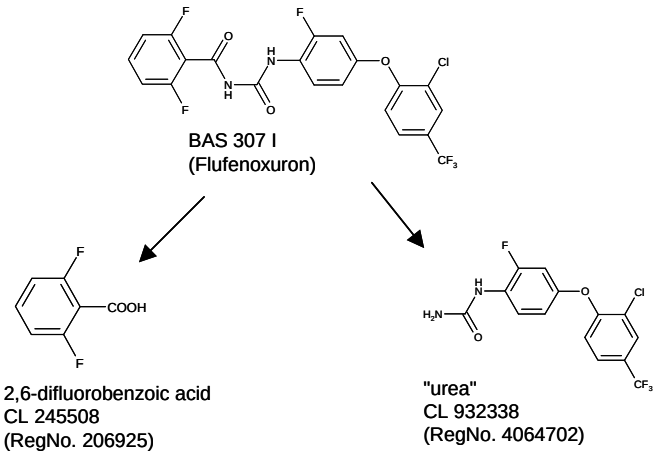
In all photolysis and water/sediment studies, the cleavage of the molecule is the first degradation step. The split can occur at two alternative locations within the molecule. In the aqueous photolysis studies the formation of 2,6-difluorobenzamide (CL 211558, Reg. No. 102719) is preferred with up to 88% total applied radioactivity (TAR). In the water/sediment systems also the alternative split leading to formation of the "urea"-metabolite (and theoretically 2,6-difluorobenzoic acid as counterpart, CL 245508, Reg. No. 206925) can occur. Furthermore, in the water/sediment studies the sorption of Flufenoxuron to the sediment leads to an even faster elimination from the water phase.

The 2,6-difluorobenzamide never exceeded 4.1% TAR in the dark water/sediment study and could not be detected in the irradiated water/sediment study. It was fast degraded to further polar compounds (all <5% TAR). The final degradation products were bound residues in the sediment and formation of CO_2.

The corresponding fluoroaniline moiety, which could not be detected in the photolysis study, was represented in the water/sediment studies exclusively by the "urea" metabolite (CL 932338, Reg.No. 4064702) appearing in both, water and sediment. It hardly reached 10% TAR in the water phase and a maximum amount of 12% TAR in the sediment. This metabolite was also further degraded forming finally bound residues in the sediment or mineralizing to CO_2. The proposed route of degradation is given in Figure 3.

Overall, the experimental results showed that Flufenoxuron is completely degradable in the aquatic environment with half-lives of 4.7 days in water and 46.1 days in sediment. It can be concluded that there is no risk of persistence or accumulation neither in water nor in sediment.

Figure 3 Hydrolytic degradation of Flufenoxuron at pH 9

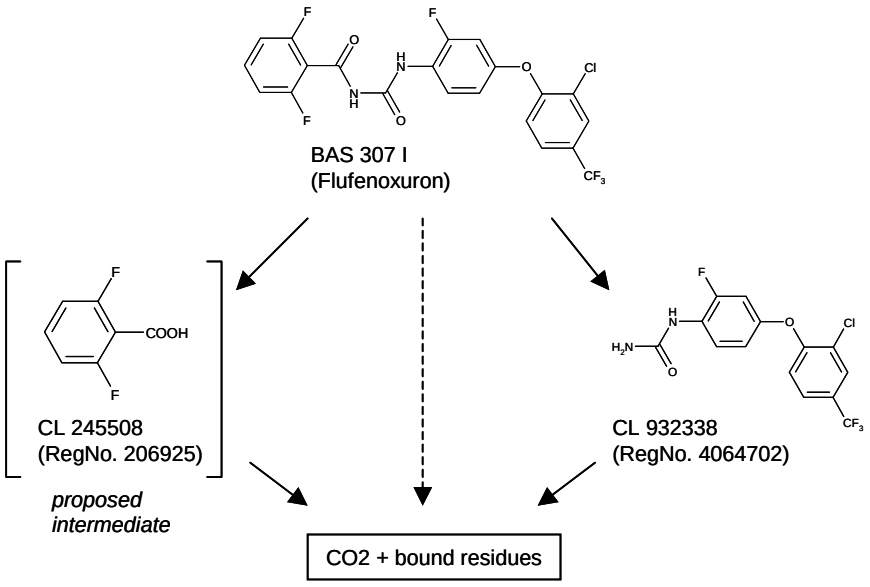


10.6.1.2 Soil

The metabolism of Flufenoxuron in soil is characterised by a splitting of the molecule into two halves. The fluoroaniline moiety forms the "urea" metabolite (CL 932338, Reg.No. 4064702), which is degraded further to form non-extractable residues and finally CO_2. With the benzamide-moiety, no distinct metabolite could be detected in soil, indicating that the degradation rate of the possibly formed difluorobenzoic acid is faster than the formation out of Flufenoxuron.

A proposed route of degradation is given in Figure 4.

Figure 4 Proposed route of degradation of Flufenoxuron in soil



The transformation rates of Flufenoxuron and its metabolite CL 932338 were estimated using the program ModelMaker, vs 3.0.4. The kinetic parameters were optimized using the MARQUARDT method (option least squares). A three-compartment model was established for the degradation of Flufenoxuron. The model consists of the parent compartment, a compartment for the "urea" metabolite (CL 932338, Reg No. 4064702) and an elimination compartment which represents all degradation processes like formation of non-extractable residues and mineralization. To calculate the half-life of the metabolite, a simple two-compartment model was established consisting of the metabolite compartment and an elimination compartment. From these calculations, good estimation for the parent and metabolite half-life were obtained in all four tested soils (

Table 26 and

Table 27).

The results of the soil experiments with Flufenoxuron under anaerobic and under irradiated conditions showed that in both cases no significant degradation could be observed. According to *Arrhenius equation*, an estimated value for DT50 at 10oC range between 252-267 and 103-129 days for flufenoxuron and its main soil degradates, Reg No. 4064702. It can therefore be concluded that soil photolysis and anaerobic conditions do not contribute to considerable extent to the degradation of Flufenxuron in soil**.**

In a new field soil dissipation study conducted in Southern Europe, a fast to moderate dissipation of Flufenoxuron was observed with DT_{50} values ranging from 6 days in Spain to 67 days in France and DT_{90} values between 20 and 222 days. Its "urea" metabolite CL 932338 (Reg.No. 4064702) was not detected in significant amounts under field conditions.

Flufenoxuron is strongly binding to soil independently of soil pH (

Table 28)

Each of the desorption steps resulted in less than 5% of the adsorbed Flufenoxuron being released, except for two higher values (about 8% to 9%) found for the lowest concentration. These values confirm the strong adsorption of Flufenoxuron to the soil matrix.

Its "urea" metabolite (CL 932338, Reg 4064702) also strongly binds to soil (Table 29). Within the five soils tested, a slight dependence of the adsorption behaviour from the soil pH could be observed with the most acidic soil (Borgeby, pH = 5.6) showing the strongest adsorption. The desorption data are given in Table 30.

Based on the fact that Flufenoxuron as well as its "urea"-metabolite (WL 129183, CL 932338, Reg.No. 4064702) have very low water solubility and show very high adsorption values (Koc) in soil and that there was no indication of any leaching processes in field trials, it can be concluded that there is no risk of leaching into deeper soil layers or groundwater after Flufenoxuron application under outdoor conditions.

10.6.1.3 Air

Flufenoxuron has a very low volatilisation potential (vapor pressure 2.32 x 10^{-8} kPa at 25 °C). Based on Atkinson calculation, Flufenoxuron would be fast degraded by photochemical processes when reaching the troposphere (DT_{50} < 17 h). Therefore, it can be concluded that there is no risk of short or long-range transport of Flufenoxuron via air.

10.6.1.4 Definition of the residue

10.6.1.4.1 Water

According to the presented results, the parent compound Flufenoxuron is the only relevant residue for quantitation in water.

In the hydrolysis study at pH 9, the major degradation product was the 2,6-difluorobenzoic acid (CL 245508, Reg.No. 206925) formed by cleavage of Flufenoxuron. At all other pH's, Flufenoxuron was stable. Under photolytic conditions the major degradation product with up to 89% was 2,6-difluorobenzamide (CL 211558, Reg.No. 102719), indicating an alternative cleavage location in the molecule.

In the water/sediment studies (in the dark and under sunlight) representing more realistic environmental conditions, only two metabolites could be detected in water and sediment.

The 2,6-difluorobenzamide (CL 211558, Reg.No. 102719) appeared in the water phase at maximum 4.1% and was not detected in sediment. The "urea" metabolite (CL 932338, Reg.No. 4064702) was formed up to 9.3% in the water phase and up to 19% in the sediment. The appearance of these two metabolites leads to the conclusion that under realistic environmental conditions, cleavage at both alternative molecule positions can occur simultaneously.

In exotoxicity studies, it was shown that the "urea" metabolite had only at the highest concentrations any effect on fish and daphnia, and no effect on algae. The 2,6-difluorobenzamide had no effect on fish, daphnia and algae even at the highest concentrations tested. Also the 2,6-difluorobenzamide proved to be not biologically active.

Therefore, the parent Flufenoxuron is proposed as the only relevant residue in water.

10.6.1.4.2 Soil

According to the presented results, the parent compound Flufenoxuron is the only relevant residue for quantitation in soil. Although the "urea" metabolite (CL 932338, Reg.No. 4064702) (cleavage product) was formed above 10% in several aerobic soils (maximum 16%) in the laboratory studies, the results of the field dissipation study showed that this metabolite was detected if at all only in trace amounts close to the determination limit. Ecotoxicity studies showed that the metabolite does not have any effect on earthworms or on the microbial activity in soil (See 4.3). Furthermore, this metabolite is not biologically active.

Under anaerobic conditions, no significant degradation of Flufenoxuron took place. No metabolites are formed under these conditions. Also during soil photolysis, no significant degradation of Flufenoxuron could be observed.

Since the adsorption to soil is very strong for Flufenoxuron (Koc > 88000) and also the "urea" metabolite (Koc > 3700), no risk for groundwater after application of Flufenoxuron exists.

Therefore, the parent Flufenoxuron is the only relevant residue in soil.

10.6.1.4.3 Air

Not relevant because very likely to present no risk of short or long-range transport of Flufenoxuron via air.

10.6.2 Effects on environmental organisms

For ease of reference, BASF code names for Flufenoxuron degradates are used hereafter. A chemical glossary with details is given in chapter 6 (pp 46-47).

10.6.2.1 Aquatic compartment

The effects of Flufenoxuron and its degradates are on aquatic organisms are summarized in Table 15.

Table 15 Summary of results of Flufenoxuron and its degradates on aquatic organisms

Test species	**Test system**	**Result [µg a.s./L]**		**Reference**
		LC_{50}/EC_{50}	**NOEC**	

Table 15 Summary of results of Flufenoxuron and its degradates on aquatic organisms

Test species	Test system	Result [µg a.s./L]		Reference
		LC_{50}/EC_{50}	NOEC	
O. mykiss [9)]	Flow-through - 96 h	> 4.9	n.d.	XXXX
Brachydanio rerio [9)]	Semi-static – 96 h	> 5.19	5.19	XXXX
Cyprinus carpio [8)]	Static - 96 h	> 10000	n.d.	XXXX
Pimephales promelas ELS [9)]	Flow-through - 34 d	n.d.	0.82	XXXX
Danio rerio	static - (full life-cycle)	n.d.	4.5	XXXX
Daphnia magna [8)]	Static - 48 h	0.0429	0.01	Funk XXXX
Daphnia magna [8)]	Static - 48 h	test 1: 0.04 test 2: 0.09	n.d.	Croucher XXXX
Daphnia carinata [8)]	Static - 48 h	test 1:< 500 test 2: 1.4	n.d.	Shumei XXXX
Gammarus pulex [9)] *Lymnea stagnalis* *Tubifex tubifex* *Chironomus lugubris*	Semi-static - 96 h Semi-static - 96 h Semi-static - 96 h Semi-static - 48 h	> 1.2 > 1.2 > 0.4 > 0.6	n.d.	Pearson, Girling XXXX
Daphnia magna [8)]	Static - 48 h	n.d.	10	Pearson, Girling XXXX
Daphnia magna [10)]	Semi-static - 21 d	n.d.	0.010	Pearson, Girling XXXX
Pseudokirchneriella subcapitata [8)]	Static - 96 h	24600 [1)]	600 [3)]	Kubitza XXXX
Pseudokirchneriella subcapitata [10)]	Static - 96 h	> 4.0	n.d.	Croucher XXXX
Chironomus riparius [8)]	Static - 28 d	0.131	0.05 [4)] 0.1 [5)]	Mattock XXXX

Table 15 Summary of results of Flufenoxuron and its degradates on aquatic organisms [Continue]

Test species	Test system	Result [µg a.s./L]		Reference
		LC_{50}/EC_{50}	NOEC	
"urea", Reg. No. 4064702				
O. mykiss 8)	Static - 96 h	570	200	XXXX
Daphnia magna 8)	Static - 48 h	1030	500 2)	Jatzek XXXX
Pseudokirchneriella subcapitata 8)	Static - 72 h	90	66	Jatzek XXXX
Chironomus riparius 8)	Static - 28 d	1200 4) 4610 5)	800 4) 1600 5)	Funk XXXX
Reg. No. 4108386				
O. mykiss 8)	Static - 96 h	2400	n.d.	XXXX
Daphnia magna 8)	Static - 48 h	6200 6) 9700 7)	n.d.	Girling XXXX Ede XXXX (amendment 1
Reg. No. 4064703				
O. mykiss 8)	Semi-static – 96 h	460	n.d.	XXXX
Daphnia magna 8)	Static - 48 h	5.9	n.d.	Girling XXXX
Pseudokirchneriella subcapitata 8)	Static - 72 h	600 1)	100	Hanstveit, Oldersma XXXX
Reg. No. 102 719				
O. mykiss 8)	Static - 96 h	> 100	100	XXXX
Daphnia magna 8)	Static - 48 h	> 1000000	25000 2)	Jatzek XXXX
Pseudokirchneriella subcapitata 8)	Static - 72 h	> 100 1)	77.7 3)	Jatzek XXXX
Reg. No. 241 208				
Daphnia magna 8)	Static - 48 h	654	500 2	Jatzek XXXX
Reg. No. 206 925				
Daphnia magna 8)	Static - 48 h	> 100	100 2	Jatzek XXXX

1) biomass; 2)$EC_{0;}$ 3) $E_bC_{10\ ;}$ 4) based on emergency; 5) based on development ; 6) based on freshly prepared test item solutions; 7) based on aged (48 h) test item solutions 8) results based on nominal concentrations; 9) results based on measured concentrations; 10) results based on initial measured concentrations

10.6.2.2 Soil Micro-organisms

The toxicity of Flufenoxuron in soil had been tested on physiological functions of soil micro-organisms (laboratory studies). The results are summarized Table 16.

Table 16 Summary of effects of Flufenoxuron and metabolites on soil micro-organisms

Test system/ Soil type	Application rate		Result	Reference
	[mg/kg]	[kg/ha]	[%] deviation from control [1)]	
C-transformation				
Flufenoxuron, tested as 100 g a.s./L DC				
Loamy sand (28 d)	0.17	0.128	-0.858	Koelzer, XXXX
	1.7	1.28	-3.66	
“urea”, Reg. No. 4064702				
Loamy sand (28 d)	0.00761	0.0057	+5.18	Koelzer, XXXX
	0.0761	0.057	-1.01	
N-transformation				
Flufenoxuron, tested as 100 g a.s./L DC				
Loamy sand (28 d)	0.17	0.128	+12.6	Koelzer, XXXX
	1.7	1.28	+6.92	
„urea“, Reg. No. 4064702 [6)]				
Loamy sand (28 d)	0.00761	0.0057	-17.2	Koelzer, XXXX
	0.0761	0.057	-17.2	

1) - = inhibition; + = stimulation 2) analysis of nitrification levels at day 28 3) analysis of nitrification levels at day 91
4) amended with ammonia, 5) amended with Lucerne 6) 1x metabolite: 20% transformation from 0.04 kg a.s./ha

10.6.2.3 Soil Macro-organisms (earthworms)

Flufenoxuron and its soil “urea” metabolite Ref No. 4064702 [previously CL 932 338] has been tested on earthworms in 14-day toxicity studies up to 1000 mg a.s./kg substrate: Furthermore, the active substance was tested in a chronic toxicity and reproduction test up to 5.0 mg a.s./kg soil dry weight. The results are summarized in Table 17.

Table 17 Summary of effects of Flufenoxuron on earthworms

Test species	Test system	Toxicity [mg/kg soil dry weight]		Reference
		LC_{50}	NOEC	
Flufenoxuron				
E. fetida	14-d toxicity test	> 1000	> 1000	Hillaby, XXXX
E. fetida	56-d repro test	n.d.	5.0	Luehrs, XXXX
"urea", Reg. No. 4640702				
E. fetida	14-d toxicity test	> 1000	316	Staebler, XXXX

n.d. = not determined

10.6.2.4 Bird

For the assessment of effects of Flufenoxuron on birds, tests with bobwhite quails (Colinus virginianus) and mallard ducks (Anas platyrhynchos) have been conducted. The results are summarized in Table 18. In the single dose acute toxicity study with bobwhite no significant reduction in the mean feed uptake was observed compared to the control up to the highest dose group. The mean body weight and the development of body weight of female birds were not statistically significant reduced when compared to the control group. No compound-related macroscopic abnormalities were detected in the gross post-mortem examination.

In the short-term dietary study with bobwhite and mallard no test item related mortality, clinical signs, reduction of feed consumption or reduction of body weight were observed.

In the sub-chronic toxicity and reproduction studies with bobwhite no mortality was observed. No compound-related symptoms occurred. Feed consumption and body weight were within the normal limits in all groups.

Table 18 Summary of effects of Flufenoxuron on birds

Test species	Test system	Results	Reference
Colinus virginianus	Acute oral toxicity	LD_{50} > 2000 mg a.s./kg b.w. NOEL = 2000 mg a.s./kg b.w.	XXXX
Colinus virginianus	Short-term dietary toxicity	LD_{50} > 5243 mg a.s./kg b.w. NOEC = 5243 mg a.s./kg b.w.	XXXX
Anas platyrhynchos	Short-term dietary toxicity	LD_{50} > 5243 mg a.s./kg b.w. NOEC = 5243 mg a.s./kg b.w.	XXXX
Colinus virginianus	Short-term dietary toxicity	NOEL = 100 mg a.s./kg feed	XXXX

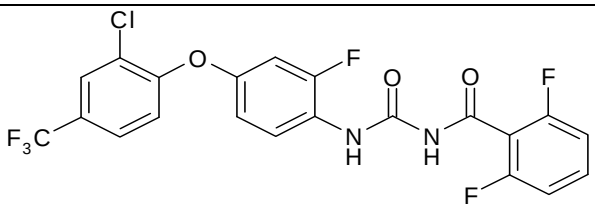
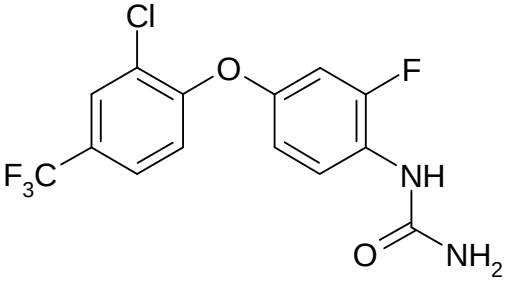
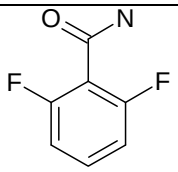
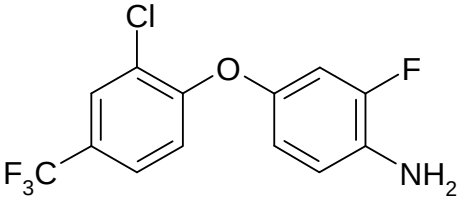
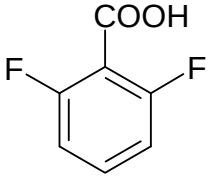
10.6.2.5 Non compartment specific effects relevant to the food chain (secondary poisoning)

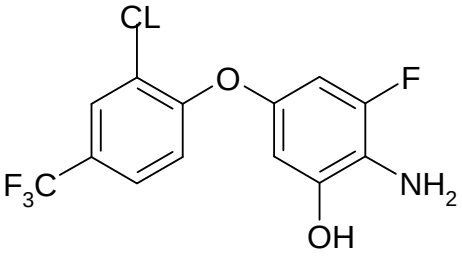
Used as a wood preservative, it is very unlikely that Flufenoxuron will present a risk for secondary poisoning.

10.7 Hazard identification for physico-chemical properties

Flufenoxuron is neither explosive nor highly flammable; it does not self-ignite and has no oxidizing properties.

10.8 Chemical glossary

Chemical structure	Names and Numbers	Matrix
	Flufenoxuron Reg.No. 243154 BAS 307 I CL 811678 WL 115110	TGAI
	**Reg.No**.4064702 **Other internal code(s):** CL 932338 WL 129183 **Molecular formula**: C_{14} H_9 Cl F_4 N_2 O_2 **Molecular mass**: 348.69 g/mol **Chemical name:** N-[4-[2-chloro-4-(trifluoro-methyl) phenoxy]-2-fluoro-phenyl urea	Soil Rat (minor metabolite)
	**Reg.No**.102719 **Other internal code(s):** CL 211558 **Molecular formula**: C_7 H_5 F_2 N O **Molecular mass**: 157.12 g/mol **Chemical name**: 2,6-difluorobenzamide	Water Sediment Hydrolysis Rat (minor metabolite)
	**Reg.No**.:241208 **Other internal code(s):** CL 359882 WL 115096 **Molecular formula**: C_{13} H_8 Cl F_4 N O **Molecular mass**: 305.60 g/mol **Chemical name:** 4-[2-chloro-4-(trifluoro-methyl)phenoxy-2-fluoro-benzenamine	Hydrolysis Rat (minor metabolite) Dog (minor metabolite)
	**Reg.No**. 206955 **Other internal code(s):** CL 245508 **Molecular formula**: C_7 H_4 F_2 O_2 **Molecular mass**: 158.1 g/mol **Chemical name**: 2,6-difluorobenzoic acid	Hydrolysis Rat (major metabolite)

Chemical structure	Names and Numbers	Matrix
	**Reg.No.**4110959 **Other internal code(s):** CL 944956 WL 132612 **Molecular formula**: C_{13} H_8 CL F_4 N O_2 **Molecular weight**: 321.7 g/mol **Chemical name**: 2-amino-5-[2-chloro-4-(trifluoromethyl)phenoxy]-3-fluorophenol	Rat (minor metabolite)

Appendix 1

Overall study results for Flufenoxuron Biotic and Abiotic degradation in environment Compartment

Table 19 - Sludge activity, Biotic degradation

Guideline / Test method	Test type[1]	Test para-meter	Inoculum Type	Test substance concentr.	Degradation		Reference
					Incub. period	Degree [%]	
OECD 301B	R	%ThOD	Sewage Sludge	3 mg/L	28 days	≤4%	Turner SJ, Watkinson RJ (1986) XXXX
OECD 301D	R	%ThCO$_2$	Sewage Sludge	20 mg/L	28 days	≤4%	

[1] Test on *inherent (I)* or *ready (R)* biodegradability according to OECD criteria

Table 20 - Hydrolysis

Guideline / Test method	pH	Temp. [°C]	Initial TS concentration, C_0 [µg.mL]	Half-life, DT_{50} [days]		Reference
None	5, 7, 9, 12, and 14	25, 40, 60, 70 and 80ºC	0.002	At 25ºC, pH 5 - 205 d pH 7 - 267 d pH 9 - 36.7 d pH 12 - 2.68 d pH 14 – 0.11 d		Langner EJ, Camilleri P (1987) *XXXX*
EC Method C7 US EPA N 161-1		50ºC and 25ºC		25ºC	50ºC	Hassink J (2003) *XXXX*
	4		1.0	434	66	
	5		1.0	682	99	
	7		0.8	234	36	
	9		1.8	88.0, 94.4	1.5, 1.0	
	9		Reg. No. 206935	59.3	--	
			Reg. No. 102719	--	3.0	

Table 21 - Photolysis in water

Guideline / Test method	Initial molar TS concen-tration	Photolysis rate constant (k^c_p)	Reaction quantum yield (ϕ^c_E)	Half-life ($t_{1/2E}$)	Reference
None	4.5x 10^{-9} mole/L	Not determined	Not determined	at Latitude 51º 20'N under June sunlight, the $t_{1/2}$ was about 11 days.	Camilleri P, Langner E J (1987) XXXX
SETAC (1995) OECD/GD (97)21	1.975 µg/L	0.14645 $days^{-1}$	4.76 x 10^{-6}	Summer – 12 days Winter – 24 to 72 days	Burgener A (2001) 2001/7000893, XXXX
Commission Directive 94/37/EEC amending Council Directive 91/414/EEC	1.6, 1.7 nM	0.15068 $days^{-1}$ 2,6-difluorobenzamide - 0.04951 $days^{-1}$	1.75 x 10^{-3}	39.2 days in April to 21.7 days in June.	Hassink J (2003) XXXX
JAMFF Guideline, 9 Nohsan 5089: 16, 1997	0.0021 µg/ml	Distilled water – 0.0976 $days^{-1}$ Pond water – 0.1024 $days^{-1}$	Not determined	Spring 35ºN Distilled water – 17.7 days Pond water – 17.0 days	Mamouni A and van der Gaauw A (2001) XXXX

Table 22 - Photolysis in Soil

Guideline / Test method	Test Conditions	Half-life ($t_{1/2E}$)	Metabolites Identified	Reference
SETAC Europe March 1995	Samples were irradiated continuously by xenon lamp for up to 16 days at 20 ± 3ºC.	under bright summer sunlight in Harrogate, UK (ca. 54ºN): 147 and 166 days	2,6-diflourobenzamide maximum of <3% TAR	Lewis CJ, Gross R (2001) XXXX

Table 23 - Photochemical degradation in air

Guideline / Test method	Test Conditions	k	$T_{1/2, OH}$	Reference
Council Directive 94/37/EC of July 22, 1994	The rate constant for reactions with OH radicals in the atmosphere was estimated using Atkinson's method. The half-life was calculated using the weighted global average OH radical concentration in the troposphere.	14.2568 x 10^{-12} cm^3 $molecule^{-1}$ s^{-1}.	0.7 days	Hassink J (XXXX

Table 24 - Laboratory degradation in soil

Guideline / Test method	Reference	Test Temp. - Duration	Soil Type/ Source	DT_{50}	Metabolites Identified
None cited.	Richardson (1987) XXXX	22 ± 2ºC 90 days	Clay Loam, UK	~140 days	
None cited.	Richardson (1990/91) XXXX	152 days	Silty clay loam, UK	Aerobic: ~120 days Anaerobic: >>150 days (86%remaining at end of study)	WL 129183: Max. 16% at 90 days WL 115096: <1%
BBA Guideline, Part IV, 4-1 (Dec. 1986)	Standen & Hill (1993) XXXX	22 ± 2ºC 150 days	Clay Loam , UK	Aerobic: 90 days Anaerobic: >>150 days (77% remaining at 150 days)	WL 129183: Max. 7.3% at 60 days WL 115096: <1% Bound residues were ca. 46% of TAR at 150 days and were characterized as fulvic acids (ca. 5% TAR), humic acids (ca. 20% TAR), and humins (ca. 20% TAR).
SETAC 1995 OECD 307	Goodyear & Gross (2001) XXXX	20 ± 2ºC 120 days	Clay Loam , UK (3)	124 days 36 days 64 days	None Bound residues were 20-25% of TAR at 150 days and were characterized as fulvic acids (5-10% TAR), humic acids (2-8% TAR), and humins (8-13% TAR).
SETAC 1995 OECD 307	Stephan & Ebert (2003) XXXX	20 ± 2ºC 120 days	Silty sand , Germany (2 for flufenoxuron, 4 for CL932338)	Flufenoxuron: 122, 115 days CL932338: 57, 56, 59, 47 days	No

Table 25 - Water/Sediment degradation

Guideline / Test method	Reference	Water/Sediment source	Analyte	Compartment	DT_{50} (days)	DT_{90} (days)
BBA, Part IV, 5-1 US-EPA N, 162-4 SETAC Europe OECD 308	Ebert D (2003) *XXXX*	Kellmetschweiher	Flufenoxuron	whole system	61	203
				water	0.3	0.9
				sediment	65	216
			CL932338	sediment	21	71
		Berghäuser Altrhein	Flufenoxuron	whole system	45	150
				water	0.4	1.2
				sediment	46	152
			CL932338	sediment	10	32
OECD Guideline, Draft Aug 2001 This study was carried out under natural light in outdoor conditions	Fent G (2003) *XXXX*	Kellmetschweiher	Flufenoxuron	whole system	42.9	142.5

Table 26 - Summary of degradation rates of Flufenoxuron in laboratory soil studies

Study Reg.Doc.#	**Soil**	**Study duration [days]**	**Temp. [°C]**	**Moisture [%MWC]**	**Estimation**	**DT50 [days]**	**DT90 [days]**	**r^2**
aerobic degradation								
Richardson 1987 XXXX	Hoath, UK	90	22	42	graphical extrapolation	~ 140	n.c.	-
Richardson 1990/91 XXXX	Woodstock, UK	152	21	40	graphical extrapolation	~ 120	n.c.	-
Standen & Hill 1993 XXXX	Woodstock, UK aniline label toluyl label	150	22	40	 graphical estimation	 ~ 90 ~ 90	 n.c. n.c.	 - -
Goodyear & Gross 2001 XXXX	Chapel Hill F., UK Newhaven C., UK Baylam, UK	120	20	45	ModelMaker 4.0	124 36 64	432 191 449	0.998 0.997 0.997
Stephan & Ebert 2003 XXXX	Bruch West, FRG Li35b, FRG	119	20	40	ModelMaker 3.0.4 first order	122 115	407* 381*	0.95 0.98
anaerobic degradation								
Richardson 1990/91 XXXX	Woodstock, UK	152	21	flooded	no significant degradation under anaerobic conditions			
Standen & Hill 1993 XXXX	Woodstock, UK	150	22	flooded				
soil photolysis								
Lewis & Gross 2001 XXXX	Newhaven C., UK	16	20	air dry	no significant degradation			

- value not reliable (too far extrapolated); MWC = maximum water holding capacity

Table 27 - Summary of degradation rates of "urea" metabolite (CL 932338) in laboratory soil studies

Study Reg.Doc.#	**Soil**	**Study duration [days]**	**Temp. [°C]**	**Moisture [%MWC]**	**Estimation**	**DT50 [days]**	**DT90 [days]**	**r^2**
aerobic degradation								
Stephan & Ebert 2003 XXXX	Bruch West, FRG Li35b, FRG Lufa 2.2, FRG Lufa 3A, FRG	119	20	40	ModelMaker 3.0.4 first order	57 56 59 47	190 186 196 156	0.97 0.99 0.99 0.99

MWC = maximum water holding capacity

Table 28 - Adsorption data for [^{14}C]-Flufenoxuron on different soils

Soil	pH ($CaCl_2$)	K_d (ml/g)	K_{OC} (ml/g)
***Hill & Standen* 1993**			
Godstone	6.1	1738	289747
Elm Farm	6.5	3206	178093
Woodstock	6.1	4250	137104
***Rosenwald* 2002**			
Chelmorton	6.1	2756 ± 1282	95030 ± 44220
Kenslow Farm	5.7	3441 ± 1782	88240 ± 45700

Table 29 - Adsorption data for ^{14}C-"urea" metabolite (CL 932338) on different soils

Soil	pH ($CaCl_2$)	K_F (ml/g)	1/n	K_{FOC} (ml/g)	K_d* (ml/g)	K_{OC}* (ml/g)
Borgeby	5.6	118.5	0.978	8467	145.2	10371
Birnbaum	6.1	37.52	0.922	4690	68.50	8563
2.2 F222002	6.3	101.7	0.918	3928	199.0	7681
Sora Bevern	6.5	63.09	0.895	3711	145.1	8536
Stetten	7.5	52.37	0.968	5237	67.56	6756

*determined at one concentration level (mean of two experiments). $K_d = C_{soil} / C_{water}$

Table 30 - Desorption data for ^{14}C-"urea" metabolite (CL 932338) on different soils

Soil	K_{FdesI} (ml/g)	1/n	$K_{FOCdesI}$ (ml/g)
Borgeby	134.8	0.951	9625
Birnbaum	42.71	0.882	5339
2.2 F222002	60.69	0.819	2343
Sora Bevern H9	129.3	0.935	7604
Stetten	33.19	0.853	3319

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	12/03/2007

Materials and methods	-
Conclusion	Modifications of summary are revised by RMS in document IIA. Please refer to Document IIA for final version.
Reliability	
Acceptability	
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Annex point(s)	Author(s)	Date Year / Month / Day	Title Source BASF DocID GLP or GEP status Published or not	Data Protection Y/N	Owner
IV A 2.6/1	XXXX	XXXX	Flufenoxuron (AC 811678) technical material: Description of the materials used to produce the product and of the production process conform EPA product properties test guidelines OPPTS 830.1600 and OPPTS 830.1620 XXXX. XXXX No, not subject to GLP regulations unpublished **Business Confidential Information – See BCI folder**	Y*	BASF
IV A 2.7/1	XXXX	XXXX	Flufenoxuron TC: Composition of the technical grade active ingredient (TGAI) XXXX. XXXX No, not subject to GLP regulations unpublished **Business Confidential Information – See BCI folder**	Y*	BASF
IV A 2.8/1	XXXX	XXXX	The analytical profile for representative manufacturing batches of Flufenoxuron technical grade active ingredient and the minimum and maximum values of each component for the re-registration of AC 811678 (Flufenoxuron) technical grade active ingredient with the European Union XXXX XXXX Yes unpublished **Business Confidential Information – See BCI folder**	Y*	BASF
IV A 2.8/2	XXXX	XXXX	Analytical characterization of five batches Flufenoxuron technical grade XXXX. XXXX Yes unpublished **Business Confidential Information – See BCI folder**	Y*	BASF

* Data protection requested as part of Business Confidential Information

Annex point(s)	Author(s)	Date Year / Month / Day	Title Source BASF DocID GLP or GEP status Published or not	Data Protection Y/N	Owner
IV A 3.1.1/1	Camilleri P. et al.	1986	Melting point and differential thermal analysis of WL115110 XXXX No unpublished	N	BASF
IV A 3.1.1/2	Daum A.	2001	Determination of the thermal stability and the stability in air of Flufenoxuron (BAS 307 I, CL# 811 678, Reg.No. 243 154) PAI XXXX Yes unpublished	Y	BASF
IV A 3.1.2/1	Camilleri P. et al.	1986	Melting point and differential thermal analysis of WL115110 XXXX No unpublished	N	BASF
IV A 3.1.2/2	Daum A.	2001	Determination of the thermal stability and the stability in air of Flufenoxuron (BAS 307 I, CL# 811 678, Reg.No. 243 154) PAI XXXX Yes unpublished	Y	BASF
IV A 3.1.3/1	Kaestel R.	2001	Density determination of the technical material of Flufenoxuron XXXX Yes unpublished	Y	BASF
IV A 3.2/1	Langner E.J.	1988	Physico-chemical properties of WL115110 XXXX Yes unpublished	N	BASF
IV A 3.2.1/1	Rice P.	2000	Flufenoxuron (BAS 307 I): Calculation of Henry's law constant XXXX No, not subject to GLP regulations unpublished	Y	BASF
IV A 3.3/1	Kaestel R.	2001	Physical properties of Flufenoxuron (TC) XXXX Yes unpublished	Y	BASF
IV A 3.3/2	Kaestel R.	2001	Physical properties of Flufenoxuron (PAI) XXXX Yes unpublished	Y	BASF
IV A 3.4/1	Fang L.Y.	1996	CL 811678 (Flufenoxuron) spectral database XXXX No unpublished	N	BASF
IV A 3.4/2	Daum A.	2003	Spectra (UV, NMR, IR, MS) of Flufenoxuron (BAS 307 I, Reg.No. 243 154) PAI XXXX Yes unpublished	Y	BASF
IV A 3.5/1	Langner E.J.	1988	Physico-chemical properties of WL115110 XXXX Yes unpublished	N	BASF
IV A 3.5/2	Bates M.L., Rice P.	2003	CL 932338, CL 211558, and CL 359882 (metabolites of BAS 307 I, flufenoxuron): Determination of the water solubility XXXX Yes unpublished	Y	BASF
IV A 3.6/1	Camilleri P., Langner E.J.	1986	Solubility and pKa of WL115110 in water XXXX No unpublished	N	BASF
IV A 3.7/1	Daum A.	2001	Determination of the solubility in organic solvents of BAS 307 I (Flufenoxuron, Reg.No. 243 154 TGAI (identical with CL 811 678)) XXXX Yes unpublished	Y	BASF
IV A 3.9/1	Langner E.J.	1988	Physico-chemical properties of WL115110 XXXX Yes unpublished	N	BASF

Annex point(s)	Author(s)	Date Year / Month / Day	Title Source BASF DocID GLP or GEP status Published or not	Data Protection Y/N	Owner
IV A 3.9/2	Bates M. et al.	2002	CL 932338, CL 211558, and CL 359882 (metabolites of BAS 307 I, Flufenoxuron): Determination of the partition coefficient XXXX Yes unpublished	Y	BASF
IV A 3.10/1	Daum A.	2001	Determination of the thermal stability and the stability in air of Flufenoxuron (BAS 307 I, CL# 811 678, Reg.No. 243 154) PAI XXXX Yes unpublished	Y	BASF
IV A 3.11/1	Van Helvoirt J.A.M.W.	1990	Determination of the flammability of Flufenoxuron XXXX Yes unpublished	N	BASF
IV A 3.11/2	Van Helvoirt J.A.M.W.	1990	Determination of the auto-flammability of Flufenoxuron XXXX Yes unpublished	N	BASF
IV A 3.13/1	Kaestel R.	2001	Physical properties of Flufenoxuron (TC) XXXX Yes unpublished	Y	BASF
I VA 3.15/1	Van Helvoirt J.A.M.W., Cardinaals J.M.	1990	Determination of the explosive properties of Flufenoxuron XXXX Yes unpublished	N	BASF
IV A 3.16/1	Van Helvoirt J.A.M.W.	1990	Determination of the oxidizing properties of Flufenoxuron XXXX Yes unpublished	N	BASF

Annex point(s)	Author(s)	Date Year / Month / Day	Title Source BASF DocID GLP or GEP status Published or not	Data Protection Y/N	Owner
IV A 4.1/1	Fang L.Y.	1996	Validation of the high pressure liquid chromatographic method M-2636 for the determination of CL 811,678 in technical grade Flufenoxuron (CL 811,678) XXXX Yes unpublished	N	BASF
IV A 4.1/2	XXXX	XXXX	Validation of high resolution gas chromatographic method M-2691 to assay residual solvents in AC 811678 (Flufenoxuron) technical grade active ingredient XXXX Yes unpublished **Business Confidential Information – See BCI folder**	Y*	BASF
IV A 4.1/3	XXXX	XXXX	Validation of high performance liquid chromatographic method M-2647.02 to assay minor components in AC 811678 (Flufenoxuron) technical grade active ingredient XXXX Yes unpublished **Business Confidential Information – See BCI folder**	Y*	BASF
IV A 4.1/4	XXXX	XXXX	Determination of the by-compounds in technical active ingredient BAS 307 I (Flufenoxuron) by reversed phase HPLC XXXX No unpublished **Business Confidential Information – See BCI folder**	Y*	BASF
IV A 4.1/5	XXXX	XXXX	Validation of the analytical method CP 415 for the determination of the by-compounds in techn. BAS 307 I (Flufenoxuron) by HPLC XXXX Yes unpublished **Business Confidential Information – See BCI folder**	Y*	BASF
IV A 4.2/1	Kennedy E.M.	1994	Flufenoxuron (WL115110: Cascade): Determination of residues in soil - Development and validation of a liquid chromatographic method XXXX Yes unpublished	N	BASF
IV A 4.2/2	Anonymous	1996	Determination of residues of WL115110 in soil - Liquid chromatographic method XXXX No unpublished	N	BASF
IV A 4.2/3	Anonymous	1989	Determination of residues of WL 129183 in soil - liquid chromatographic method XXXX No unpublished	N	BASF
IV A 4.2/4	Jones S.	2002	Method validation of RLA 12637 HPLC/MS method for the determination of BAS 307 I (CL811678, flufenoxuron) and CL 032338 residues in soil XXXX Yes unpublished	Y	BASF
IV A 4.2/5	Smalley R.	2002	Validation of method RLA 12637 for the analysis of BAS 307 I and CL 932338 in soil down to an LOQ of 0.001mg/kg XXXX Yes unpublished	Y	BASF
IV A 4.2/6	Anonymous	1986	Determination of residues of WL115110 in water - Liquid chromatographic method XXXX No unpublished	N	BASF
IV A 4.2/7	Smalley R.	2003	Validation of method RLA 12680 for the analysis of BAS 307 I and metabolite CL 932338 in water at an LOQ of 0.01 µg/litre XXXX Yes unpublished	Y	BASF

Annex point(s)	Author(s)	Date Year / Month / Day	Title Source BASF DocID GLP or GEP status Published or not	Data Protection Y/N	Owner
IV A 4.2/8	Zangmeister W.	2003	Validation of analytical method 533: Determination of BAS 307 I (Flufenoxuron) in air by LC/MS-MS XXXX Yes unpublished	Y	BASF

Annex point(s)	Author(s)	Date Year / Month / Day	Title Source BASF DocID GLP or GEP status Published or not	Data Protection Y/N	Owner
IV A 6.1.1/1	XXXX	XXXX	WL115110 (Cascade): Acute oral toxicity XXXX XXXX Yes unpublished	N	BASF
IV A 6.1.1/2	XXXX	XXXX	Toxicology of insecticides (acyl ureas): The acute oral and percutaneous toxicity, skin and eye irritancy and skin sensitizing potential of WL115110 XXXX No unpublished	N	BASF
IV A 6.1.1/3	XXXX	XXXX	Corrigendum to XXXX: Toxicology of insecticides (acyl ureas): The acute oral and percutaneous toxicity, skin and eye irritancy and skin sensitizing potential of WL115110 XXXX Yes unpublished	N	BASF
IV A 6.1.2/1	XXXX	XXXX	Toxicology of insecticides (acyl ureas): The acute oral and percutaneous toxicity, skin and eye irritancy and skin sensitizing potential of WL115110 XXXX No unpublished	N	BASF
IV A 6.1.2/2	XXXX	XXXX	Corrigendum to XXXX: Toxicology of insecticides (acyl ureas): The acute oral and percutaneous toxicity, skin and eye irritancy and skin sensitizing potential of WL115110 XXXX Yes unpublished	N	BASF
IV A 6.1.3/1	XXXX	XXXX	WL 115110: Acute inhalation toxicity study in rats XXXX Yes unpublished	N	BASF
IV A 6.1.3/2	XXXX	XXXX	Addendum to XXXX: WL 115110: Acute inhalation toxicity study in rats XXXX Yes unpublished	N	BASF
IV A 6.1.4/1	XXXX	XXXX	Toxicology of insecticides (acyl ureas): The acute oral and percutaneous toxicity, skin and eye irritancy and skin sensitizing potential of WL115110 XXXX No unpublished	N	BASF
IV A 6.1.4/2	XXXX	XXXX	Corrigendum to XXXX: Toxicology of insecticides (acyl ureas): The acute oral and percutaneous toxicity, skin and eye irritancy and skin sensitizing potential of WL115110 XXXX Yes unpublished	N	BASF
IV A 6.1.5/1	XXXX	XXXX	Toxicology of insecticides (acyl ureas): The acute oral and percutaneous toxicity, skin and eye irritancy and skin sensitizing potential of WL115110 XXXX No, studies were conducted prior to the implementation of GLP but are scientifically valid unpublished	N	BASF
IV A 6.1.5/2	XXXX	XXXX	Corrigendum to XXXX: Toxicology of insecticides (acyl ureas): The acute oral and percutaneous toxicity, skin and eye irritancy and skin sensitizing potential of WL115110 XXXX Yes unpublished	N	BASF
IV A 6.1.5/3	XXXX	XXXX	BAS 307 I (Flufenoxuron) – Maximization Test in Guinea pigs. XXXX Yes unpublished	Y	BASF
IV A 6.2/1	XXXX	XXXX	The fate of (14C-aniline)-WL115110 in the fischer 344 rat following a single low oral dose of 3.5 mg per kg bodyweight XXXX Yes unpublished	N	BASF

Annex point(s)	Author(s)	Date Year / Month / Day	Title Source BASF DocID GLP or GEP status Published or not	Data Protection Y/N	Owner
IV A 6.2/2	XXXX	XXXX	Corrigendum to SBGR.87.186: The fate of (14C-aniline)-WL115110 in the fischer 344 rat following a single low oral dose of 3.5 mg per kg bodyweight XXXX Yes unpublished	N	BASF
IV A 6.2/3	XXXX	XXXX	Addendum to XXXX: The fate of (14C-aniline)-WL115110 in the fischer 344 rat following a single low oral dose of 3.5 mg per kg bodyweight XXXX Yes unpublished	N	BASF
IV A 6.2/4	XXXX	XXXX	Excretion of an oral dose of (Aniline 14C) WL 115110 in bile duct-cannulated rats XXXX Yes unpublished	N	BASF
IV A 6.2/5	XXXX	XXXX	The fate of (14C-aniline)-WL115110 in the fischer 344 rat following a single high oral dose of 350 mg per kg XXXX Yes unpublished	N	BASF
IV A 6.2/6	XXXX	XXXX	Corrigendum/addendum to XXXX: The fate of (14C-aniline)-WL115110 in the fischer 344 rat following a single high oral dose of 350 mg per kg XXXX Yes unpublished	N	BASF
IV A 6.2/7	XXXX	XXXX	Addendum to XXXX: The fate of (14C-aniline)-WL115110 in the fischer 344 rat following a single high oral dose of 350 mg per kg XXXX Yes unpublished	N	BASF
IV A 6.2/8	XXXX	XXXX	(14C-aniline)-WL115110: Accumulation and depletion from tissues following 28 successive, daily oral low doses (3.5 mg per kg) to female fischer 344 rats XXXX Yes unpublished	N	BASF
IV A 6.2/9	XXXX	XXXX	Corrigendum to XXXX: (14C-aniline)-WL115110: Accumulation and depletion from tissues following 28 successive, daily oral low doses (3.5 mg per kg) to female fischer 344 rats XXXX Yes unpublished	N	BASF
IV A 6.2/10	XXXX	XXXX	(14C-aniline)-WL115110: Accumulation and depletion from tissues following 28 successive, daily oral low doses (3.5 mg per kg) to female fischer 344 rats. II. Nature of the residue in fat XXXX Yes unpublished	N	BASF
IV A 6.2/11	XXXX	XXXX	Corrigendum to XXXX: (14C-aniline)-WL115110: Accumulation and depletion from tissues following 28 successive, daily oral low doses (3.5 mg per kg) to female fischer 344 rats II. Nature of the residue in fat XXXX Yes unpublished	N	BASF
IV A 6.2/12	XXXX	XXXX	The metabolism of 14C-WL115110 in rats XXXX Yes unpublished	N	BASF
IV A 6.2/13	XXXX	XXXX	Report amendment no. 1: The metabolism of 14C-WL115110 in rats XXXX Yes unpublished	N	BASF
IV A 6.2/14	XXXX	XXXX	WL115110 (Cascade): Residues in the body fat of rats following ingestion in diet for 100 days XXXX Yes unpublished	N	BASF

Annex point(s)	Author(s)	Date Year / Month / Day	Title Source BASF DocID GLP or GEP status Published or not	Data Protection Y/N	Owner
IV A 6.2/15	XXXX	XXXX	The absorption and disposition of 14C-WL 115110 in the dog after a single oral administration XXXX Yes unpublished	N	BASF
IV A 6.2/16	XXXX	XXXX	Amendment no. 1: The absorption and disposition of 14C-WL115110 in the dog after a single oral administration XXXX Yes Unpublished	N	BASF
IV A 6.2/17	XXXX	XXXX	Amendment no. 2: The absorption and disposition of 14C-WL115110 in the dog after a single oral administration XXXX Yes unpublished	N	BASF
IV A 6.2/18	XXXX	XXXX	WL115110 kinetic accumulation and elimination study in the dog XXXX Yes unpublished	N	BASF
IV A 6.2/19	XXXX	XXXX	WL115110: Percutaneous penetration of the 10 DC formulation in the rat in vivo XXXX Yes unpublished	N	BASF
IV A 6.3.1/1	XXXX	XXXX	WL115110: A 28 day feeding study in rats XXXX No unpublished	N	BASF
IV A 6.3.1/2	XXXX	XXXX	Corrigendum 1 WL115110: A 28 day feeding study in rats XXXX No unpublished	N	BASF
IV A 6.3.1/3	XXXX	XXXX	Flufenoxuron (WL115110): A 28 day range-finding feeding study in mice XXXX No unpublished	N	BASF
IV A 6.4.1/1	XXXX	XXXX	WL115110: A 90 day feeding study in rats XXXX Yes unpublished	N	BASF
IV A 6.4.1/2	XXXX	XXXX	Corrigenda/Addenda to XXXX: WL115110: A 90 day feeding study in rats XXXX Yes unpublished	N	BASF
IV A 6.4.1/3	XXXX	XXXX	Corrigenda/Addenda to XXXX: WL115110: A 90 day feeding study in rats XXXX Yes unpublished	N	BASF
IV A 6.4.1/4	XXXX	XXXX	WL115110: A 90 day feeding study in mice XXXX No unpublished	N	BASF
IV A 6.4.1/5	XXXX	XXXX	Corrigenda/Addenda to XXXX: WL115110: A 90 day feeding study in mice XXXX No unpublished	N	BASF
IV A 6.4.1/6	XXXX	XXXX	Corrigenda/Addenda to XXXX: WL115110: A 90 day feeding study in mice XXXX No unpublished	N	BASF
IV A 6.4.1/7	XXXX	XXXX	WL115110: A 13 week oral toxicity study in dogs XXXX No unpublished	N	BASF
IV A 6.4.1/8	XXXX	XXXX	Addendum to XXXX - WL115110: A 13 week oral toxicity study in dogs XXXX Yes unpublished	N	BASF
IV A 6.4.1/9	XXXX	XXXX	Supplement to XXXX (WL115110: 13 week oral toxicity study in dogs). A 13 week no effect level XXXX No unpublished	N	BASF

Annex point(s)	Author(s)	Date Year / Month / Day	Title Source BASF DocID GLP or GEP status Published or not	Data Protection Y/N	Owner
IV A 6.4.1/10	XXXX	XXXX	Supplement to XXXX (WL115110 : 13 week oral toxicity study in dogs) XXXX No unpublished	N	BASF
IV A 6.4.1/11	XXXX	XXXX	WL 115110: 52 week oral toxicity study in dogs XXXX Yes unpublished	N	BASF
IV A 6.4.1/12	XXXX	XXXX	Addendum to XXXX - WL 115110: 52 week oral toxicity study in dogs XXXX No unpublished	N	BASF
IV A 6.5/1	XXXX	XXXX	WL115110: A two year chronic toxicity feeding study in rats XXXX Yes unpublished	N	BASF
IV A 6.5/2	XXXX	XXXX	Addendum to XXXX - Volume 4 of 5: WL115110: A 2 year chronic toxicity feeding study in rats XXXX Yes unpublished	N	BASF
IV A 6.5/3	XXXX	XXXX	Corrigenda/addenda to XXXX - WL115110: A 2 year chronic toxicity feeding study in rats XXXX Yes unpublished	N	BASF
IV A 6.6.1/1	Brooks T.M.	1986	Microbial mutagenicity studies with WL115110 XXXX No unpublished	N	BASF
IV A 6.6.1/2	Brooks T.M.	1991	Addendum to XXXX: Microbial mutagenicity of WL115110 XXXX No unpublished	N	BASF
IV A 6.6.1/3	Engelhardt G., Leibold E.	2005	Salmonella typhimurium / Escherichia coli - Reverse mutation assay (standard plate test and preincubation test) with BAS 307 I (Flufenoxuron) XXXX Yes unpublished	Y	BASF
IV A 6.6.2/1	Meyer A.L.	1987	Genotoxicity studies with WL115110 : in vitro chromosome studies with WL115110 XXXX No unpublished	N	BASF
IV A 6.6.2/2	Meyer A.L.	1991	Addendum to XXXX: Genotoxicity studies with WL115110 : in vitro chromosome studies with WL115110 XXXX No unpublished	N	BASF
IV A 6.6.2/3	Meyer A.L.	1988	Genotoxicity studies with WL115110: in vitro chromosome studies with WL115110 and glutathione using chinese hamster ovary (CHO) cells XXXX No unpublished	N	BASF
IV A 6.6.2/4	Meyer A.L.	1991	Addendum to XXXX: Genotoxicity studies with WL115110: in vitro chromosome studies with WL115110 and glutathione using chinese hamster ovary (CHO) cells XXXX No unpublished	N	BASF
IV A 6.6.2/5	Meyer A.L.	1988	Genotoxicity studies with WL115110: in vitro chromosome studies with WL115110 using a rat liver (RL4) cell line XXXX No unpublished	N	BASF
IV A 6.6.2/6	Meyer A.L.	1991	Corrigendum/Addendum to XXXX: Genotoxicity studies with WL115110: in vitro chromosome studies with WL115110 using a rat liver (RL4) cell line XXXX No unpublished	N	BASF

Annex point(s)	Author(s)	Date Year / Month / Day	Title Source BASF DocID GLP or GEP status Published or not	Data Protection Y/N	Owner
IV A 6.6.2/7	McEnaney S.	1992	Study to evaluate the chromosome damaging potential of WL115110 by its effects on cultured human lymphocytes using an in vitro cytogenetics assay XXXX Yes unpublished	N	BASF
IV A 6.6.3/1	Clare M.G.	1986	In vitro mutagenicity studies with WL115110 (insecticide) using cultured chinese hamster V79 cells XXXX No unpublished	N	BASF
IV A 6.6.3/2	Brooks T.M.	1991	Addendum 1 in vitro mutagenicity studies with WL115110 (insecticide) using cultured Chinese hamster V79 cells XXXX No unpublished	N	BASF
IV A 6.6.4/1	XXXX	XXXX	Genotoxicity studies with WL115110 : In vivo chromosome studies with rat bone marrow cells XXXX Yes unpublished	N	BASF
IV A 6.6.4/2	XXXX	XXXX	Report amendment no. 1 - Genotoxicity studies with WL115110 : In vivo chromosome studies with rat bone marrow cells XXXX Yes unpublished	N	BASF
IV A 6.6.4/3	XXXX	XXXX	Report amendment no.2 - Genotoxicity studies with WL115110: In vivo chromosome studies with rat bone marrow cells XXXX) Yes unpublished	N	BASF
IV A 6.6.4/4	XXXX	XXXX	Micronucleus test on WL115110 in mice XXXX Yes unpublished	N	BASF
IV A 6.6.5/1	XXXX	XXXX	Mutagenicity test on WL115110 in the in vivo/in vitro rat primary hepatocyte unscheduled DNA synthesis assay - Revised final report XXXX No unpublished	N	BASF
IV A 6.7/1	XXXX	XXXX	WL115110: A two year oncogenicity feeding study in rats XXXX Yes unpublished	N	BASF
IV A 6.7/2	XXXX	XXXX	Addendum to XXXX - WL115110: A two year oncogenicity feeding study in rats XXXX Yes unpublished	N	BASF
IV A 6.7/3	XXXX	XXXX	Corrigenda/addenda to XXXX - WL115110: A 2 year oncogenicity feeding study in rats XXXX Yes unpublished	N	BASF
IV A 6.7/4	XXXX	XXXX	WL115110: A 2 year oncogenicity feeding study in mice XXXX Yes unpublished	N	BASF
IV A 6.7/5	XXXX	XXXX	Corrigenda/addenda to XXXX - WL115110: A 2 year oncogenicity feeding study in mice XXXX Yes unpublished	N	BASF
IV A 6.7/6	XXXX	XXXX	Corrigenda/addenda to XXXX - WL115110: A 2 year oncogenicity feeding study in mice XXXX Yes unpublished	N	BASF

Annex point(s)	Author(s)	Date Year / Month / Day	Title Source BASF DocID GLP or GEP status Published or not	Data Protection Y/N	Owner
IV A 6.7/7	XXXX	XXXX	Corrigenda/addenda to XXXX - WL115110: A 2 year oncogenicity feeding study in mice XXXX Yes unpublished	N	BASF
IV A 6.7/8	Haseman J.K. et al.	1985	Neoplasms observed in untreated and corn oil gavage control groups of F344/N rats and (C57BL/6N x C3H/HeN)F1 (B6C3F1) mice Literature XXXX No Published in Journal National Cancer Institute, Vol 75, No.5, 975-984	N	Not Applicable
IV A 6.7/9	XXXX	XXXX	WL115110: Oncogenicity study by dietary administration to B6C3F1 mice XXXX Yes unpublished	N	BASF
IV A 6.8.1/1	XXXX	XXXX	Reissued report XXXX: WL115110 teratogenicity study in rats XXXX Yes unpublished	N	BASF
IV A 6.8.1/2	XXXX	XXXX	Addendum to XXXX - WL115110: Teratogenicity study in rats XXXX Yes unpublished	N	BASF
IV A 6.8.1/3	XXXX	XXXX	Response to BGVV concern regarding variations in branching of the great vessels of the heart in rat fetuses XXXX No, not subject to GLP regulations unpublished	N	BASF
IV A 6.8.1/4	XXXX	XXXX	Reissued report XXXX - WL115110: Teratogenicity study in rabbits XXXX Yes unpublished	N	BASF
IV A 6.8.1/5	XXXX	XXXX	Addendum to XXXX - WL115110: Teratogenicity study in rabbits XXXX Yes Unpublished	N	BASF
IV A 6.8.2/1	XXXX	XXXX	The effect of WL115110 on the reproductive function of two generations in the rat XXXX Yes unpublished	N	BASF
IV A 6.8.2/2	XXXX	XXXX	Addendum to SLL 138/891394: The effects of WL115110 on the reproductive function of two generations in the rat XXXX Yes unpublished	N	BASF
IV A 6.8.2/3	XXXX	XXXX	Amendment no. one: The effects of WL115110 on the reproductive function of two generations in the rat XXXX Yes unpublished	N	BASF
IV A 6.8.2/4	XXXX	XXXX	Dietary investigative study in pregnant rats rearing young to weaning. Compound: WL 115110 XXXX No Unpublished	N	BASF
IV A 6.8.2/5	XXXX	XXXX	WL115110: A cross-fostering study, supplementary to a previous two generation rat reproduction study XXXX Yes unpublished	N	BASF
IV A 6.8.2/6	XXXX	XXXX	WL 115110: A CKA embryotoxicity study in rats XXXX No unpublished	N	BASF
IV A 6.9/1	XXXX	XXXX	BAS 307 I - Subacute neurotoxicity study in Wistar rats; Administration in the diet for 4 weeks XXXX Yes unpublished	Y	BASF

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IV A 6.10/1	XXXX	XXXX	WL129183: Acute oral toxicity XXXX Yes unpublished	N	BASF
IV A 6.10/2	Brooks T.M., Wiggins D.E.	1990	Bacterial mutagenicity studies with WL129183 Sittingbourne Research Centre; Kent ME9 8AG; United Kingdom FX-470-018 Yes unpublished	N	BASF
IV A 6.10/3	XXXX	XXXX	WL115096: Acute oral toxicity XXXX Yes unpublished	N	BASF
IV A 6.10/4	XXXX	XXXX	The acute oral and percutaneous toxicity WL125892 XXXX No unpublished	N	BASF
IV A 6.10/5	XXXX	XXXX	WL125892: A 28 day oral toxicity study in Fischer 344 rats XXXX No unpublished	N	BASF
IV A 6.10/6	Brooks T.M., Wiggins D.E.	1990	Bacterial mutagenicity studies with WL115096 XXXX Yes unpublished	N	BASF
IV A 6.10/7	Brooks T.M., Wiggins D.E.	1987	Bacterial mutagenicity studies with WL125892 XXXX No unpublished	N	BASF
IV A 6.10/8	Engelhardt G., Leibold E.	2005	In vitro gene mutation test with Reg. No. 241208 (Metabolite of BAS 307 I, Flufenoxuron) in CHO cells (HPRT locus assay) XXXX Yes unpublished	Y	BASF
IV A 6.10/9	Engelhardt G.	2005	Amendment No. 1 to the report: In vitro gene mutation test with Reg. No. 241208 (Metabolite of BAS 307 I, Flufenoxuron) in CHO cells (HPRT locus assay) XXXX Yes unpublished	Y	BASF
IV A 6.10/10	Brooks T.M., Wiggins D.E.	1992	WL115096: In vitro chromosome studies with cultured chinese hamster ovary (CHO) cells XXXX Yes unpublished	N	BASF
IV A 6.10/11	XXXX	XXXX	In vivo unscheduled DNA synthesis (UDS) assay with Reg. No. 241208 (Metabolite of BAS 307 I, Flufenoxuron) in rat hepatocytes - Single oral administration XXXX Yes unpublished	Y	BASF
IV A 6.10/12	XXXX	XXXX	Amendment No. 1 to the report: In vivo unscheduled DNA synthesis (UDS) assay with Reg. No. 241208 (Metabolite of BAS 307 I, Flufenoxuron) in rat hepatocytes - Single oral administration XXXX Yes unpublished	Y	BASF
IV A 6.10/13	Brooker P. et al.	1987	Analysis of metaphase chromosomes obtained from CHO cells cultured in vitro and treated with WL125892 XXXX No unpublished	N	BASF
IV A 6.10/14	XXXX	XXXX	WL125892 (95-06-0752): Micronucleus test in the mouse XXXX Yes unpublished	N	BASF

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IV A 6.10/15	Engelhardt G., Leibold E.	2005	The low pH 6.7 in vitro cell transformation assay with Reg. No. 241208 (Metabolite of BAS 307 I, Flufenoxuron) in Syrian hamster Embryo cells (SHE Assay) XXXX Yes unpublished	Y	BASF
IV A 6.10/16	Engelhardt G.,	2005	Amendment No. 1 to the report: The low pH 6.7 in vitro cell transformation assay with Reg. No. 241208 (Metabolite of BAS 307 I, Flufenoxuron) in Syrian hamster Embryo cells (SHE Assay) XXXX Yes unpublished	Y	BASF
I VA 6.10/17	XXXX	XXXX	Bacterial mutagenicity studies with 2,6-Difluorobenzamide (DFBAM) XXXX No unpublished **Business Confidential Information – See BCI folder**	Y*	BASF
IV A 6.10/18	XXXX	XXXX	WL128196: Bacterial mutagenicity studies XXXX Yes unpublished **Business Confidential Information – See BCI folder**	Y*	BASF
IV A 6.10/19	XXXX	XXXX	Bacterial mutagenicity studies with WL131767 XXXX Yes unpublished **Business Confidential Information – See BCI folder**	Y*	BASF
IV A 6.10/20	Evelyn K.A., Malloy H.T.	1938	Microdetermination of oxyhemoglobin, methemoglobin, and sulfhemoglobin in a single sample of blood Literature XXXX No Published in The Journal of Biological Chemistry, Volume 126, 655-662	N	Not Applicable
IV A 6.10/21	XXXX	XXXX	Haemoglobin binding of WL 115110 (Cascade) and its precursor WL 125892: A pilot study in the rat XXXX No unpublished	N	BASF
IV A 6.10/22	XXXX	XXXX	Replicative DNA synthesis (RDS) test using rat livers on WL115110 XXXX No unpublished	N	BASF
IV A 6.12.1/1	Deweerdt J., Mommee J.C.	1997	SNPE Chimie - Health surveillance program in Flufenoxuron production plant XXXX No unpublished	N	SNPE
IV A 6.12.1/2	Flynn A.	2003	Medical information (Great Lakes) XXXX No unpublished	N	Great Lakes
IV A 6.12.1/3	Evrard P.	2004	Medical information (Isochem) XXXX No unpublished	N	Isochem

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IV A 7.1.1.1.1/1	Langner E.J., Camilleri P.	1987	Hydrolysis of WL115110 in aqueous media XXXX No unpublished	N	BASF
IV A 7.1.1.1.1/2	Hassink J.	2003	Hydrolysis of BAS 307 I XXXX Yes unpublished	Y	BASF
IV A 7.1.1.1.2/1	Camilleri P., Langner E.J.	1987	Photodecomposition of aqueous solutions of Flufenoxuron by sunlight XXXX No unpublished	N	BASF
IV A 7.1.1.1.2/2	Langner E.J.	1991	Corrigendum to SBGR.87.150: Photodecomposition of aqueous solutions of Flufenoxuron by sunlight XXXX No unpublished	N	BASF
IV A 7.1.1.1.2/3	Burgener A.	2001	14C-Flufenoxuron (BAS 307 I): Quantum yield of direct phototransformation in water XXXX Yes unpublished	Y	BASF
IV A 7.1.1.1.2/4	Hassink J.	2003	Aqueous photolysis of BAS 307 I XXXX Yes unpublished	Y	BASF
IV A 7.1.1.1.2/5	Mamouni A., van der Gaauw A.	2001	14C-Flufenoxuron (BAS 307 I): Photolysis in natural water XXXX Yes unpublished	Y	BASF
IV A 7.1.1.1.2/6	Mamouni A., van der Gaauw A.	2001	Amendment no.1: 14C-Flufenoxuron (BAS 307 I): Photolysis in natural water XXXX Yes unpublished	Y	BASF
IV A 7.1.1.2.1/1	Turner S.J., Watkinson R.J.	1986	WL115110: An assessment of the ready biodegradability XXXX No unpublished	N	BASF
IV A 7.1.2.2.2/1	Ebert D.	2003	Degradation of BAS 307 I (Flufenoxuron) in water/sedimentsystems under aerobic conditions XXXX Yes unpublished	Y	BASF
IV A 7.1.2.2.2/2	Fent G.	2003	Degradation and distribution of BAS 307 I in a water-sediment system under outdoor conditions XXXX Yes unpublished	Y	BASF
IV A 7.2.1/1	Richardson K.A.	1987	The effect of soil pH on the degradation of 14C-WL115110 XXXX No unpublished	N	BASF
IV A 7.2.2.1/1	Richardson K.A.	1990	A comparison of the degradation of (aniline-14C)-WL115110 in soil under aerobic and anaerobic conditions XXXX Yes unpublished	N	BASF
IV A 7.2.2.1/2	Richardson K.A.	1991	A comparison of the degradation of (aniline-14C)-WL115110 in soil under aerobic and anaerobic conditions XXXX Yes unpublished	N	BASF
IV A 7.2.2.1/3	Standen M.E., Hill A.D.	1993	Cascade (WL115110): A comparison of the degradation of (aniline-14C)- and (toluyl-14C)-Cascade in soil under aerobic and anaerobic conditions XXXX Yes unpublished	N	BASF

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IV A 7.2.2.1/4	Goodyear A., Gross R.	2001	14C-Flufenoxuron (BAS 307 I): Aerobic soil rate of degradation in three soils XXXX Yes unpublished	Y	BASF
IV A 7.2.2.1/5	Stephan A., Ebert D.	2003	Degradation rates of BAS 307 I (Flufenoxuron) and Reg.No. 406 4702 (CL932338) under aerobic conditions in different soils (DT50/DT90) XXXX Yes unpublished	Y	BASF
IV A 7.2.2.1/6	Beigel C.	2004	Calculation of the DT50 values at 10°C of BAS 307 I (Flufenoxuron) and Reg.No. 4064702 (CL 932338) in different soils under aerobic conditions XXXX No, not subject to GLP regulations unpublished	Y	BASF
IV A 7.2.2.2/1	Smalley R.	2003	Field soil dissipation of BAS 307 I in the formulation BAS 307 QA I on bare soil in France (S) and Spain, 2001-2002 XXXX Yes unpublished	Y	BASF
IV A 7.2.2.3/1	Standen M.E., Hill A.D.	1993	Cascade (WL115110): A comparison of the degradation of (aniline-14C)- and (toluyl-14C)-Cascade in soil under aerobic and anaerobic conditions XXXX Yes unpublished	N	BASF
IV A 7.2.2.3/2	Goodyear A., Gross R.	2001	14C-Flufenoxuron (BAS 307 I): Aerobic soil rate of degradation in three soils XXXX Yes unpublished	Y	BASF
IV A 7.2.2.4/1	Richardson K.A.	1990	A comparison of the degradation of (aniline-14C)-WL115110 in soil under aerobic and anaerobic conditions XXXX Yes unpublished	N	BASF
IV A 7.2.2.4/2	Richardson K.A.	1991	A comparison of the degradation of (aniline-14C)-WL115110 in soil under aerobic and anaerobic conditions XXXX Yes unpublished	N	BASF
IV A 7.2.2.4/3	Standen M.E., Hill A.D.	1993	Cascade (WL115110): A comparison of the degradation of (aniline-14C)- and (toluyl-14C)-Cascade in soil under aerobic and anaerobic conditions Sittingbourne Research Centre; Kent ME9 8AG; United Kingdom FX-620-037 Yes unpublished	N	BASF
IV A 7.2.2.4/4	Lewis C.J., Gross R.	2001	14C-Flufenoxuron (BAS 307 I): Soil photolysis under artificial sunlight XXXX Yes unpublished	Y	BASF
IV A 7.2.3.1/1	Hill A.D., Standen M.E.	1993	[Carbonyl-14C] WL115110 (Cascade): Adsorption/desorption in three soils XXXX Yes unpublished	N	BASF
IV A 7.2.3.1/2	Rosenwald J.	2002	Adsorption/desorption of 14C-Flufenoxuron (BAS 307 I) in three soils XXXX Yes unpublished	Y	BASF
IV A 7.2.3.1/3	Zirnstein M.	2003	Adsorption/desorption - Study of BAS 307 I metabolite (Reg.No. 406 4702) on five European soils XXXX Yes unpublished	Y	BASF
IV A 7.3.1/1	Hassink J.	2003	Photochemical oxidative degradation of Flufenoxuron BAS 307 I (QSAR estimates) XXXX No, not subject to GLP regulations unpublished	Y	BASF

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IV A 7.3.2/1	Hassink J.	2003	Volatilisation of BAS 307 I after application of BAS 307 10 I on soil and on plant surfaces XXXX Yes unpublished	Y	BASF
IV A 7.4.1.1/1	XXXX	XXXX	WL115110: Acute toxicity to Salmo gairdneri, Daphnia magna and Selenastrum capricornutum XXXX Yes unpublished	N	BASF
IV A 7.4.1.1/2	XXXX	XXXX	Acute toxicity of Flufenoxuron (AC 811678) technical to zebra fish (Brachydanio rerio) under flow-through test conditions XXXX Yes unpublished	Y	BASF
IV A 7.4.1.1/3	XXXX	XXXX	Acute toxicity of SKI-8503 to Cyprinus carpio XXXX No unpublished	N	BASF
IV A 7.4.1.1/4	XXXX	XXXX	4-Amino-3-Fluorophenol: Acute toxicity to Daphnia magna and Salmo gairdneri XXXX Yes unpublished	N	BASF
IV A 7.4.1.1/5	XXXX	XXXX	4-Amino-3-Fluorophenol : Acute toxicity to Daphnia magna and Salmo gairdneri XXXX) Yes unpublished	N	BASF
IV A 7.4.1.1/6	XXXX	XXXX	WL125892: Acute toxicity to Salmo gairdneri and Daphnia magna XXXX Yes unpublished	N	BASF
IV A 7.4.1.1/7	XXXX	XXXX	Reg.No. 406 4702 (metabolite of BAS 307 I) - Acute toxicity study on the rainbow trout (Oncorhynchus mykiss) in a static system over 96 hours XXXX Yes unpublished	Y	BASF
IV A 7.4.1.1/8	XXXX	XXXX	Reg.No. 102719 (metabolite of BAS 307 I) - Acute toxicity study on the rainbow trout (Oncorhynchus mykiss) in a static system over 96 hours XXXX Yes unpublished	Y	BASF
IV A 7.4.1.2/1	Funk M.	2003	Effect of radiolabelled BAS 307 I on the immobility of Daphnia magna STRAUS in a 48 hours static, acute toxicity test XXXX Yes unpublished	Y	BASF
IV A 7.4.1.2/2	XXXX	XXXX	WL115110: Acute toxicity to Salmo gairdneri, Daphnia magna and Selenastrum capricornutum XXXX Yes unpublished	N	BASF
IV A 7.4.1.2/3	Shumei W.	1987	Acute toxicity of SKI-8503 on Daphnia carinata XXXX No unpublished	N	BASF
IV A 7.4.1.2/4	Pearson N., Girling A.E.	1989	Flufenoxuron (WL115110): Acute toxicity to Gammarus pulex, Lymnaea stagnalis, Tubifex tubifex and chiromonus lugubris XXXX Yes unpublished	N	BASF
IV A 7.4.1.2/5	XXXX	XXXX	4-Amino-3-Fluorophenol: Acute toxicity to Daphnia magna and Salmo gairdneri XXXX Yes unpublished	N	BASF

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IV A 7.4.1.2/6	XXXX	XXXX	4-Amino-3-Fluorophenol : Acute toxicity to Daphnia magna and Salmo gairdneri XXXX) Yes unpublished	N	BASF
IV A 7.4.1.2/7	XXXX	XXXX	WL125892: Acute toxicity to Salmo gairdneri and Daphnia magna XXXX Yes unpublished	N	BASF
IV A 7.4.1.2/8	Jatzek H.-J.	2003	Reg.No. 406 4702 (metabolite of BAS 307 I) - Determination of the acute effect on the swimming ability of the water flea Daphnia magna STRAUS XXXX Yes unpublished	Y	BASF
IV A 7.4.1.2/9	Jatzek H.-J.	2003	Reg.No. 102 719 (metabolite of BAS 307 I) - Determination of the acute effect on the swimming ability of the water flea Daphnia magna STRAUS XXXX Yes unpublished	Y	BASF
IV A 7.4.1.2/10	Jatzek H.-J.	2003	Reg.No. 241 208 (metabolite of BAS 307 I) - Determination of the acute effect on the swimming ability of the water flea Daphnia magna STRAUS XXXX Yes unpublished	Y	BASF
IV A 7.4.1.2/11	Jatzek H.-J.	2003	Reg.No. 206925 (metabolite of BAS 307 I, Flufenoxuron) - Determination of the acute effect on the swimming ability of the water flea Daphnia magna STRAUS XXXX Yes unpublished	Y	BASF
IV A 7.4.1.3/1	Kubitza J.	2003	Effect of BAS 307 I (Flufenoxuron) on the growth of the green alga Pseudokirchneriella subcapitata XXXX Yes unpublished	Y	BASF
IV A 7.4.1.3/2	XXXX	XXXX	WL115110: Acute toxicity to Salmo gairdneri, Daphnia magna and Selenastrum capricornutum XXXX Yes unpublished	N	BASF
IV A 7.4.1.3/3	Hanstveit A.O., Oldersma H.	1993	Effect of WL 125892 on the growth of alga Selenastrum capricornutum (OECD 201) XXXX Yes unpublished	N	BASF
IV A 7.4.1.3/4	Jatzek H.-J.	2003	Reg.No. 102 719 (metabolite of BAS 307 I) - Determination of the inhibitory effect on the cell multiplication of unicellular green algae XXXX Yes unpublished	Y	BASF
IV A 7.4.1.3/5	Jatzek H.-J.	2003	Reg.No. 406 4702 (metabolite of BAS 307 I) - Determination of the inhibitory effect on the cell multiplication of unicellular green algae XXXX Yes unpublished	Y	BASF
IV A 7.4.1.4/1	Lebertz H., Yan Z.	2001	Flufenoxuron (BAS 307I): Activated sludge, respiration inhibition test XXXX Yes unpublished	Y	BASF
IV A 7.4.3.1/1	XXXX	XXXX	Flufenoxuron (Cascade): An early life stage test with the fathead minnow Pimephales promelas (Rafinesque) XXXX Yes unpublished	N	BASF
IV A 7.4.3.2/1	XXXX	XXXX	Flufenoxuron 100 DC (BAS 307 10 I): Zebrafish (Danio rerio), static full life cycle test with sediment XXXX Yes unpublished	Y	BASF

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IV A 7.4.3.3.1/1	XXXX	XXXX	Flufenoxuron: The accumulation and elimination by rainbow trout (Oncorhynchus mykiss) in a continuous flow test XXXX Yes unpublished	N	BASF
IV A 7.4.3.3.1/2	XXXX	XXXX	Bioaccumulation and metabolism of 14C-BAS 307 I (Flufenoxuron) in rainbow trout XXXX Yes unpublished	Y	BASF
IV A 7.4.3.3.1/3	Junker M.	2004	Bioaccumulation of BAS 307 I (Flufenoxuron) – applied as formulated product BAS 307 QA I – in an aquatic ecosystem XXXX Yes unpublished	Y	BASF
IV A 7.4.3.4/1	Pearson N., Girling A.	1989	Flufenoxuron: Chronic toxicity to Daphnia magna XXXX Yes unpublished	N	BASF
IV A 7.4.3.4/2	Harrison E.G.	1988	Effects of Cascade emulsifiable concentrate (EC) and water dispersable (WDC) formulations on zooplankton in enclosures in experimental ponds XXXX Yes unpublished	N	BASF
IV A 7.4.3.5.1/1	Mattock S. et al.	2001	Effects of 14C labelled Flufenoxuron on the development of sediment-dwelling larvae of Chironomus riparius in a water-sediment system XXXX Yes unpublished	Y	BASF
IV A 7.4.3.5.1/2	Funk M.	2003	Effect of Reg.No. 4064702 (metabolite of BAS 307 I, Flufenoxuron) on the development of sediment dwelling larvae of Chironomus riparius in a water-sediment system XXXX Yes unpublished	Y	BASF
IV A 7.4.3.5.1/3	Toy R.	1993	Flufenoxuron: Toxic effects of soils treated with Cascade 100 g/L DC (SF07055) on Chironomus riparius XXXX Yes unpublished	Y	BASF
IV A 7.4.3.5.1/4	Egeler, P. and Seck, C	2006	Flufenoxuron (BAS 307 I): Chronic toxicity to the aquatic Oligochaete *Lumbriculus variegatus* exposed to spiked sediment in a 28 d study. XXXX Yes unpublished	Y	BASF
IV A 7.4.3.5.1/5	Weltje, L. and Pupp, A.	2007	Chronic toxicity of flufenoxuron (BAS 307 I) to the non-biting midge *Chironomus riparius* exposed via spiked-sediment. XXXX Yes unpublished	Y	BASF
IV A 7.5.1.1/1	Koelzer U.	2003	Assessment of the side effects of BAS 307 QA I on the activity of the soil microflora, nitrogen turnover XXXX Yes unpublished	Y	BASF
IV A 7.5.1.1/2	Koelzer U.	2003	Assessment of the side effects of BAS 307 QA I on the activity of the soil microflora, short-term respiration XXXX Yes unpublished	Y	BASF
IV A 7.5.1.1/3	Koelzer U.	2003	Effects of CL 932338 (metabolite of BAS 307 I) on the activity of the soil microflora, nitrogen transformation test XXXX Yes unpublished	Y	BASF
IV A 7.5.1.2/1	Hillaby J.M.	1987	The toxicity of WL115110 to the earthworm, Eisenia foetida L. (Oligocheata: Lumbriculidae) in laboratory tests XXXX Yes unpublished	N	BASF

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IV A 7.5.1.3/1	Sack D.	2003	BAS 307 QA I: Effects on non-target plants in the greenhouse - A limit test XXXX Yes unpublished	Y	BASF
IV A 7.5.1.2/2	Staebler D.	2003	Acute toxicity of CL 932 338 (metabolite of BAS 307 I) on earthworms, Eisenia fetida using an artificial soil test XXXX Yes unpublished	Y	BASF
IV A 7.5.2.1/1	Luehrs U.	2001	Effects of Flufenoxuron technical (AC 811678) on reproduction and growth of earthworms Eisenia fetida (Savigny 1826) in artificial soil XXXX Yes unpublished	Y	BASF
IV A 7.5.3.1.1/1	XXXX	XXXX	The acute oral toxicity (LD50) of WL 115110 to the bobwhite quail XXXX Yes unpublished	N	BASF
IV A 7.5.3.1.2/1	XXXX	XXXX	The subacute dietary toxicity (LC50) ofWL 115110 to the bobwhite quail XXXX Yes Unpublished	N	BASF
IV A 7.5.3.1.2/2	XXXX	XXXX	The subacute dietary toxicity (LC50) of WL 115110 to the mallard duck XXXX Yes unpublished	N	BASF
IV A 7.5.3.1.3/1	XXXX	XXXX	WL 115110: The effects of dietary inclusion on reproduction and tissue residues in the bobwhite quail XXXX Yes unpublished	N	BASF
IV A 7.5.3.1.3/2	XXXX	XXXX	WL 115110 = Flufenoxuron new statistical evaluation of a 1-generation reproduction study on the bobwhite quail (Colinus virginianus) XXXX No, not subject to GLP regulations unpublished	Y	BASF
IV A 7.5.4.1/1	XXXX	XXXX	Effects of Flufenoxuron technical (AC 811678) (Acute contact and oral LD50) on honey bees (Apis mellifers L.) (Hymenoptera, Apidae) in the laboratory XXXX Yes unpublished	Y	BASF

Annex point(s)	Author(s)	Date Year / Month / Day	Title Source BASF DocID GLP or GEP status Published or not	Data Protection Y/N	Owner
IV A 8.4/1	Schenk W.	2001	Possible procedures for the decontamination of water from Flufenoxuron XXXX No unpublished	Y	BASF

Annex point(s)	Author(s)	Date Year / Month / Day	Title Source BASF DocID GLP or GEP status Published or not	Data Protection Y/N	Owner
IV A 2.8/2	X	x	Analytical characterization of five batches Flufenoxuron technical grade X. x Yes unpublished **Business Confidential Information – See BCI folder**	Y*	BASF
IV A 2.6/1	X	x	Flufenoxuron (AC 811678) technical material: Description of the materials used to produce the product and of the production process conform EPA product properties test guidelines OPPTS 830.1600 and OPPTS 830.1620 X. x No, not subject to GLP regulations unpublished **Business Confidential Information – See BCI folder**	Y*	BASF
IV A 2.8/1	X	x	The analytical profile for representative manufacturing batches of Flufenoxuron technical grade active ingredient and the minimum and maximum values of each component for the re-registration of AC 811678 (Flufenoxuron) technical grade active ingredient with the European Union X x Yes unpublished **Business Confidential Information – See BCI folder**	Y*	BASF
IV A 2.7/1	X.	x	Flufenoxuron TC: Composition of the technical grade active ingredient (TGAI) X. x No, not subject to GLP regulations unpublished **Business Confidential Information – See BCI folder**	Y*	BASF

* Data protection requested as part of Business Confidential Information

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IV A 3.9/2	Bates M. et al.	2002	CL 932338, CL 211558, and CL 359882 (metabolites of BAS 307 I, Flufenoxuron): Determination of the partition coefficient XXXX Yes unpublished	Y	BASF
IV A 3.5/2	Bates M.L., Rice P.	2003	CL 932338, CL 211558, and CL 359882 (metabolites of BAS 307 I, flufenoxuron): Determination of the water solubility XXXX Yes unpublished	Y	BASF
IV A 3.1.1/1	Camilleri P. et al.	1986	Melting point and differential thermal analysis of WL115110 XXXX No unpublished	N	BASF
IV A 3.1.2/1	Camilleri P. et al.	1986	Melting point and differential thermal analysis of WL115110 XXXX No unpublished	N	BASF
IV A 3.6/1	Camilleri P., Langner E.J.	1986	Solubility and pKa of WL115110 in water XXXX No unpublished	N	BASF
IV A 3.1.1/2	Daum A.	2001	Determination of the thermal stability and the stability in air of Flufenoxuron (BAS 307 I, CL# 811 678, Reg.No. 243 154) PAI XXXX Yes unpublished	Y	BASF
IV A 3.1.2/2	Daum A.	2001	Determination of the thermal stability and the stability in air of Flufenoxuron (BAS 307 I, CL# 811 678, Reg.No. 243 154) PAI XXXX Yes unpublished	Y	BASF
IV A 3.4/2	Daum A.	2003	Spectra (UV, NMR, IR, MS) of Flufenoxuron (BAS 307 I, Reg.No. 243 154) PAI XXXX Yes unpublished	Y	BASF
IV A 3.7/1	Daum A.	2001	Determination of the solubility in organic solvents of BAS 307 I (Flufenoxuron, Reg.No. 243 154 TGAI (identical with CL 811 678)) XXXX Yes unpublished	Y	BASF
IV A 3.10/1	Daum A.	2001	Determination of the thermal stability and the stability in air of Flufenoxuron (BAS 307 I, CL# 811 678, Reg.No. 243 154) PAI XXXX Yes unpublished	Y	BASF
IV A 3.4/1	Fang L.Y.	1996	CL 811678 (Flufenoxuron) spectral database XXXX No unpublished	N	BASF
IV A 3.1.3/1	Kaestel R.	2001	Density determination of the technical material of Flufenoxuron XXXX Yes unpublished	Y	BASF
IV A 3.3/1	Kaestel R.	2001	Physical properties of Flufenoxuron (TC) XXXX Yes unpublished	Y	BASF
IV A 3.3/2	Kaestel R.	2001	Physical properties of Flufenoxuron (PAI) XXXX Yes unpublished	Y	BASF
IV A 3.13/1	Kaestel R.	2001	Physical properties of Flufenoxuron (TC) XXXX Yes unpublished	Y	BASF
IV A 3.2/1	Langner E.J.	1988	Physico-chemical properties of WL115110 XXXX Yes unpublished	N	BASF

Annex point(s)	Author(s)	Date Year / Month / Day	Title Source BASF DocID GLP or GEP status Published or not	Data Protection Y/N	Owner
IV A 3.5/1	Langner E.J.	1988	Physico-chemical properties of WL115110 XXXX Yes unpublished	N	BASF
IV A 3.9/1	Langner E.J.	1988	Physico-chemical properties of WL115110 XXXX Yes unpublished	N	BASF
IV A 3.2.1/1	Rice P.	2000	Flufenoxuron (BAS 307 I): Calculation of Henry's law constant XXXX No, not subject to GLP regulations unpublished	Y	BASF
IV A 3.11/1	Van Helvoirt J.A.M.W.	1990	Determination of the flammability of Flufenoxuron XXXX Yes unpublished	N	BASF
IV A 3.11/2	Van Helvoirt J.A.M.W.	1990	Determination of the auto-flammability of Flufenoxuron XXXX Yes unpublished	N	BASF
IV A 3.16/1	Van Helvoirt J.A.M.W.	1990	Determination of the oxidizing properties of Flufenoxuron XXXX Yes unpublished	N	BASF
I VA 3.15/1	Van Helvoirt J.A.M.W., Cardinaals J.M.	1990	Determination of the explosive properties of Flufenoxuron XXXX Yes unpublished	N	BASF

Annex point(s)	Author(s)	Date Year / Month / Day	Title Source BASF DocID GLP or GEP status Published or not	Data Protection Y/N	Owner
IV A 4.1/3	X	x	Validation of high performance liquid chromatographic method M-2647.02 to assay minor components in AC 811678 (Flufenoxuron) technical grade active ingredient X x Yes unpublished **Business Confidential Information – See BCI folder**	Y*	BASF
IV A 4.2/2	Anonymous	1996	Determination of residues of WL115110 in soil - Liquid chromatographic method XXXX No unpublished	N	BASF
IV A 4.2/3	Anonymous	1989	Determination of residues of WL 129183 in soil - liquid chromatographic method XXXX No unpublished	N	BASF
IV A 4.2/6	Anonymous	1986	Determination of residues of WL115110 in water - Liquid chromatographic method XXXX No unpublished	N	BASF
IV A 4.1/1	Fang L.Y.	1996	Validation of the high pressure liquid chromatographic method M-2636 for the determination of CL 811,678 in technical grade Flufenoxuron (CL 811,678) XXXX Yes unpublished	N	BASF
IV A 4.1/2	X	x	Validation of high resolution gas chromatographic method M-2691 to assay residual solvents in AC 811678 (Flufenoxuron) technical grade active ingredient X x Yes unpublished **Business Confidential Information – See BCI folder**	Y*	BASF
IV A 4.1/4	X	x	Determination of the by-compounds in technical active ingredient BAS 307 I (Flufenoxuron) by reversed phase HPLC X. x No unpublished **Business Confidential Information – See BCI folder**	Y*	BASF
IV A 4.1/5	X	x	Validation of the analytical method CP 415 for the determination of the by-compounds in techn. BAS 307 I (Flufenoxuron) by HPLC X. x Yes unpublished **Business Confidential Information – See BCI folder**	Y*	BASF
IV A 4.2/4	Jones S.	2002	Method validation of RLA 12637 HPLC/MS method for the determination of BAS 307 I (CL811678, flufenoxuron) and CL 032338 residues in soil XXXX Yes unpublished	Y	BASF
IV A 4.2/1	Kennedy E.M.	1994	Flufenoxuron (WL115110: Cascade): Determination of residues in soil - Development and validation of a liquid chromatographic method XXXX Yes unpublished	N	BASF
IV A 4.2/5	Smalley R.	2002	Validation of method RLA 12637 for the analysis of BAS 307 I and CL 932338 in soil down to an LOQ of 0.001mg/kg XXXX Yes unpublished	Y	BASF
IV A 4.2/7	Smalley R.	2003	Validation of method RLA 12680 for the analysis of BAS 307 I and metabolite CL 932338 in water at an LOQ of 0.01 µg/litre XXXX Yes unpublished	Y	BASF

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IV A 4.2/8	Zangmeister W.	2003	Validation of analytical method 533: Determination of BAS 307 I (Flufenoxuron) in air by LC/MS-MS XXXX Yes unpublished	Y	BASF

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IV A 6.6.4/1	X	x	Genotoxicity studies with WL115110 : In vivo chromosome studies with rat bone marrow cells X x Yes unpublished	N	BASF
IV A 6.6.4/2	X	x	Report amendment no. 1 - Genotoxicity studies with WL115110 : In vivo chromosome studies with rat bone marrow cells X x Yes unpublished	N	BASF
IV A 6.6.4/3	X	x	Report amendment no.2 - Genotoxicity studies with WL115110: In vivo chromosome studies with rat bone marrow cells X x (Amendment 2) Yes unpublished	N	BASF
IV A 6.2/14	X	x	WL115110 (Cascade): Residues in the body fat of rats following ingestion in diet for 100 days X x Yes unpublished	N	BASF
IV A 6.7/2	X	x	Addendum to XXXX - WL115110: A two year oncogenicity feeding study in rats X x Yes unpublished	N	BASF
IV A 6.4.1/3	X	x	Corrigenda/Addenda to XXXX: WL115110: A 90 day feeding study in rats X x Yes unpublished	N	BASF
IV A 6.4.1/6	X	x	Corrigenda/Addenda to XXXX: WL115110: A 90 day feeding study in mice X x No unpublished	N	BASF
IV A 6.5/3	X	x	Corrigenda/addenda to XXXX - WL115110: A 2 year chronic toxicity feeding study in rats X x Yes unpublished	N	BASF
IV A 6.7/3	X	x	Corrigenda/addenda to XXXX - WL115110: A 2 year oncogenicity feeding study in rats X x Yes unpublished	N	BASF
IV A 6.7/6	X	x	Corrigenda/addenda to XXXX - WL115110: A 2 year oncogenicity feeding study in mice X x Yes unpublished	N	BASF
IV A 6.10/21	X	x	Haemoglobin binding of WL 115110 (Cascade) and its precursor WL 125892: A pilot study in the rat X x No unpublished	N	BASF
IV A 6.7/9	X	x	WL115110: Oncogenicity study by dietary administration to B6C3F1 mice X x Yes unpublished	N	BASF

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IV A 6.10/13	Brooker P. et al.	1987	Analysis of metaphase chromosomes obtained from CHO cells cultured in vitro and treated with WL125892 XXXX No unpublished	N	BASF
IV A 6.6.1/1	Brooks T.M.	1986	Microbial mutagenicity studies with WL115110 XXXX No unpublished	N	BASF
IV A 6.6.1/2	Brooks T.M.	1991	Addendum to SBGR.86.026: Microbial mutagenicity of WL115110 XXXX No unpublished	N	BASF
IV A 6.6.3/2	Brooks T.M.	1991	Addendum 1 in vitro mutagenicity studies with WL115110 (insecticide) using cultured Chinese hamster V79 cells XXXX No unpublished	N	BASF
IV A 6.10/7	Brooks T.M., Wiggins D.E.	1987	Bacterial mutagenicity studies with WL125892 XXXX No unpublished	N	BASF
I VA 6.10/17	X.	x	Bacterial mutagenicity studies with 2,6-Difluorobenzamide (DFBAM) X x No unpublished **Business Confidential Information – See BCI folder**	Y*	BASF
I VA 6.10/11	X	x	Bacterial mutagenicity studies with 2,6-Difluorobenzamide (DFBAM) X x No unpublished **Business Confidential Information – See BCI folder**	Y*	BASF
IV A 6.10/2	Brooks T.M., Wiggins D.E.	1990	Bacterial mutagenicity studies with WL129183 XXXX Yes unpublished	N	BASF
IV A 6.10/6	Brooks T.M., Wiggins D.E.	1990	Bacterial mutagenicity studies with WL115096 XXXX Yes unpublished	N	BASF
IV A 6.10/19	X	x	Bacterial mutagenicity studies with WL131767 X x Yes unpublished **Business Confidential Information – See BCI folder**	Y*	BASF
IV A 6.10/18	X	x	WL128196x: Bacterial mutagenicity studies X x Yes unpublished **Business Confidential Information – See BCI folder**	Y*	BASF
IV A 6.10/10	Brooks T.M., Wiggins D.E.	1992	WL115096: In vitro chromosome studies with cultured chinese hamster ovary (CHO) cells XXXX Yes unpublished	N	BASF
IV A 6.8.1/3	X	x	Response to BGVV concern regarding variations in branching of the great vessels of the heart in rat fetuses X x No, not subject to GLP regulations unpublished	N	BASF
IV A 6.6.5/1	X	x	Mutagenicity test on WL115110 in the in vivo/in vitro rat primary hepatocyte unscheduled DNA synthesis assay - Revised final report X x No unpublished	N	BASF

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IV A 6.6.3/1	Clare M.G.	1986	In vitro mutagenicity studies with WL115110 (insecticide) using cultured chinese hamster V79 cells XXXX No unpublished	N	BASF
IV A 6.4.1/9	X	x	Supplement to IRI report no. XXXX (WL115110: 13 week oral toxicity study in dogs). A 13 week no effect level X x No unpublished	N	BASF
IV A 6.4.1/10	X	x	Supplement to IRI report no. XXXX (WL115110 : 13 week oral toxicity study in dogs) X x No unpublished	N	BASF
IV A 6.12.1/1	Deweerdt J., Mommee J.C.	1997	SNPE Chimie - Health surveillance program in Flufenoxuron production plant XXXX No unpublished	N	SNPE
IV A 6.10/14	X	x	WL125892 (95-06-0752): Micronucleus test in the mouse X x Yes unpublished	N	BASF
IV A 6.2/16	X	x	Amendment no. 1: The absorption and disposition of 14C-WL115110 in the dog after a single oral administration X x Yes Unpublished	N	BASF
IV A 6.2/17	X	x	Amendment no. 2: The absorption and disposition of 14C-WL115110 in the dog after a single oral administration X x Yes unpublished	N	BASF
IV A 6.6.1/3	Engelhardt G., Leibold E.	2005	Salmonella typhimurium / Escherichia coli - Reverse mutation assay (standard plate test and preincubation test) with BAS 307 I (Flufenoxuron) XXXX Yes unpublished	Y	BASF
IV A 6.10/8	Engelhardt G., Leibold E.	2005	In vitro gene mutation test with Reg. No. 241208 (Metabolite of BAS 307 I, Flufenoxuron) in CHO cells (HPRT locus assay) XXXX Yes unpublished	Y	BASF
IV A 6.10/9	Engelhardt G.	2005	Amendment No. 1 to the report: In vitro gene mutation test with Reg. No. 241208 (Metabolite of BAS 307 I, Flufenoxuron) in CHO cells (HPRT locus assay) XXXX Yes unpublished	Y	BASF
IV A 6.10/11	X	x	In vivo unscheduled DNA synthesis (UDS) assay with Reg. No. 241208 (Metabolite of BAS 307 I, Flufenoxuron) in rat hepatocytes - Single oral administration X x Yes unpublished	Y	BASF
IV A 6.10/12	X	x	Amendment No. 1 to the report: In vivo unscheduled DNA synthesis (UDS) assay with Reg. No. 241208 (Metabolite of BAS 307 I, Flufenoxuron) in rat hepatocytes - Single oral administration X x Yes unpublished	Y	BASF

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IV A 6.10/15	Engelhardt G., Leibold E.	2005	The low pH 6.7 in vitro cell transformation assay with Reg. No. 241208 (Metabolite of BAS 307 I, Flufenoxuron) in Syrian hamster Embryo cells (SHE Assay) XXXX Yes unpublished	Y	BASF
IV A 6.10/16	Engelhardt G.,	2005	Amendment No. 1 to the report: The low pH 6.7 in vitro cell transformation assay with Reg. No. 241208 (Metabolite of BAS 307 I, Flufenoxuron) in Syrian hamster Embryo cells (SHE Assay) XXXX Yes unpublished	Y	BASF
IV A 6.3.1/1	X	x	WL115110: A 28 day feeding study in rats X x No unpublished	N	BASF
IV A 6.8.2/6	X	x	WL 115110: A CKA embryotoxicity study in rats X x No unpublished	N	BASF
IV A 6.4.1/1	X	xx	WL115110: A 90 day feeding study in rats X x Yes unpublished	N	BASF
IV A 6.4.1/4	X	x	WL115110: A 90 day feeding study in mice X x No unpublished	N	BASF
IV A 6.10/5	X	x	WL125892: A 28 day oral toxicity study in Fischer 344 rats X x No unpublished	N	BASF
IV A 6.5/1	X.	x	WL115110: A two year chronic toxicity feeding study in rats X x Yes unpublished	N	BASF
IV A 6.7/1	X	x	WL115110: A two year oncogenicity feeding study in rats X x Yes unpublished	N	BASF
IV A 6.5/2	X	x	Addendum to XXXX - Volume 4 of 5: WL115110: A 2 year chronic toxicity feeding study in rats X X Yes unpublished	N	BASF
IV A 6.7/4	X	x	WL115110: A 2 year oncogenicity feeding study in mice X x Yes unpublished	N	BASF
IV A 6.3.1/3	X	x	Flufenoxuron (WL115110): A 28 day range-finding feeding study in mice X x No unpublished	N	BASF
IV A 6.4.1/2	X	x	Corrigenda/Addenda to XXXX: WL115110: A 90 day feeding study in rats X x Yes unpublished	N	BASF

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IV A 6.4.1/5	X	x	Corrigenda/Addenda to XXXX: WL115110: A 90 day feeding study in mice X x No unpublished	N	BASF
IV A 6.7/5	X	x	Corrigenda/addenda to XXXX - WL115110: A 2 year oncogenicity feeding study in mice X x Yes unpublished	N	BASF
IV A 6.10/20	Evelyn K.A., Malloy H.T.	1938	Microdetermination of oxyhemoglobin, methemoglobin, and sulfhemoglobin in a single sample of blood Literature XXXX No Published in The Journal of Biological Chemistry, Volume 126, 655-662	N	Not Applicable
IV A 6.12.1/3	Evrard P.	2004	Medical information (Isochem) XXXX No unpublished	N	Isochem
IV A 6.7/7	X	x	Corrigenda/addenda to XXXX - WL115110: A 2 year oncogenicity feeding study in mice X x Yes unpublished	N	BASF
IV A 6.12.1/2	Flynn A.	2003	Medical information (Great Lakes) XXXX No unpublished	N	Great Lakes
IV A 6.1.5/3	X	x	BAS 307 I (Flufenoxuron) – Maximization Test in Guinea pigs. X x Yes unpublished	Y	BASF
IV A 6.1.1/1	X	x	WL115110 (Cascade): Acute oral toxicity X x Yes unpublished	N	BASF
IV A 6.10/1	X	x	WL129183: Acute oral toxicity X x Yes unpublished	N	BASF
IV A 6.10/3	X	x	WL115096: Acute oral toxicity X x Yes unpublished	N	BASF
IV A 6.4.1/7	X	xx	WL115110: A 13 week oral toxicity study in dogs X x No unpublished	N	BASF
IV A 6.2/18	X	x	WL115110 kinetic accumulation and elimination study in the dog X x Yes unpublished	N	BASF
IV A 6.4.1/11	X	x	WL 115110: 52 week oral toxicity study in dogs X x Yes unpublished	N	BASF
IV A 6.4.1/8	X	x	Addendum to XXXX - WL115110: A 13 week oral toxicity study in dogs X x Yes unpublished	N	BASF

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IV A 6.4.1/12	X	x	Addendum to XXXX - WL 115110: 52 week oral toxicity study in dogs X x No unpublished	N	BASF
IV A 6.7/8	Haseman J.K. et al.	1985	Neoplasms observed in untreated and corn oil gavage control groups of F344/N rats and (C57BL/6N x C3H/HeN)F1 (B6C3F1) mice Literature x No Published in Journal National Cancer Institute, Vol 75, No.5, 975-984	N	Not Applicable
IV A 6.2/15	X	x	The absorption and disposition of 14C-WL 115110 in the dog after a single oral administration X x Yes unpublished	N	BASF
IV A 6.2/12	X	x	The metabolism of 14C-WL115110 in rats X x Yes unpublished	N	BASF
IV A 6.8.1/1	X	x	Reissued report XXXX: WL115110 teratogenicity study in rats X x Yes unpublished	N	BASF
IV A 6.8.1/2	X	x	Addendum to XXXX - WL115110: Teratogenicity study in rats X x Yes unpublished	N	BASF
IV A 6.8.1/4	X	x	Reissued report XXXX - WL115110: Teratogenicity study in rabbits X x Yes unpublished	N	BASF
IV A 6.2/5	X	xx	The fate of (14C-aniline)-WL115110 in the fischer 344 rat following a single high oral dose of 350 mg per kg X x Yes unpublished	N	BASF
IV A 6.2/1	X	x	The fate of (14C-aniline)-WL115110 in the fischer 344 rat following a single low oral dose of 3.5 mg per kg bodyweight X x Yes unpublished	N	BASF
IV A 6.2/3	X	x	Addendum to XXXX: The fate of (14C-aniline)-WL115110 in the fischer 344 rat following a single low oral dose of 3.5 mg per kg bodyweight XXXX Yes unpublished	N	BASF
IV A 6.2/6	X	x	Corrigendum/addendum to XXXX: The fate of (14C-aniline)-WL115110 in the fischer 344 rat following a single high oral dose of 350 mg per kg X x Yes unpublished	N	BASF
IV A 6.2/7	X	x	Addendum to XXXX: The fate of (14C-aniline)-WL115110 in the fischer 344 rat following a single high oral dose of 350 mg per kg X x Yes unpublished	N	BASF
IV A 6.2/2	X	x	Corrigendum to XXXX: The fate of (14C-aniline)-WL115110 in the fischer 344 rat following a single low oral dose of 3.5 mg per kg bodyweight X x Yes unpublished	N	BASF

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IV A 6.2/9	X	x	Corrigendum to XXXX: (14C-aniline)-WL115110: Accumulation and depletion from tissues following 28 successive, daily oral low doses (3.5 mg per kg) to female fischer 344 rats X x Yes unpublished	N	BASF
IV A 6.2/11	X	x	Corrigendum to XXXX: (14C-aniline)-WL115110: Accumulation and depletion from tissues following 28 successive, daily oral low doses (3.5 mg per kg) to female fischer 344 rats II. Nature of the residue in fat X x Yes unpublished	N	BASF
IV A 6.8.2/2	X	x	Addendum to XXXX: The effects of WL115110 on the reproductive function of two generations in the rat X x Yes unpublished	N	BASF
IV A 6.8.2/3	X	x	Amendment no. one: The effects of WL115110 on the reproductive function of two generations in the rat X x Yes unpublished	N	BASF
IV A 6.8.2/1	X	x	The effect of WL115110 on the reproductive function of two generations in the rat X x Yes unpublished	N	BASF
IV A 6.8.2/4	X	x	Dietary investigative study in pregnant rats rearing young to weaning. Compound: WL 115110 X x No Unpublished	N	BASF
IV A 6.9/1	X	x	BAS 307 I - Subacute neurotoxicity study in Wistar rats; Administration in the diet for 4 weeks X. x Yes unpublished	Y	BASF
IV A 6.2/4	X	x	Excretion of an oral dose of (Aniline 14C) WL 115110 in bile duct-cannulated rats X x Yes unpublished	N	BASF
IV A 6.8.2/5	X	x	WL115110: A cross-fostering study, supplementary to a previous two generation rat reproduction study X x Yes unpublished	N	BASF
IV A 6.2/13	X	x	Report amendment no. 1: The metabolism of 14C-WL115110 in rats X x Yes unpublished	N	BASF
IV A 6.1.3/1	X	x	WL 115110: Acute inhalation toxicity study in rats X x Yes unpublished	N	BASF
IV A 6.1.3/2	X	x	Addendum to XXXX: WL 115110: Acute inhalation toxicity study in rats X x Yes unpublished	N	BASF

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IV A 6.6.2/7	McEnaney S.	1992	Study to evaluate the chromosome damaging potential of WL115110 by its effects on cultured human lymphocytes using an in vitro cytogenetics assay XXXX Yes unpublished	N	BASF
IV A 6.6.2/1	Meyer A.L.	1987	Genotoxicity studies with WL115110 : in vitro chromosome studies with WL115110 XXXX No unpublished	N	BASF
IV A 6.6.2/3	Meyer A.L.	1988	Genotoxicity studies with WL115110: in vitro chromosome studies with WL115110 and glutathione using chinese hamster ovary (CHO) cells XXXX No unpublished	N	BASF
IV A 6.6.2/5	Meyer A.L.	1988	Genotoxicity studies with WL115110: in vitro chromosome studies with WL115110 using a rat liver (RL4) cell line XXXX No unpublished	N	BASF
IV A 6.6.2/2	Meyer A.L.	1991	Addendum to SBGR.86.216: Genotoxicity studies with WL115110 : in vitro chromosome studies with WL115110 XXXX No unpublished	N	BASF
IV A 6.6.2/4	Meyer A.L.	1991	Addendum to SBGR.87.117: Genotoxicity studies with WL115110: in vitro chromosome studies with WL115110 and glutathione using chinese hamster ovary (CHO) cells XXXX No unpublished	N	BASF
IV A 6.6.2/6	Meyer A.L.	1991	Corrigendum/Addendum to SBGR.87.118: Genotoxicity studies with WL115110: in vitro chromosome studies with WL115110 using a rat liver (RL4) cell line XXXX No unpublished	N	BASF
IV A 6.10/22	X	x	Replicative DNA synthesis (RDS) test using rat livers on WL115110 X x No unpublished	N	BASF
IV A 6.2/10	X	x	(14C-aniline)-WL115110: Accumulation and depletion from tissues following 28 successive, daily oral low doses (3.5 mg per kg) to female fischer 344 rats. II. Nature of the residue in fat X x Yes unpublished	N	BASF
IV A 6.2/8	X	x	(14C-aniline)-WL115110: Accumulation and depletion from tissues following 28 successive, daily oral low doses (3.5 mg per kg) to female fischer 344 rats X x Yes unpublished	N	BASF
IV A 6.6.4/4	X	x	Micronucleus test on WL115110 in mice X x Yes unpublished	N	BASF
IV A 6.1.1/2	X	x	Toxicology of insecticides (acyl ureas): The acute oral and percutaneous toxicity, skin and eye irritancy and skin sensitizing potential of WL115110 X x No unpublished	N	BASF

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IV A 6.1.2/1	X	x	Toxicology of insecticides (acyl ureas): The acute oral and percutaneous toxicity, skin and eye irritancy and skin sensitizing potential of WL115110 X x No unpublished	N	BASF
IV A 6.1.4/1	X	x	Toxicology of insecticides (acyl ureas): The acute oral and percutaneous toxicity, skin and eye irritancy and skin sensitizing potential of WL115110 X x No unpublished	N	BASF
IV A 6.1.5/1	X	x	Toxicology of insecticides (acyl ureas): The acute oral and percutaneous toxicity, skin and eye irritancy and skin sensitizing potential of WL115110 X x No, studies were conducted prior to the implementation of GLP but are scientifically valid unpublished	N	BASF
IV A 6.1.1/3	X	x	Corrigendum to XXXX: Toxicology of insecticides (acyl ureas): The acute oral and percutaneous toxicity, skin and eye irritancy and skin sensitizing potential of WL115110 X x Yes unpublished	N	BASF
IV A 6.1.2/2	X	x	Corrigendum to XXXX: Toxicology of insecticides (acyl ureas): The acute oral and percutaneous toxicity, skin and eye irritancy and skin sensitizing potential of WL115110 X x Yes unpublished	N	BASF
IV A 6.1.4/2	X	x	Corrigendum to XXXX: Toxicology of insecticides (acyl ureas): The acute oral and percutaneous toxicity, skin and eye irritancy and skin sensitizing potential of WL115110 X x Yes unpublished	N	BASF
IV A 6.1.5/2	X	x	Corrigendum to XXXX: Toxicology of insecticides (acyl ureas): The acute oral and percutaneous toxicity, skin and eye irritancy and skin sensitizing potential of WL115110 X x Yes unpublished	N	BASF
IV A 6.10/4	X	xx	The acute oral and percutaneous toxicity WL125892 X x No unpublished	N	BASF
IV A 6.3.1/2	X	x	Corrigendum 1 WL115110: A 28 day feeding study in rats X x No unpublished	N	BASF

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IV A 7.2.2.1/6	Beigel C.	2004	Calculation of the DT50 values at 10°C of BAS 307 I (Flufenoxuron) and Reg.No. 4064702 (CL 932338) in different soils under aerobic conditions XXXX No, not subject to GLP regulations unpublished	Y	BASF
IV A 7.1.1.1.2/3	Burgener A.	2001	14C-Flufenoxuron (BAS 307 I): Quantum yield of direct phototransformation in water XXXX Yes unpublished	Y	BASF
IV A 7.1.1.1.2/1	Camilleri P., Langner E.J.	1987	Photodecomposition of aqueous solutions of Flufenoxuron by sunlight XXXX No unpublished	N	BASF
IV A 7.4.3.3.1/2	X	x	Bioaccumulation and metabolism of 14C-BAS 307 I (Flufenoxuron) in rainbow trout X x Yes unpublished	Y	BASF
IV A 7.4.1.1/1	X	xx	WL115110: Acute toxicity to Salmo gairdneri, Daphnia magna and Selenastrum capricornutum X x Yes unpublished	N	BASF
IV A 7.4.1.2/2	X	x	WL115110: Acute toxicity to Salmo gairdneri, Daphnia magna and Selenastrum capricornutum X x Yes unpublished	N	BASF
IV A 7.4.1.3/2	X	x	WL115110: Acute toxicity to Salmo gairdneri, Daphnia magna and Selenastrum capricornutum X x Yes unpublished	N	BASF
IV A 7.1.2.2.2/1	Ebert D.	2003	Degradation of BAS 307 I (Flufenoxuron) in water/sedimentsystems under aerobic conditions XXXX Yes unpublished	Y	BASF
IV A 7.4.1.1/5	X	x	4-Amino-3-Fluorophenol : Acute toxicity to Daphnia magna and Salmo gairdneri X x (Amendment 1) Yes unpublished	N	BASF
IV A 7.4.1.2/5	X	x	4-Amino-3-Fluorophenol : Acute toxicity to Daphnia magna and Salmo gairdneri X x (Amendment 1) Yes unpublished	N	BASF
IV A 7.4.3.5.1/4	Egeler, P. and Seck, C.	2006	Flufenoxuron (BAS 307 I): Chronic toxicity to the aquatic Oligochaete *Lumbriculus variegatus* exposed to spiked sediment in a 28 d study. XXXX Yes unpublished	Y	BASF
IV A 7.1.2.2.2/2	Fent G.	2003	Degradation and distribution of BAS 307 I in a water-sediment system under outdoor conditions XXXX Yes unpublished	Y	BASF
IV A 7.4.1.2/1	Funk M.	2003	Effect of radiolabelled BAS 307 I on the immobility of Daphnia magna STRAUS in a 48 hours static, acute toxicity test XXXX Yes unpublished	Y	BASF

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IV A 7.4.3.5.1/2	Funk M.	2003	Effect of Reg.No. 4064702 (metabolite of BAS 307 I, Flufenoxuron) on the development of sediment dwelling larvae of Chironomus riparius in a water-sediment system XXXX Yes unpublished	Y	BASF
IV A 7.4.3.3.1/1	X	x	Flufenoxuron: The accumulation and elimination by rainbow trout (Oncorhynchus mykiss) in a continuous flow test X x Yes unpublished	N	BASF
IV A 7.4.1.1/4	X	x	4-Amino-3-Fluorophenol: Acute toxicity to Daphnia magna and Salmo gairdneri X x Yes unpublished	N	BASF
IV A 7.4.1.1/6	X	x	WL125892: Acute toxicity to Salmo gairdneri and Daphnia magna X x Yes unpublished	N	BASF
IV A 7.4.1.2/4	X	x	4-Amino-3-Fluorophenol: Acute toxicity to Daphnia magna and Salmo gairdneri X x Yes unpublished	N	BASF
IV A 7.4.1.2/6	X	x	WL125892: Acute toxicity to Salmo gairdneri and Daphnia magna X x Yes unpublished	N	BASF
IV A 7.2.2.1/4	Goodyear A., Gross R.	2001	14C-Flufenoxuron (BAS 307 I): Aerobic soil rate of degradation in three soils XXXX Yes unpublished	Y	BASF
IV A 7.2.2.3/2	Goodyear A., Gross R.	2001	14C-Flufenoxuron (BAS 307 I): Aerobic soil rate of degradation in three soils XXXX Yes unpublished	Y	BASF
IV A 7.4.1.1/2	X	x	Acute toxicity of Flufenoxuron (AC 811678) technical to zebra fish (Brachydanio rerio) under flow-through test conditions X x Yes unpublished	Y	BASF
IV A 7.4.1.3/3	Hanstveit A.O., Oldersma H.	1993	Effect of WL 125892 on the growth of alga Selenastrum capricornutum (OECD 201) XXXX Yes unpublished	N	BASF
IV A 7.4.3.4/2	Harrison E.G.	1988	Effects of Cascade emulsifiable concentrate (EC) and water dispersable (WDC) formulations on zooplankton in enclosures in experimental ponds XXXX Yes unpublished	N	BASF
IV A 7.1.1.1.1/2	Hassink J.	2003	Hydrolysis of BAS 307 I XXXX Yes unpublished	Y	BASF
IV A 7.1.1.1.2/4	Hassink J.	2003	Aqueous photolysis of BAS 307 I XXXX Yes unpublished	Y	BASF

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IV A 7.3.1/1	Hassink J.	2003	Photochemical oxidative degradation of Flufenoxuron BAS 307 I (QSAR estimates) XXXX No, not subject to GLP regulations unpublished	Y	BASF
IV A 7.3.2/1	Hassink J.	2003	Volatilisation of BAS 307 I after application of BAS 307 10 I on soil and on plant surfaces XXXX Yes unpublished	Y	BASF
IV A 7.2.3.1/1	Hill A.D., Standen M.E.	1993	[Carbonyl-14C] WL115110 (Cascade): Adsorption/desorption in three soils XXXX Yes unpublished	N	BASF
IV A 7.5.1.2/1	Hillaby J.M.	1987	The toxicity of WL115110 to the earthworm, Eisenia foetida L. (Oligocheata: Lumbriculidae) in laboratory tests XXXX Yes unpublished	N	BASF
IV A 7.4.3.1/1	X	x	Flufenoxuron (Cascade): An early life stage test with the fathead minnow Pimephales promelas (Rafinesque) X x Yes unpublished	N	BASF
IV A 7.4.1.2/7	Jatzek H.-J.	2003	Reg.No. 406 4702 (metabolite of BAS 307 I) - Determination of the acute effect on the swimming ability of the water flea Daphnia magna STRAUS XXXX Yes unpublished	Y	BASF
IV A 7.4.1.2/8	Jatzek H.-J.	2003	Reg.No. 102 719 (metabolite of BAS 307 I) - Determination of the acute effect on the swimming ability of the water flea Daphnia magna STRAUS XXXX Yes unpublished	Y	BASF
IV A 7.4.1.2/9	Jatzek H.-J.	2003	Reg.No. 241 208 (metabolite of BAS 307 I) - Determination of the acute effect on the swimming ability of the water flea Daphnia magna STRAUS XXXX Yes unpublished	Y	BASF
IV A 7.4.1.2/10	Jatzek H.-J.	2003	Reg.No. 206925 (metabolite of BAS 307 I, Flufenoxuron) - Determination of the acute effect on the swimming ability of the water flea Daphnia magna STRAUS XXXX Yes unpublished	Y	BASF
IV A 7.4.1.3/4	Jatzek H.-J.	2003	Reg.No. 102 719 (metabolite of BAS 307 I) - Determination of the inhibitory effect on the cell multiplication of unicellular green algae XXXX Yes unpublished	Y	BASF
IV A 7.4.1.3/5	Jatzek H.-J.	2003	Reg.No. 406 4702 (metabolite of BAS 307 I) - Determination of the inhibitory effect on the cell multiplication of unicellular green algae XXXX Yes unpublished	Y	BASF
IV A 7.4.3.3.1/3	X.	X	Bioaccumulation of BAS 307 I (Flufenoxuron) – applied as formulated product BAS 307 QA I – in an aquatic ecosystem XXXX Yes unpublished	Y	BASF
IV A 7.5.1.1/1	Koelzer U.	2003	Assessment of the side effects of BAS 307 QA I on the activity of the soil microflora, nitrogen turnover XXXX Yes unpublished	Y	BASF
IV A 7.5.1.1/2	Koelzer U.	2003	Assessment of the side effects of BAS 307 QA I on the activity of the soil microflora, short-term respiration XXXX Yes unpublished	Y	BASF

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IV A 7.5.1.1/3	Koelzer U.	2003	Effects of CL 932338 (metabolite of BAS 307 I) on the activity of the soil microflora, nitrogen transformation test XXXX Yes unpublished	Y	BASF
IV A 7.4.1.3/1	Kubitza J.	2003	Effect of BAS 307 I (Flufenoxuron) on the growth of the green alga Pseudokirchneriella subcapitata XXXX Yes unpublished	Y	BASF
IV A 7.1.1.1.2/2	Langner E.J.	1991	Corrigendum to SBGR.87.150: Photodecomposition of aqueous solutions of Flufenoxuron by sunlight XXXX No unpublished	N	BASF
IV A 7.1.1.1.1/1	Langner E.J., Camilleri P.	1987	Hydrolysis of WL115110 in aqueous media XXXX No unpublished	N	BASF
IV A 7.4.1.4/1	Lebertz H., Yan Z.	2001	Flufenoxuron (BAS 307I): Activated sludge, respiration inhibition test XXXX Yes unpublished	Y	BASF
IV A 7.2.2.4/4	Lewis C.J., Gross R.	2001	14C-Flufenoxuron (BAS 307 I): Soil photolysis under artificial sunlight XXXX Yes unpublished	Y	BASF
IV A 7.5.2.1/1	Luehrs U.	2001	Effects of Flufenoxuron technical (AC 811678) on reproduction and growth of earthworms Eisenia fetida (Savigny 1826) in artificial soil XXXX Yes unpublished	Y	BASF
IV A 7.1.1.1.2/5	Mamouni A., van der Gaauw A.	2001	14C-Flufenoxuron (BAS 307 I): Photolysis in natural water XXXX Yes unpublished	Y	BASF
IV A 7.1.1.1.2/6	Mamouni A., van der Gaauw A.	2001	Amendment no.1: 14C-Flufenoxuron (BAS 307 I): Photolysis in natural water XXXX Yes unpublished	Y	BASF
IV A 7.4.3.5.1/1	Mattock S. et al.	2001	Effects of 14C labelled Flufenoxuron on the development of sediment-dwelling larvae of Chironomus riparius in a water-sediment system XXXX Yes unpublished	Y	BASF
IV A 7.4.3.4/1	Pearson N., Girling A.	1989	Flufenoxuron: Chronic toxicity to Daphnia magna XXXX Yes unpublished	N	BASF
IV A 7.4.1.2/3	Pearson N., Girling A.E.	1989	Flufenoxuron (WL115110): Acute toxicity to Gammarus pulex, Lymnaea stagnalis, Tubifex tubifex and chiromonus lugubris XXXX Yes unpublished	N	BASF
IV A 7.2.1/1	Richardson K.A.	1987	The effect of soil pH on the degradation of 14C-WL115110 XXXX No unpublished	N	BASF
IV A 7.2.2.1/1	Richardson K.A.	1990	A comparison of the degradation of (aniline-14C)-WL115110 in soil under aerobic and anaerobic conditions XXXX Yes unpublished	N	BASF
IV A 7.2.2.1/2	Richardson K.A.	1991	A comparison of the degradation of (aniline-14C)-WL115110 in soil under aerobic and anaerobic conditions XXXX Yes unpublished	N	BASF

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IV A 7.2.2.4/1	Richardson K.A.	1990	A comparison of the degradation of (aniline-14C)-WL115110 in soil under aerobic and anaerobic conditions XXXX Yes unpublished	N	BASF
IV A 7.2.2.4/2	Richardson K.A.	1991	A comparison of the degradation of (aniline-14C)-WL115110 in soil under aerobic and anaerobic conditions XXXX Yes unpublished	N	BASF
IV A 7.5.3.1.3/1	X	x	WL 115110: The effects of dietary inclusion on reproduction and tissue residues in the bobwhite quail X x Yes unpublished	N	BASF
IV A 7.5.3.1.1/1	X	x	The acute oral toxicity (LD50) of WL 115110 to the bobwhite quail X x Yes unpublished	N	BASF
IV A 7.5.3.1.2/1	X	x	The subacute dietary toxicity (LC50) ofWL 115110 to the bobwhite quail X x Yes Unpublished	N	BASF
IV A 7.5.3.1.2/2	X	x	The subacute dietary toxicity (LC50) of WL 115110 to the mallard duck X x Yes unpublished	N	BASF
IV A 7.2.3.1/2	Rosenwald J.	2002	Adsorption/desorption of 14C-Flufenoxuron (BAS 307 I) in three soils XXXX Yes unpublished	Y	BASF
IV A 7.5.1.3/1	Sack D.	2003	BAS 307 QA I: Effects on non-target plants in the greenhouse - A limit test XXXX Yes unpublished	Y	BASF
IV A 7.4.3.2/1	X	x	Flufenoxuron 100 DC (BAS 307 10 I): Zebrafish (Danio rerio), static full life cycle test with sediment X. x Yes unpublished	Y	BASF
IV A 7.5.4.1/1	X	x	Effects of Flufenoxuron technical (AC 811678) (Acute contact and oral LD50) on honey bees (Apis mellifers L.) (Hymenoptera, Apidae) in the laboratory X x Yes unpublished	Y	BASF
IV A 7.4.1.1/3	X	x	Acute toxicity of SKI-8503 to Cyprinus carpio X x No unpublished	N	BASF
IV A 7.2.2.2/1	Smalley R.	2003	Field soil dissipation of BAS 307 I in the formulation BAS 307 QA I on bare soil in France (S) and Spain, 2001-2002 XXXX Yes unpublished	Y	BASF
IV A 7.5.1.2/2	Staebler D.	2003	Acute toxicity of CL 932 338 (metabolite of BAS 307 I) on earthworms, Eisenia fetida using an artificial soil test XXXX Yes unpublished	Y	BASF
IV A 7.2.2.1/3	Standen M.E., Hill A.D.	1993	Cascade (WL115110): A comparison of the degradation of (aniline-14C)- and (toluyl-14C)-Cascade in soil under aerobic and anaerobic conditions XXXX Yes unpublished	N	BASF

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IV A 7.2.2.3/1	Standen M.E., Hill A.D.	1993	Cascade (WL115110): A comparison of the degradation of (aniline-14C)- and (toluyl-14C)-Cascade in soil under aerobic and anaerobic conditions XXXXX Yes unpublished	N	BASF
IV A 7.2.2.4/3	Standen M.E., Hill A.D.	1993	Cascade (WL115110): A comparison of the degradation of (aniline-14C)- and (toluyl-14C)-Cascade in soil under aerobic and anaerobic conditions XXXXX Yes unpublished	N	BASF
IV A 7.2.2.1/5	Stephan A., Ebert D.	2003	Degradation rates of BAS 307 I (Flufenoxuron) and Reg.No. 406 4702 (CL932338) under aerobic conditions in different soils (DT50/DT90) XXXX Yes unpublished	Y	BASF
IV A 7.4.3.5.1/3	Toy R.	1993	Flufenoxuron: Toxic effects of soils treated with Cascade 100 g/L DC (SF07055) on Chironomus riparius XXXX Yes unpublished	Y	BASF
IV A 7.1.1.2.1/1	Turner S.J., Watkinson R.J.	1986	WL115110: An assessment of the ready biodegradability XXXXX No unpublished	N	BASF
IV A 7.4.3.5.1/5	Weltje, L. and Pupp, A.	2007	Chronic toxicity of flufenoxuron (BAS 307 I) to the non-biting midge *Chironomus riparius* exposed via spiked-sediment. XXXX Yes unpublished	Y	BASF
IV A 7.2.3.1/3	Zirnstein M.	2003	Adsorption/desorption - Study of BAS 307 I metabolite (Reg.No. 406 4702) on five European soils XXXX Yes unpublished	Y	BASF
IV A 7.4.1.1/7	X	x	Reg.No. 406 4702 (metabolite of BAS 307 I) - Acute toxicity study on the rainbow trout (Oncorhynchus mykiss) in a static system over 96 hours X. x Yes unpublished	Y	BASF
IV A 7.4.1.1/8	X	x	Reg.No. 102719 (metabolite of BAS 307 I) - Acute toxicity study on the rainbow trout (Oncorhynchus mykiss) in a static system over 96 hours X. x Yes unpublished	Y	BASF
IV A 7.5.3.1.3/2	X	x	WL 115110 = Flufenoxuron new statistical evaluation of a 1-generation reproduction study on the bobwhite quail (Colinus virginianus) X x No, not subject to GLP regulations unpublished	Y	BASF

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IV A 8.4/1	Schenk W.	2001	Possible procedures for the decontamination of water from Flufenoxuron XXXXX No unpublished	Y	BASF
IV A 7.4.1.2/3	Shumei W.	1987	Acute toxicity of SKI-8503 on Daphnia carinata XXXXX No unpublished	N	BASF