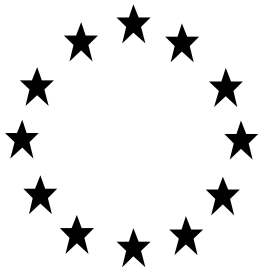
# Directive 98/8/EC concerning the placing biocidal products on the market

***Inclusion of active substances in Annex I or IA to Directive 98/8/EC***

Assessment Report[i]



# Flufenoxuron

# Product-type PT8

# (Wood Preservatives)

September 2011

**Annex I - FR**

**Flufenoxuron (PT8)**

**Assessment Report**

**Finalised in the Standing Committee on Biocidal Products at its meeting on 22/09/2011 in view of its inclusion in Annex I to Directive 98/8/EC**

# CONTENT

# 1 STATEMENT OF SUBJECT MATTER AND PURPOSE

## 1.1 PROCEDURE FOLLOWED

This assessment report has been established as a result of the evaluation of flufenoxuron as product-type 8 (wood preservative), carried out in the context of the work programme for the review of existing active substances provided for in Article 16(2) of Directive 98/8/EC concerning the placing of biocidal products on the market[1], with a view to the possible inclusion of this substance into Annex I to the Directive.

Flufenoxuron (CAS no. 101463-69-8) was notified as an existing active substance, by BASF AG, hereafter referred to as the applicant, in product-type 8.

Commission Regulation (EC) No 1451/2007 of 4th December 2007[2] lays down the detailed rules for the evaluation of dossiers and for the decision-making process in order to include or not an existing active substance into Annex I or IA to the Directive.

In accordance with the provisions of Article 14 of that Regulation, the Commission designated France as Rapporteur Member State to carry out the assessment of flufenoxuron on the basis of the dossier submitted by the applicant. The deadline for submission of a complete dossier for flufenoxuron as an active substance in product-type was 28th March 2004, in accordance with Article 9 paragraph 2 of Regulation (EC) No 1451/2007.

On 19th March 2004, the French competent authorities received a dossier from the applicant. The Rapporteur Member State accepted the dossier as complete for the purpose of the evaluation, taking into account the supported uses, and confirmed the acceptance of the dossier on 28th September 2004.

On 03 March 2009, the Rapporteur Member State submitted, in accordance with the provisions of Article 10(5) and (7) of Regulation (EC) No 2032/2003, to the Commission and the applicant a copy of the evaluation report, hereafter referred to as the competent authority report.

The Commission made the report available to all Member States by electronic means on 7 April 2009. The competent authority report included a recommendation for the inclusion of flufenoxuron in Annex I to the Directive for PT 8.

In accordance with Article 12 of Regulation (EC) No 2032/2003, the Commission made the competent authority report publicly available by electronic means on 7 April 2009. This report did not include such information that was to be treated as confidential in accordance with Article 19 of Directive 98/8/EC.

In order to review the competent authority report and the comments received on it, consultations of technical experts from all Member States (peer review) were organised by the Commission. Revisions

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[1] Directive 98/8/EC of the European Parliament and of the Council of 16 February 1998 concerning the placing biocidal products on the market, OJ L 123, 24.4.98, p.1

[2] OJ L 325, 11.12.2007, p. 3

agreed upon were presented at technical and competent authority meetings and the competent authority report was amended accordingly.

On the basis of the final competent authority report, the Commission proposed the inclusion of flufenoxuron in Annex I to Directive 98/8/EC and consulted the Standing Committee on Biocidal Product on 22/09/2011.

In accordance with Article 11(4) of Regulation (EC) No 2032/2003, the present assessment report contains the conclusions of the Standing Committee on Biocidal Products, as finalised during its meeting held on 22/09/2011.

## 1.2 PURPOSE OF THE ASSESSMENT REPORT

This assessment report has been developed and finalised in support of the decision to include flufenoxuron in Annex I to Directive 98/8/EC for product-type 8. The aim of the assessment report is to facilitate the authorisation in Member States of individual biocidal products in product-type 8 that contain flufenoxuron. In their evaluation, Member States shall apply the provisions of Directive 98/8/EC, in particular the provisions of Article 5 as well as the common principles laid down in Annex VI.

For the implementation of the common principles of Annex VI, the content and conclusions of this assessment report, which is available at the Commission website[3], shall be taken into account.

However, where conclusions of this assessment report are based on data protected under the provisions of Directive 98/8/EC, such conclusions may not be used to the benefit of another applicant, unless access to these data has been granted.

## 1.3 OVERALL CONCLUSION IN THE CONTEXT OF DIRECTIVE 98/8/EC

The overall conclusion from the evaluation is that it may be expected that there are products containing flufenoxuron for the product-type 8, which will fulfil the requirements laid down in Article 10(1) and (2) of Directive 98/8/EC. This conclusion is however subject to:

i. compliance with the particular requirements in the following sections of this assessment report,

ii. the implementation of the provisions of Article 5(1) of Directive 98/8/EC, and

iii. the common principles laid down in Annex VI to Directive 98/8/EC.

Furthermore, these conclusions were reached within the framework of the uses that were proposed and supported by the applicant (see Appendix II). Extension of the use pattern beyond those described will

[3] http://ec.europa.eu/comm/environment/biocides/index.htm

require an evaluation at product authorisation level in order to establish whether the proposed extensions of use will satisfy the requirements of Article 5(1) and of the common principles laid down in Annex VI to Directive 98/8/EC.

# 2 OVERALL SUMMARY AND CONCLUSIONS

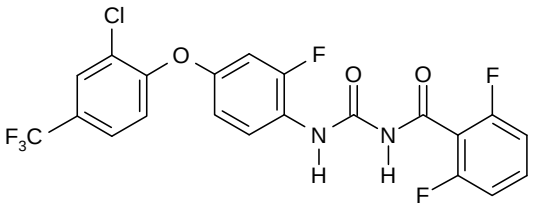
## 2.1 PRESENTATION OF THE ACTIVE SUBSTANCE

### 2.1.1 Identity, Physico-Chemical properties & Methods of Analysis

#### 2.1.1.1 Active substance

The main identification characteristics and physico-chemical properties of the active substance flufenoxuron are given in Appendix I and the listing of endpoints. The identity of impurities is provided in the confidential part of the dossier. None of the manufacturing impurities are considered to be of potential toxicological or environmental concern.

**Identity of the active substance flufenoxuron**

| | |
|---|---|
| Active substance | Flufenoxuron |
| Function | PT8 (wood preservative), insecticide |
| Common name, | Flufenoxuron |
| Other names, Synonym | BAS 307 I |
| IUPAC Name | 1-[4-(2-chloro-alpha, alpha,alpha-trifluoro-para-tolyloxy)-2-fluorophenyl]-3-(2,6-difluorobenzoyl)urea |
| C.A. Name | N-[[[4-[2-chloro-4-(trifluoromethyl)phenoxy]-2-fluorophenyl]amino]carbony]-2,6-difluorobenzamide |
| CAS-No. | 101463-69-8 |
| EC-No. | 417-680-3 |
| Other No. (CIPAC, ELINCS) | CIPAC No. 470 |
| Purity | 960 g/kg |
| Impurities and additives | The identity and concentrations of the impurities in flufenoxuron, and the additives are confidential. |
| Molecular formula | $C_{21}H_{11}ClF_6N_2O_3$ |
| Molecular weight (g/mol) | 488.8 g/mol |
| Structural formula |  |
| SMILES: | Fc1cccc(F)c1C(=O)NC(=O)Nc2ccc(Oc3ccc(C(F)(F)F)cc3Cl)cc2F |

The methods of analysis for the active substance as manufactured, and for the determination of impurities, have been validated. Analytical methods in environmental matrices have been validated but shown to be not sufficiently sensitive with respect to the levels of concern in surface water, as the limit of quantification of the presented methods is no less than 0.01 µg/L and the lowest NOEC value (*Daphnia magna*, 21 days) for water is estimated at $4.49 \times 10^{-3}$ µg/L. Another method for flufenoxuron analysis in water has to be developed before authorisation of products.

#### 2.1.1.2 Biocidal products

For the purposes of Annex I listing, two solvent based formulations in their commercial form have been proposed as the representative products by the applicant:

##### *2.1.1.2.1 Basiment Holzwurm BV Konzentrat*

Basiment Holzwurm BV Konzentrat: an emulsifiable concentrate containing 0.1% (w/w) of flufenoxuron, to be diluted in water before use (1 part: 9 parts water).

##### *2.1.1.2.2 Basiment Holzwurm BV U 1551*

Basiment Holzwurm BV U 1551 (also named Basileum Holzwurm BV U 1551): a ready-to-use liquid, with a flufenoxuron concentration of 0.02% (w/w).

### 2.1.2 Intended Uses and Efficacy

#### 2.1.2.1 Field of use / Function / Mode of action

Flufenoxuron is designed for an insecticide use for curative and preventive wood preservation (product type 8). The claimed intended uses are industrial and non-industrial (residential) applications by professionals or amateurs, for a preventive and curative indoor and outdoor treatment (use classes 1 to 3).

Flufenoxuron is an insecticide belonging to the benzoylurea family. It is a growth regulator that interferes in chitin production during cuticle development.

#### 2.1.2.2 Objects to be protected, target organisms

Flufenoxuron efficacy was examined for the following target organisms:

| Application mode | Target organism | Active substances rate |
|---|---|---|
| Preventive impregnation treatment (vacuum pressure, double vacuum pressure, injection applied by industrials) | *wood boring beetles* (*H. bajulus* as the representative target organism) | 0.75 g flufenoxuron/$m^3$ sapwood loading (1 kg Wocosen™ 100 SL/FL per $m^3$ wood). (EN47+EN73) |
| Curative superficial | *Hylotrupes bajulus* | 0.064 g flufenoxuron /$m^2$ claimed by the applicant has been considered to secure the efficient rate |

| | | |
|---|---|---|
| treatment (brushing or spraying by professionals, brushing by general public) | | |

An efficacy for preventive superficial treatment has also been claimed (dipping or spraying by industrials, spraying or brushing by professionals, brushing by general public). However, as the effectiveness has not been proved in the product dossiers (the only test provided has been refused as it does not meet EN599-1 criteria), the efficiency of superficial treatment in preventive application will have to be demonstrated at the Member State level for the product authorisation stage.

#### 2.1.2.3 Resistance

Based on the elements presented by the applicant, the risk for development of resistance for the target insects is very low.

### 2.1.3 Classification

#### 2.1.3.1 Active substance

***Current classification***

The active ingredient is not included yet in the Annex VI in the CLP regulation.

***Proposed classification***

On the basis of a review of submitted data, the following classification is proposed by the RMS. This classification was adopted at the RAC 16 in June 2011.

| **Directive 67/548/EEC** | | |
|---|---|---|
| Class of danger | N | Dangerous for the environment |
| Risk phrases | R33 | Danger of cumulative effects |
| | R64 | May cause harm to breastfed babies. |
| | R50/53 | Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment. |
| Safety phrases | S2 | Keep out of the reach of children. |
| | S22 | Do not breathe dust. |
| | S36/37 | Wear suitable protective clothing and gloves. |
| | S46 | If swallowed, seek medical advice immediately and show this container or label. |
| | S60 | This material and its container must be disposed of as hazardous waste. |
| | S61 | Avoid release to the environment. Refer to special instructions/Safety data sheets. |
| **Regulation 1272/2008** | | |
| Classification and Hazard statements | Lact. H362 | May cause harm to breast-fed children |
| | Aquatic acute 1 /H400 | Very toxic to aquatic life |
| | Aquatic chronic 1 /H410 | Very toxic to aquatic life with long lasting effect<br>M- factor =10 000 |

### 2.1.3.2 Biocidal products

**Proposed classification and labelling of Basiment Holzwurm BV Konzentrat**

| **Directive 1999/45/EC** | | |
|---|---|---|
| Class of danger | Xi: | Irritant |
| | N: | Dangerous for the environment |
| Risk phrases: | R36: | Irritant to eyes. |
| | R38: | Irritant to skin. |
| | R50/53: | Very toxic to aquatic organisms; may cause long-term adverse effects in the aquatic environment. |
| Safety phrases: | S2: | Keep out of the reach of children. |
| | S13: | Keep away from food, drink and animal feeding stuffs. |
| | S20: | When using, do not eat or drink. |
| | S23: | Do not breathe vapour. |
| | S24/25: | Avoid contact with skin and eyes. |
| | S26: | In case of contact with eyes, rinse immediately with plenty of water and seek medical advice. |
| | S28: | After contact with skin, wash immediately with plenty of soap-suds. |
| | S36/37/39: | Wear suitable protective clothing, gloves and eye/face protection. |
| | S45: | In case of accident or if you feel unwell, seek medical advice immediately. |
| | S60: | This material and its container must be disposed of as hazardous waste. |
| | S61: | Avoid release to the environment. Refer to special instructions/Safety data sheets. |
| | S62: | If swallowed, do not induce vomiting; seek medical advice immediately and show this container or label. |
| | S64: | If swallowed, rinse mouth with water (only if the person is conscious). |
| Justification: | For toxicological properties, R64 and R33 are not applied to Basiment Holzwurm BV Konzentrat as this product contains 0.1% of active ingredient flufenoxuron. | |
| **Regulation 1272/2008** | | |
| Classification and | Eye Irrit. 2 H319 | Causes serious eye irritation |
| | Skin Irrit.2 H315 | Causes skin irritation |

| | | |
|---|---|---|
| Hazard statements | Aquatic acute 1 /H400 | Very toxic to aquatic life |
| | Aquatic chronic 1 /H410 | Very toxic to aquatic life with long lasting effect |

**Proposed classification and labelling of Basiment Holzwurm BV U 1551/155A:**

The formulation of Basiment Holzwurm BV U 1551 is being slightly modified under the name Basiment Holzwurm BV U 155 A which contains more acceptable formulants. However, the efficacy and toxicology studies presented in the dossier relate to the U 1551 product.

| **Directive 1999/45/EC** | | |
|---|---|---|
| Class of danger | Xi: | Irritant |
| | N: | Dangerous for the environment |

| | | |
|---|---|---|
| Risk phrases: | R38: | Irritant to skin. |
| | R65: | Harmful: may cause lung damage if swallowed |
| | R66: | Repeated exposure may cause skin dryness or cracking |
| | R50/53: | Very toxic to aquatic organisms; may cause long-term adverse effects in the aquatic environment. |
| Safety phrases: | S2: | Keep out of the reach of children. |
| | S13: | Keep away from food, drink and animal feeding stuffs. |
| | S20: | When using, do not eat or drink. |
| | S23: | Do not breathe vapour. |
| | S24: | Avoid contact with skin. |
| | S28: | After contact with skin, wash immediately with plenty of soap-suds. |
| | S36/37/39: | Wear suitable protective clothing, gloves and eye/face protection. |
| | S45: | In case of accident or if you feel unwell, seek medical advice immediately. |
| | S60: | This material and its container must be disposed of as hazardous waste. |
| | S61: | Avoid release to the environment. Refer to special instructions/Safety data sheets.[1)] |
| | S62: | If swallowed, do not induce vomiting; seek medical advice immediately and show this container or label. |
| | S64: | If swallowed, rinse mouth with water (only if the person is conscious). |
| Justification: | For toxicological properties, R64 and R33 are not applied to Basiment Holzwurm BV U 1551/155A as this product contains 0.02% of active ingredient flufenoxuron. | |
| **Regulation 1272/2008** | | |
| Classification and Hazard statements | Skin Irrit.2 H315 | Causes skin irritation |
| | EUH066 | Repeated exposure may cause skin dryness or cracking |
| | Asp. Tox.1 H304 | May be fatal if swallowed and enters airways |
| | Aquatic acute 1 /H400 | Very toxic to aquatic life |
| | Aquatic chronic 1 /H410 | Very toxic to aquatic life with long lasting effect |

[1)] Alternatively, if general public may use the product, the safety advice phrase “S29: do not empty into drains” applies.

## 2.2 SUMMARY OF THE RISK ASSESSMENT

### 2.2.1 Human health risk assessment

#### 2.2.1.1 Hazard identification and effects assessment

**Toxicokinetics**

Several studies were performed with flufenoxuron in rats and dogs at two concentrations (3.5 and 350 mg/kg bw).

- Absorption

Based on a study in cannulated rats, an oral absorption of 80 % was retained.

No dermal absorption data are available on the active substance alone. Nevertheless, based on its physico-chemical properties (molecular weight at 488.8 g/mol and log Pow > 4) and according to the TGD on Risk Assessment, flufenoxuron is a borderline case for considering a dermal absorption of 10%. A study was conducted in rats *in vivo* with the 10 DC formulation containing 0.1 g a.i/ml and its 1:900 dilution in water and showed a dermal penetration lower than 5 %. Despite its poor reliability (Klimisch score: 3) due to a low recovery of radioactivity for the dilution, this study is supporting a low dermal absorption. This is also strengthened by the results of the test conducted with the PT18 formulation (containing 3 % of flufenoxuron) showing a dermal penetration up to 6 %. Based on this data, the RMS considers that a dermal absorption of 10 % is sufficient for the purpose of annex I inclusion but will need to be confirmed by the submission of an adequate study at product authorisation level.

As no experimental data are available by inhalation, a default absorption value of 100 % was considered.

- Distribution

Once absorbed, flufenoxuron is well distributed in the whole organism, mainly in gastro-intestinal tract, fat tissue, bone marrow and skin.

- Metabolism

Small amounts of flufenoxuron were metabolised in rats. Unchanged substance was the major component in the tissues (in particular in the fat where it was the single component detected) and faeces.

- Excretion

At low concentration (3.5 mg/kg bw), the excretion is slow, mainly via faeces and in a less extent via the urine. Flufenoxuron was also excreted in milk in lactating female rats in a cross-fostering study.

**Acute toxicity**

Flufenoxuron has a low acute oral ($LD_{50}$> 3000 mg/kg bw), dermal ($LD_{50}$> 2000 mg/kg bw) or inhalation toxicity ($LC_{50}$ > 5.1 mg/l/4h) in rats.

**Local toxicity**

Flufenoxuron is neither a skin nor an eye irritant.

Flufenoxuron is not a skin sensitiser to guinea pigs.

**Repeated dose toxicity**

- Oral route

A 28-day toxicity study was performed in rats exposed to flufenoxuron through the diet and showed modifications of clinical chemistry (triglyceride, albumin or beta-globulin). **Based on these effects, a NOAEL of 49 mg/kg bw/day for males and a NOAEL of 1067 mg/kg bw/day for females were derived.**

In a 28-day toxicity study in mice exposed to flufenoxuron through the diet, no adverse treatment-related effects were reported up to 50,000 ppm (equivalent to 9,820-12,157 mg/kg bw/day for males and females, respectively).

Subchronic oral toxicity studies carried out in rats (90 days), mice (90 days) and dogs (90 days and 1 year) highlighted the main health effect of flufenoxuron: an anemia, probably haemolytic, characterised by decreasing haemoglobin and hematocrit levels, concomitant with compensatory hematopoiesis. This effect was particularly observed in dogs.

In the 90-day study in dogs, a decrease in haemoglobin levels was observed in males from 500 ppm (equivalent to 18-21 mg/kg bw/day) at week 9. After 12 and 15 weeks, significant haematological effects were confined to the 50,000 ppm group male (equivalent to 1,961-2,039 mg/kg bw/day). This effect was associated with bone marrow hyperplasia and higher pigment deposition in liver, kidneys, spleen and bone marrow. In addition to anemia, an increase in methemoglobin levels was observed at and above 18-21 mg/kg bw/day.

Similar effects were observed in the 52-week study in dogs: a mild anemia, revealed by significant changes in haemoglobin level and erythrocytes parameters appeared in both sexes at 50,000 ppm (equivalent to 2018-1879 mg/kg bw/day) after 5 weeks of treatment. Methemoglobinemia and sulfhaemoglobulin were also increased at 50,000 ppm in both sexes at most time points of investigation and to a minimal degree also in females at 500 ppm (equivalent to 19 mg/kg bw/day). Evidence of compensatory hematopoiesis revealed by bone marrow hyperplasia was observed in all animals at 50,000 ppm and in one female at 500 ppm and was accompanied by pigment deposition in the bone marrow, spleen, liver and kidney. Platelet counts were statistically significantly increased in males at 50,000 ppm from week 13 and at 500 ppm from week 27. In addition, effects in the liver were reported (increased liver weights associated with hepatocellular fatty vacuolisation at 50,000 ppm). **Based on the haematological findings, the one-year feeding study in dogs supports a NOAEL of 100 ppm (equivalent to 3.5 mg/kg bw/d in males and 3.7 mg/kg bw/d in females).**

Chronic administration of flufenoxuron in rats (24-month chronic toxicity study) through the diet resulted in changes in haematological and clinical chemistry parameters. Chronic effects of flufenoxuron could also be determined from the oncogenicity studies in rats and mice. Hepatic effects and reduced body weights were the main findings in the oncogenicity in rats and in one of the two carcinogenicity study in mice. In the second study in mice, increase of uterus distension was the only systemic effect observed.

- Inhalation route

A justification for non-submission data was accepted for inhalation, 28 and 90 days, based on the low acute toxicity of the substance and its low volatility and the fact that the final product should be a liquid

(no powder exposition) which is not intended to be used as an aerosol generating droplets with a diameter < 50 µm. This condition will have to be checked at the product authorisation stage.

- Dermal route

A justification for non-submission of data was also accepted for repeated-dose toxicity by dermal route since acute toxicity studies did not indicate any adverse findings when flufenoxuron was tested by the dermal route at limit dose levels.

**Genotoxicity**

- *In vitro* tests

A complete genotoxicity test battery was performed on flufenoxuron and its main metabolites. Flufenoxuron was not genotoxic in Ames tests. Other negative results were obtained in mammalian cell tests but these were carried out with too low concentrations (not enough toxic and below the maximal concentrations recommended by the OECD guidelines). A mammalian chromosome aberration test suggested that in the presence of S-9 mix activation, a reactive metabolic intermediate, clastogenic to CHO cells, is generated. When glutathione was added to CHO cells, the positive response with S-9 mix was no more observed. Nevertheless, the tested dose was not sufficiently cytotoxic to validate this test performed with glutathione.

Weak mutagenic potential with S9-mix in strains TA98 and TA100 were observed with two flufenoxuron metabolites in Ames tests.

- *In vivo* tests

The lack of any genotoxic effects following exposure to flufenoxuron was confirmed *in vivo* in a rat bone marrow chromosomal aberration assay, a mouse bone marrow micronucleus assay and an *in vivo/in vitro* UDS test, with rat liver cells.

**Carcinogenicity**

No oncogenic effect was observed in a 24-month study in rats up to 2,290 and 2,900 mg/kg bw/d in males and females, respectively. Two carcinogenicity studies in mice were carried out with flufenoxuron. In the first study, an increased incidence of hepatocellular carcinoma was observed in all treated male groups (from 56 mg/kg bw/d) and in low dose females (73 mg/kg bw/d). Nevertheless, this increase in hepatocellular carcinoma was within the US National Toxicology Program (NTP) historical control range. Therefore it is considered to be associated with an unusually low incidence of these tumors in control males and not directly related to treatment. Furthermore, at the top dose of 50,000 ppm (equivalent to a daily intake of 7356 mg/kg bw/day in males), the hepatocellular carcinomas were observed in a very toxic context. In this same study, increasing splenic haemangiosarcomas were observed in female mice at the highest tested dose (equivalent to a daily intake of 7780 mg/kg bw/day in females) *(controls: 0; 50000 ppm: 7/50 females)*. However, these effects appeared at a dose which is about 7.5-fold higher than the limit dose recommended for chronic toxicity test in the OECD guidelines (1000 mg/kg bw/day) and exceeded the maximum tolerated dose for flufenoxuron (excessive hepatocellular toxicity and body weight depression).

In the second study performed in mice, exposed to lower doses (maximum 10000 ppm i.e. 1591.1 mg/kg bw/day for females), no oncogenic activity was observed. Therefore, the effects observed in the first study appeared at a very high dose level in a toxic context and are considered insufficient to warrant a classification for carcinogenicity. The NOAEL for oncogenicity was hence 10,000 ppm (equivalent to 1591.1 mg/kg bw/day).

**Reproductive toxicity**

- Developmental toxicity

No teratogenic effect was observed in rats and rabbits.

- Fertility

No effect on fertility was observed in male or female rats. However, in a multigeneration study, an increasing number of litter losses (associated with changes in litter size and cumulative pup losses) and difficulties for newborn to gain weight were observed. Two other studies were carried out in order to investigate the reason of the increased post-partum mortality of pups. No effects on pup survival were observed when flufenoxuron was administered from day 3 of gestation to weaning or from 10 weeks prior mating until parturition. Furthermore, in the cross-fostering study, no effect during lactation was identified when the control pups were reared by the dams exposed during gestation. Nevertheless, in this study, a rapid decrease of flufenoxuron levels in milk and fat upon cessation of treatment was noted. All these results indicate that the adverse effects on pup survival observed in the 2-generation study are likely due to a chronic exposure of dams leading to an accumulation of flufenoxuron and an adverse effect via lactation (transfer of flufenoxuron though the milk and/or perturbation of the lactation). Furthermore, the bioaccumulative potential of flufenoxuron and the fact that effects on pups do not occur immediately after birth supports this hypothesis.

Two possible mechanisms were proposed to explain the reduction/losses in pup weight and viability:

- Inhibition of maternal lactation and reduced milk fat content as the result of reduced triglyceride levels in the dams,
- Reduced triglyceride levels in the pups secondary to reduced maternal milk quality and direct exposure to flufenoxuron via maternal milk and, later, via maternal diet.

Indeed, in the repeated-dose toxicity studies in rats (28 days, 90 days and 24 months), flufenoxuron induced reduced triglycerides levels. Furthermore, flufenoxuron was found to have a high affinity for fat (toxicokinetic studies) and was detected in the milk of lactating rats in the cross-fostering study. The hypothesis of a perturbation of the mammary development and lactation process could also be supported by the fact that some of the dead pups showed absent or minimal stomach content in the 2-generation study and that some dams had difficulties to lactate properly (in spite of substantial differences in study design from 2-generation study) after exposure to flufenoxuron during days 8 to 17 of gestation in the CKA test.

Based on the presence of flufenoxuron in the milk produced by the treated dams and effects on pup survival and their development during lactation, a classification **R64 (May cause harm to breastfed babies) is proposed.**

**Neurotoxicity**

According to a 28-day neurotoxicity study in rats, flufenoxuron is not neurotoxic.

**Human data**

Medical surveillance was performed in a manufacturing plant in France for over a total of six years. During this period, no unusual or abnormal health effect were observed among the operators and other employees involved in flufenoxuron production (total of 50 people). Only one case of skin allergy (hives on face, abdomen and thighs followed by repeated pharyngitis) was reported but no medical tests had been performed to confirm flufenoxuron as causative agent.

In another manufacturing plant in the United Kingdom, no unusual or abnormal health effects among 15 operators or other employees involved in flufenoxuron production were reported in two production campaigns during 2002 and 2003.

The risk assessment conducted for the active substance covers also the risk due to metabolites and impurities.

### 2.2.1.2 Exposure assessment

Exposure was assessed for the flufenoxuron-containing wood preservative products Basiment Holzwurm BV Konzentrat and Basiment Holzwurm BV U 1551. Both primary and secondary exposures were taken into account, for industrial, professional (residential), non professional users and consumers.

Basiment Holzwurm BV Konzentrat is a 0.1 % EC formulation which is diluted 10-fold (0.01 % a.s.) in water before application. Basiment Holzwurm BV U 1551 is a ready-to-use solvent-based formulation containing 0.02 % flufenoxuron.

**In the exposure assessment, the "water based formulation" refers to the Basiment Holzwurm BV Konzentrat which is a solvent based formulation diluted in water for using and solvent based formulation refers to the Basiment Holzwurm BV U 1551.**

Handling and application of wood preservatives in an industrial, professional or amateur environment can result in direct exposure via skin contact or via inhalation. Contamination by ingestion should not occur under usual working practices as long as a minimum of hygiene standards are observed. The oral route is therefore not included as a potential direct route for exposure during the use of wood preservatives (in contrast to indirect exposure via secondary contact, see Section 2.3.1.3.2). Exposure via the environment is another potential route, which is however rather an indirect than a direct one.

| Exposure path | Industrial use | Professional use | General public | Via the environment |
|---|---|---|---|---|
| Inhalation | √ | √ | √ | *x* |
| Dermal | √ | √ | √ | *x* |
| Oral | *x* | *x* | *x* | *x* |

#### 2.2.1.2.1 Primary exposure

##### *2.2.1.2.1.1 Industrial procedures*

2.2.1.2.1.1.1 Double-vacuum impregnation of timber

This procedure can be subdivided into several activities with and without exposure potential as described below.

**Mixing/loading**

Mixing/loading is a fully automated process in a closed system. Mixing occurs in large tanks to which the product and water are automatically supplied in the required quantities via hoses. There is no manual interaction needed. Loading/unloading of the impregnation chamber from and back to the mixing tank also occurs in an automated, closed system, without any need for manual interaction by the operator. Treating solutions are recycled. The concentration of active ingredient may be checked from time to time and adjusted by additional supply of product, all within the same automated, closed system.

The **process of mixing/loading** in a double-vacuum impregnation system is **not associated with significant exposure** of the operator, neither by inhalation nor via dermal contact. No exposure calculation is provided for this activity.

**Application**

The application process itself occurs in the vacuum pressure impregnation chamber, which is part of the closed system. Two activities may potentially lead to exposure to the product: opening of the impregnation chamber and handling of treated wood. For this scenario the TNG on Human Exposure to Biocidal Products provides a model to estimate dermal and inhalation exposure (Handling, Model 1).

**Post-application and disposal**

Daily maintenance is included in application process.

Another potential source for contamination with residual product is cleaning the inner surface of the impregnation chamber. In some impregnation plants cleaning is done once a year, in others they never clean. The cleaning process lasts for a few hours. For this scenario the TNG on Human Exposure to Biocidal Products provides a model to estimate dermal and inhalation exposure (Handling, Model 1).

2.2.1.2.1.1.2 Vacuum pressure impregnation of timber

Vacuum pressure treatment of timber follows the same activities as double-vacuum impregnation. So exposure during one cycle of process is identical for vacuum pressure process and double vacuum process.

Differences occur only in the process. Vacuum pressure process contains one phase of vacuum per cycle whereas double-vacuum pressure process contains two phases of vacuum per cycle.

According to the TNsG part 2, page 77, vacuum pressure process has a cycle time of 3 hours and double vacuum process has a cycle time of 1 hour. Only three cycles are performed each day for simple vacuum process when six cycles are performed for double vacuum process. On this basis exposure for double vacuum process is considered as a worst-case scenario covering exposure during simple vacuum process. So, no specific scenario has been developed for simple vacuum process.

2.2.1.2.1.1.3 Dipping of timber

This procedure can be subdivided into several activities with or without exposure as described below.

**Mixing/loading**

Mixing/loading is a fully automated process in a closed system. Mixing occurs in large tanks to which the product and water are automatically supplied in the required quantities via hoses. There is no manual interaction needed. Loading of the dipping tank from the mixing tank also occurs in an automated, closed system, without any need for manual interaction by the operator. The concentration of active ingredient may be checked from time to time and adjusted by additional supply of product, all within the same automated, closed system.

The **process of mixing/loading** for dipping of wood in industrial premises is **not associated with significant exposure** of the operator, neither by inhalation nor via dermal contact. No exposure calculation is provided for this activity.

**Application**

The application process itself occurs in dipping tanks with no direct manipulations during treatment of wood. Handling of treated wood may potentially lead to exposure to the product. For this scenario the TNG on Human Exposure to Biocidal Products provides a model to estimate dermal and inhalation exposure (Handling, Model 1).

**Post-application and disposal**

Daily maintenance is included in application process.

Another potential source for contamination with residual product is cleaning the inner surface of the dipping tank. In some dipping plants cleaning is done once a year, in others they never clean. The cleaning process lasts for a few hours. For this scenario the TNG on Human Exposure to Biocidal Products provides a model to estimate dermal and inhalation exposure (Handling, Model 1).

2.2.1.2.1.1.4 Automated spraying/deluge

No specific exposure data are available on automated enclosed spraying. According to the User Guidance for Human Exposure to Biocidal Products (TNG, 2002, p44), exposure during dipping process is a good approximation of the exposure during automated spraying/deluge application. Therefore the exposure assessment is covered by industrial dipping scenario.

It should be underlined that exposure of operators by automated spraying is likely to be less than by dipping, as the automated spraying is fully enclosed and minimal spray mist is released.

### *2.2.1.2.1.2 Professional procedures*

There are several application techniques for indoor (*in situ*) remedial wood preservation by professionals. These are mainly spraying, brushing and injection. Out of these scenarios, spraying is considered to represent the worst case. The following exposure estimates for professional *in situ* treatment is therefore limited to the spraying technique. It is considered that indoor application covers outdoor application, where inhalation exposure might be only slightly reduced.

Additionally, flufenoxuron containing formulations may be used for small-scale dipping of wood in use (e.g. fences, windows).

2.2.1.2.1.2.1 *In situ* spraying wooden structures (medium pressure spraying with electric powered spray equipment)

This procedure can be subdivided into several activities with or without exposure as described below.

**Mixing/loading**

A tank of appropriate size is filled once a day with spraying solution either by pumping from a larger reservoir (ready to use formulation) or by mixing appropriate amounts of formulation and water. This activity is considered to potentially result in contamination by dermal contact (mainly hands) and by inhalation. Several models are provided by the TNG on Human Exposure to Biocidal Products to estimate exposure levels (Mixing and loading, e.g. Models 4, 5). Further, the spraying model mentioned below (Model 2) does include exposure during mixing/loading.

**Application**

Spray application indoor is associated with significant exposure. Professionals may spray all over the year, 5 days a week. The average daily duration is about 40 min. The TNG on Human Exposure to Biocidal Products provides a model to estimate exposure levels during medium pressure spray application (Spraying, Model 2). The model data include exposure during mixing/loading and application.

**Post-application and disposal**

A relevant post-application task which may lead to some degree of exposure is the cleaning of the spray equipment. Cleaning of the equipment is assumed to be done once a day and lasts for about 15 min. It might result in some skin exposure. The cleaning phase is not covered by any of the proposed TNG on human exposure to biocidal products. Therefore, the Riskofderm toolkit has been used.

2.2.1.2.1.2.2 Small-scale dipping of timber

This procedure can be subdivided into several activities with or without exposure as described below.

**Mixing/loading**

A small-scale dipping tank is filled at maximum once a day with treating solution either by pumping from a larger reservoir (ready to use formulation) or by mixing appropriate amounts of formulation and water. This activity is considered to potentially result in contamination by dermal contact (mainly hands) and by inhalation. Several models are provided by the TNG on Human Exposure to Biocidal Products to estimate exposure levels (e.g.: Mixing/loading, Model 7).

**Application**

Dipping is typically performed outdoor (protected with a roof) and maybe associated with some, mainly dermal, exposure. Professionals may apply this technique during most part of the year. The average daily duration is about 30 min. The TNG on Human Exposure to Biocidal Products provides a model to estimate exposure levels during dipping of wooden articles (Dipping, Model 1).

**Post-application and disposal**

There is no technical equipment which might require maintenance work. The dipping tank may be cleaned occasionally - possibly once a year or less. Cleaning may last for a relatively short time (e.g. 1 hour or less). There is a certain potential for contamination mainly due to dermal contact. However, compared to an industrial dipping tank the expected contamination during cleaning should be lower, due to the lower size of the tank and consequently the lower time needed. Therefore, the exposure during

this activity is not specifically assessed. As a worst-case scenario it can be referred to the cleaning of industrial dipping tanks.

#### *2.2.1.2.1.3 Industrial and professional procedures exposure summary*

Table 2.2.1-1: Summary table for exposure estimates to flufenoxuron resulting from industrial and professional procedures

| **Professional uses Scenarios** | **Systemic dose per day** |
|---|---|
| *Primary exposure double vacuum pressure (water-based formulation)* [1)] | |
| Tier 1 (gloves) | $4.25 \times 10^{-2}$ mg/kg bw/d |
| Tier 2 (gloves, coverall and RPE) | $8.87 \times 10^{-3}$ mg/kg bw/d |
| *Primary exposure double vacuum pressure (solvent-based formulation)* [1)] | |
| Tier 1 (gloves) | $3.65 \times 10^{-3}$ mg/kg bw/d |
| Tier 2 (gloves, coverall and RPE) | $4.48 \times 10^{-4}$ mg/kg bw/d |
| *Primary exposure dipping process (water-based formulation)* [2)] | |
| Tier 1 (gloves) | $4.25 \times 10^{-2}$mg/kg bw/d |
| Tier 2 (gloves, coverall and RPE) | $8.87 \times 10^{-3}$ mg/kg bw/d |
| *Primary exposure dipping process (solvent-based formulation)* [2)] | |
| Tier 1 (gloves) | $3.65 \times 10^{-3}$ mg/kg bw/d |
| Tier 2 (gloves, coverall and RPE) | $4.48 \times 10^{-4}$ mg/kg bw/d |
| *Primary exposure in situ spraying wooden structures (water-based formulation)* [3)] | |
| Tier 1 (no PPE) | $5.19 \times 10^{-3}$ mg/kg bw/d |
| Tier 2 (gloves, coverall and RPE) | $1.88 \times 10^{-3}$ mg/kg bw/d |
| *Primary exposure in situ spraying wooden structures (solvent-based formulation)* [3)] | |
| Tier 1 (no PPE) | $1.04 \times 10^{-2}$ mg/kg bw/d |
| Tier 2 (gloves, coverall and RPE) | $3.77 \times 10^{-3}$ mg/kg bw/d |
| *Primary exposure small-scale dipping (pouring liquid) (water-based formulation)* | |
| Tier 1 (gloves, coverall no RPE) | $1.70 \times 10^{-3}$ mg/kg bw/d |
| Tier 2 (gloves, coverall and RPE) | $8.88 \times 10^{-4}$ mg/kg bw/d |
| *Primary exposure small-scale dipping (pumping liquid) (water-based formulation)* | |
| Tier 1 (gloves, coverall no RPE) | $1.48 \times 10^{-3}$ mg/kg bw/d |
| Tier 2 (gloves, coverall and RPE) | $4.67 \times 10^{-4}$ mg/kg bw/d |
| *Primary exposure small-scale dipping (solvent-based formulation)* | |
| Tier 1 (gloves) | $2.31 \times 10^{-3}$ mg/kg bw/d |
| Tier 2 (gloves, coverall and RPE) | $8.97 \times 10^{-4}$ mg/kg bw/d |

*[1] Double vacuum is considered as a worst-case, also covering simple vacuum impregnation process. Exposures for vacuum application are two-fold lower than those for double vacuum application.*

*[2] According to the User Guidance for Human Exposure to Biocidal Products (TNG, 2002, p44), exposure during dipping process is a good approximation of the exposure during automated spraying/deluge application.*

*[3] In situ spraying is considered as a worst-case, also covering brushing and injection*

#### *2.2.1.2.2 Non-professional (Do-it yourself in situ) applications*

The relevant application technique for do-it-yourself *in situ* treatment of wood are brushing and spraying, both indoor and outdoor.

These procedures can be subdivided into several activities with or without exposure as described below.

**Mixing/loading**

Products in the do-it-yourself market are sold as ready-to-use products. Mixing/loading is therefore not a relevant activity for this user group and therefore not assessed.

**Application**

*Brushing:*

Brushing indoor or outdoor may be associated with some exposure, mainly by skin contact. Amateurs apply wood preservatives very rarely, not more than once or twice a year. The average daily duration of the task is 155 min. The TNG on Human Exposure to Biocidal Products provides several models to estimate exposure levels during brush painting which are considered to be suitable for this scenario:

- for overhead indoor brush painting (Consumer product painting, Model 1)
- for outdoor painting of sheds and fences (Consumer product painting, Model 2 and 3).

Model 2 gives separate data for water-based and solvent-based products but contains no data for inhalation. Dermal data are only provided as potential exposure.

Model 3 contains data for inhalation exposure and for hand and feet exposure inside gloves and shoes.

*Spraying:*

The TNG on Human Exposure to Biocidal Products proposes several models for consumer product spraying. Consumer Models 2 (ready-to-use aerosol and trigger spray for surface spraying) and Model 3 (refillable pressure sprayers) are considered to be most suitable for estimating the exposure of amateurs during the application of wood preservatives by spraying.

**Post-application/Maintenance/Cleaning**

Freshly treated, wet wood is assumed not to be touched. If nevertheless accidental contact by the operator occurs, it will be of very short duration and to a small skin area only. It is assumed that it will in any case cause much lower contamination than during application and/or cleaning. Exposure through accidental contact with wet wood is not calculated. Contamination of other residents by contact with treated, wet wood is considered to be secondary or indirect exposure and is treated separately (see document IIB).

The only others relevant post-application task which may lead to some degree of exposure is the cleaning of the brush and the cleaning of spraying equipment. In accordance to above description of

brushing, cleaning of the equipment (brush) by amateurs is done once to twice a year at maximum and lasts for no more than 15 min. It might result in some exposure to hands. The exposure during cleaning is not covered by any of the proposed TNG models; therefore an internal calculation is provided. As for brush application there is no existing scenario for assessment of exposure during cleaning of spraying equipment. So the Riskofderm toolkit has been used.

**Table 2.2.1-2: Summary table for non-professional exposure estimates to flufenoxuron resulting from application of wood preservative**

| **Non-Professional uses Scenarios** | **systemic dose (mg/kg bw/d)** |
|---|---|
| *overhead indoor brushing model 1* | |
| Tier 1 | $1.55 \times 10^{-2}$ |
| *outdoor brushing of sheds and fences model 2* | |
| Tier 1 | $1.16 \times 10^{-2}$ |
| *outdoor brushing of sheds and fences model 3* | |
| Tier 1 | $6.52 \times 10^{-3}$ |
| *spraying indoor/outdoor model 2* | |
| Tier 1 | $8.55 \times 10^{-3}$ |
| *trigger spray indoor/outdoor model 2* | |
| Tier 1 | $3.42 \times 10^{-3}$ |
| *hand held pressurised sprayer indoor/outdoor model 3* | |
| Tier 1 | $5.39 \times 10^{-3}$ |
| *electric powered sprayer outdoor model 3* | |
| Tier 1 | $3.15 \times 10^{-3}$ |

#### 2.2.1.2.3 Secondary exposure

Secondary exposure is assessed as proposed by the TNsG on Human Exposure to Biocidal Products. Among these, there are scenarios which may be considered to represent worst cases for all of the relevant exposure routes. These are:

- for dermal route: manual handling of wet wood; playing children on preserved (dried) wood, cleaning of work wear at home,
- for oral route: infants chewing preserved timber off-cuts,
- and for inhalation route: processing of treated wood, exposure in a room with treated wood.

Other possible secondary exposure scenarios are assumed to represent lower exposure risks. In particular, the question of potential exposure through the environment e.g. food and drinking water can be addressed:

- The dose rate of flufenoxuron active substance consists of a few g a.s./$m^3$ treated wood and the quantity of active ingredient perceived for the whole of EU amounts to <1 tonne p.a.
- Flufenoxuron products will only be used as wood preservatives for Hazard Classes 1 - 3, so treated timber will not be in contact with the soil. Consequently potential emission to soil or

surface or groundwater can only arise through leaching and run-off after rainfall. This is dealt with in the Environmental Exposure Assessment and shown to be minimal.

- Flufenoxuron has a high sorption to soil and sediment (independent of pH), is of very low mobility in soil, and is not expected to reach groundwater.
- Flufenoxuron is of extremely low solubility in water (1.36-3.69 µg/l at pH 5-9)
- No food contact clearance is being sought at this time, so flufenoxuron treated wood would not come into direct contact with foodstuffs (e.g. fruit and vegetables). If this were to be considered later, suitable residue analysis studies would be conducted in order to obtain clearance.

Exposure and risk for livestock that could lick treated timber and so be exposed to the preservative will have to be taken into account during product authorisation stage if it is relevant.

As agreed during the TM IV09, the risk to pets will be considered at the product authorisation stage if relevant and appropriate risk management measures (e.g labelling instructions) could be taken at national level.

#### *2.2.1.2.3.1 Professional manual handling of treated wet wood*

Handling Model 1 of the TNsG on Human Exposure to Biocidal Products describes the intermittent manual contact with treated wet wood. In principle this model is to be used for industrial wood preservation processes, as the incorporated studies have been conducted in such industrial environments. However, it is considered to be a suitable surrogate for the exposure estimation due to secondary contact to wet wood, outside the industrial facility. The data in the model do not only cover contact to wet wood but also to any other contaminated surfaces in the facility. Applying this model to secondary exposure outside the facility is therefore expected to result in an overestimation of the real exposure. The model presents the exposure data as mg product per treatment cycle. Depending on the type of process, the cycle duration varies from 30 min. to 3 hours. This time range is considered to reasonably reflect the daily secondary contact to wet wood. Model calculation is therefore conducted for 1 cycle. Inhalation exposure outside the facility is considered to be of less relevance compared to inside the facility during the treatment process. Only the dermal exposure part of the model is therefore included in the calculation.

The model gives data for potential dermal (body) exposure but exposure to hands and feet are given as actual exposure only (inside gloves and shoes). Further, the model gives data for penetration through clothing. The calculations therefore contain the option for wearing or not wearing of protective clothing but assume always the wearing of gloves and shoes. Although the model contains data for using new and used gloves, the calculations consider used gloves only.

As the model gives separate data for water based and for solvent based formulations, both options are considered.

Handling of wet wood by persons other than the operator in the industrial facility is not a daily event but may happen occasionally. As a worst case, it is considered to be a chronic exposure.

#### *2.2.1.2.3.2 Processing of treated wood*

Processing activities with treated but completely dried wood can be performed by professionals as well as by amateurs. Exposure to flufenoxuron may occur by dermal contact or by inhalation of wood dust.

The most critical activities are sawing and grinding, which may generate substantial amounts of dust. Professional exposure is assumed to be up to chronic, whereas exposure to amateurs may happen only rarely and is therefore best described as acute.

The highest *professional exposure* to the preservative via inhalation is limited by the limit concentrations for wood dust at workplaces. These are regulated by different bodies. The German "Gefahrstoffverordnung" has established a general limit value for wood dust of 2 mg/m$^3$ air, which might be exceeded for short periods by a factor of 4 (resulting in 8 mg/m$^3$). The EU limit value for hardwood dust is fixed at 5 mg/m$^3$. Similarly, the American Conference of Governmental Industrial Hygienists (ACGIH) has established a long term Threshold Limit Value (TLV) for certain hardwood dust of 1 mg/m$^3$ and for softwood dust of 5 mg/m$^3$, whereas for short-term exposure to softwood dust the TLV is at 10 mg/m$^3$. Exceeding of a limit value would require respiratory protection. For the following exposure estimates it is assumed that in a professional environment appropriate technical measures are taken to minimize dust development. On the other hand, processing work with pre-treated wood may last for several hours or an entire work day. Therefore the more stringent limit value of 2 mg/m$^3$ according to the German regulation is applied to calculate the highest acceptable exposure to wood dust for professionals.

*Amateurs* are assumed to work for relatively short periods with pre-treated wood but usually have no appropriate equipment to reduce dust development. Exposure estimates for amateurs are therefore based on the higher limit value for wood dust of 10 mg/m$^3$.

Operators (professional or consumers) are exposed by dermal contact with treated dry wood. Exposure was estimated using model specified in the TNsG (USER GUIDANCE version 1, p51) on human exposure. The scenario considers that 20% of the palms of hands are contaminated at 100% of the concentration of flufenoxuron residue on wood surface. As a worst case approach, the migration factor of active substance from dry wood to hand is considered to be 100%.

#### *2.2.1.2.3.3 Inhalation exposure in presence of treated wood in a room*

Adult and children can be exposed to release from treated wood of residue of active substance in the air. This is considered a chronic exposure. As a worst cast scenario it is assumed that adult and children are exposed during 24h at a saturated vapour concentration. Considering a vapour pressure of 6.52 x $10^{-12}$ Pa, the airborne concentration of active substance is about 1.31 x $10^{-9}$ mg a.s. /m$^3$.

#### *2.2.1.2.3.4 Cleaning work wear at home*

Persons at risk are adults. The relevant exposure route is dermal. Cleaning of treatment equipment has been integrated in the process scenarios. Another cleaning activity with the potential for some contamination is the washing of contaminated work clothing (e.g. a coverall). Washing is assumed to occur mechanically without any exposure risk to humans. Contact with effluent is unlikely to occur. The only likely exposure can occur during handling of the dirty clothing while preparing it for washing. The exposure route is dermal (mainly to hands) and is dependent on the area concentration of dislodgeable residues on the surface of the clothing and the transfer coefficient to the human skin. For the following it is assumed, that the clothing to be washed is a coverall used by a professional applicator (considered to represent the worst case). The total surface of a medium size coverall was determined to be 22,700 cm$^2$. Body contamination (without hands and feet) as calculated for above described professional exposure scenarios are re-expressed as mg a.s./day.

The highest coverall contamination is obtained by intermittent contact with wet wood during industrial processes with a 95%-ile value of 25.5 mg/day. It is further assumed that the coverall is washed after one working week, corresponding to 5 working days, and the total residues accumulate during this time and account for 5-times the daily deposits. The total contamination for one working week therefore accounts for 127.4 mg/week. Part of this residues will be on the surface of the tissue and therefore dislodgeable, but part will be within the tissue and therefore non-dislodgeable. As a worst case it is assumed that up to 30% of the total residues are dislodgeable (the transfer coefficient for contamination (dried fluid) from cotton, knitwear to wet hands according to TNsG, Part 2, p.204). Therefore the

dislodgeable residues on coveralls can account for up to 38.2 mg/week. For an adult the total area of both hands (front and back) is 840 $cm^2$.

As another worst case assumption, 100% of the dislodgeable residues in the touched area are considered to be transferred to the skin.

#### *2.2.1.2.3.5 Toddlers and infants playing on preserved timber*

Persons at risk are children. The following scenario describes exposure due to secondary contact with treated, dried wood. The relevant exposure route is dermal. Occasionally, oral exposure might also occur, e.g. in case a playing child puts its contaminated hand into the mouth. However, it is reasonable to assume that this would result in a much lower exposure compared to the scenario described below (chewing preserved timber off-cuts). It is therefore not specifically assessed. Inhalation exposure is considered to be negligible due to the low vapor pressure of flufenoxuron. Dermal exposure duration can be up to chronic, assuming that playing in this environment may happen daily. The same degree of exposure is assumed to occur every day throughout the entire lifespan of the wooden structure. It is considered to represent the worst case scenario for secondary, dermal exposure due to contact with dried, treated wood.

As described for the previous scenario, dermal exposure depends on the dislodgeable residues and the transfer coefficient. Highest levels of dislodgeable residues are assumed to result from surface treatment procedures rather than from vacuum-/pressure-type techniques. The maximum absorbed flufenoxuron in wood treated by industrial dipping amounts to 0.0064 $mg/cm^2$. Fully dried and fixed preserved wood is expected to strongly bind the preservative agent. Therefore, only a small fraction of the absorbed preservative must be assumed to be dislodgeable due to dermal contact. The TNsG on Human Exposure to Biocidal Products suggests a dislodgeable portion (transfer efficiency) of 2% for dried fluid on rough sawn wood. This is considered to be rather conservative, particularly when assuming daily contact and an even daily exposure throughout the entire lifespan of the wooden structure. Transfer coefficients for this activity on wooden structure can be derived from the Standard Operating Procedures (SOPs) for Residential Exposure Assessment, published by US-EPA in 1997. Section 8.2.2 of this document describes the exposure scenario for "Post application dermal dose from pesticide residues on hard surfaces". This document proposes TCs of 8700 $cm^2$/hr for toddlers (1-6 year old) and 6000 $cm^2$/hr for infants (0.5-1.5 year old). The average body weights for these two groups as suggested in this document are 15 and 10 kg, respectively and a daily duration of exposure of 4 hours is proposed. No protection by clothing is assumed.

#### *2.2.1.2.3.6 Infants chewing preserved timber off-cuts*

Persons at risk are infants. The relevant exposure route is oral. This is an incidental event and exposure duration is therefore best described as acute. This scenario is considered to represent the worst case for secondary oral exposure. Timber off-cuts may originate from vacuum impregnated wood or from surface treated (e.g. dipping) wood. The content of active ingredient in the two types of treated timber differs, due to different degrees of absorption of the preservative. The two following scenarios calculate exposure based on absorption data for wood treated by double vacuum technique and by dipping.

Double vacuum impregnated timber: the maximum absorption of product is 50 $L/m^3$ (according to the TNG on Human Exposure to Biocidal Products). It is assumed that all of this is bound in the outermost 10% of the timber volume and that this part is accessible to infants for chewing. It is further assumed that only a small fraction of the total preservative become released by chewing, as most of it is bound inside of the piece of wood. A reasonable assumption is that 100% may become released. Further, a piece of the size of 2 $cm^3$ is assumed to be chewed.

Dipping: this technique is considered to be representative for all surface treatments. The extent of absorption is 0.05 L product/$m^2$ (according to the TNG on Human Exposure to Biocidal Products). Only

an outermost, very thin layer (1 mm or less) binds the preservative. In contrast to vacuum impregnated wood, surface treated wood may release a higher fraction of the preservative during chewing. It is assumed that 100% of absorbed a.s. becomes released. A chip of 6 $cm^2$ from the outermost layer is chewed. This scenario reflects the worst case, as a chip from the timber surface contains by far the highest concentration of the preservative.

#### *2.2.1.2.3.7 Summary for secondary exposure scenario*

**Table 2.2.1-3: Summary table for secondary exposure scenario**

| **Secondary exposure Scenarios** | **systemic dose (mg/kg bw/d)** |
|---|---|
| *Professional manual handling of treated wet wood (water based)* | |
| Tier 1 (gloves and shoes) | $6.63 \times 10^{-3}$ |
| Tier 2 (protective clothing, gloves and shoes) | $1.03 \times 10^{-3}$ |
| *Professional manual handling of treated wet wood (solvent based)* | |
| Tier 1 (gloves and shoes) | $1.33 \times 10^{-2}$ |
| Tier 2 (protective clothing, gloves and shoes) | $3.03 \times 10^{-3}$ |
| *Processing of treated wood by professionals* | |
| Tier 1 (no PPE) | $9.02 \times 10^{-4}$ |
| *Processing of treated wood by amateurs* | |
| Tier 1 (no PPE) | $8.98 \times 10^{-4}$ |
| *Adult Inhalation exposure in presence of treated wood in a room* | |
| Tier 1 | $6.54 \times 10^{-10}$ |
| *Children Inhalation exposure in presence of treated wood in a room* | |
| Tier 1 | $1.35 \times 10^{-8}$ |
| *Cleaning work wear at home* | |
| Tier 1 | $2.3 \times 10^{-3}$ |
| *Toddler playing on preserved timber* | |
| Tier 1 | $2.32 \times 10^{-2}$ |
| *Infants playing on preserved timber* | |
| Tier 1 | $2.40 \times 10^{-2}$ |
| *Infants chewing preserved timber off-cuts (double vacuum treatment)* | |
| Tier 1 | $6.00 \times 10^{-4}$ |
| *Infants chewing preserved timber off-cuts (dipping treatment)* | |
| Tier 1 | $2.84 \times 10^{-3}$ |

### 2.2.1.3 Risk characterisation

The human health risk characterisation is performed using both the AEL and the MOE approaches.

Furthermore, as no uses of treated wood is intended in animal housing or in food contact, no Acceptable Daily Intake (ADI) was derived to perform a dietary risk assessment for human consumers of food of animal origin.

#### 2.2.1.3.1 *AELs determination*

For each exposure scenario, an appropriate AEL is determined on the basis of the exposure frequency.

Accordingly, three types of AELs are classically derived: $AEL_{acute}$, $AEL_{medium\text{-}term}$ and $AEL_{long\text{-}term}$ corresponding to short-, medium- and long-term exposures respectively.

AELs are usually derived by applying the following formula:

$$AEL = \frac{NOAEL}{Assessment\ \ factors}$$

In the case of flufenoxuron, the $AEL_{acute}$ was derived on the basis of the NOAEL of 49 mg/kg bw/day obtained in the 28-day oral rat study.

The $AEL_{medium\text{-}term}$ and $AEL_{long\text{-}term}$ were derived on the basis of the NOAEL of 3.5 mg/kg bw/day from the 1-year oral dog study.

As flufenoxuron did not induce any local effects by dermal and inhalation route, no local AEC was derived.

Regarding the assessment factors, a default value of 100 (including an inter-species factor of 10 and an intra-species factor of 10) was applied. This value is used as the reference margin of exposure ($MOE_{ref}$). Furthermore, an oral absorption rate of 80% was taken into account for deriving AELs.

The following AELs were therefore derived:

- $AEL_{acute}$ = 49 x 0.8 / 100 = 0.4 mg/kg bw/day
- $AEL_{medium/long\text{-}term}$ = 3.5 x 0.8 / 100 = 0.028 mg/kg bw/day

In the AEL approach, a risk is considered as acceptable if AEL > exposure.

In practice, exposure is expressed as a percentage of the AEL (%AEL). The risk is therefore considered as acceptable if %AEL < 100.

In the MOE approach, a risk is considered as acceptable if MOE > $MOE_{ref}$ (where $MOE = \frac{NOAEL}{Exposure}$ ).

### *2.2.1.3.2 Risk characterisation for primary exposure scenarios*

For professional scenarios, the exposures were compared to the long-term AEL. For non-professional scenarios, the acute AEL is considered as appropriate since it is assumed that the non-professional apply wood preservatives not more than once or twice a year.

The results of the risk characterisation are summarised in tabular format in Table 2.2.1.3.2-1 for industrial/professional primarily exposed to flufenoxuron and in table 2.2.1.3.2-2 for non-professional users.

Table 2.2.1.3.2-1 : Summary of exposure and risk assessment for industrial/professional users.

| Exposure Scenario | Systemic dose (mg/kg bw/d) | Relevant NOAEL (mg/kg bw/d) | AEL (mg/kg bw/d) | $MOE_{ref}$ | % AEL | MOE |
|---|---|---|---|---|---|---|
| Double vacuum pressure and dipping process for water-based formulation | | | | | | |
| Tier 1 (gloves) | $4.25 \times 10^{-2}$ | 2.8* | 0.028 | 100 | **151.8** | **65.9** |
| Tier 2 (gloves, coverall and RPE) | $8.87 \times 10^{-3}$ | 2.8* | 0.028 | 100 | 31.7 | 315.7 |
| Double vacuum pressure and dipping process for solvent-based formulation | | | | | | |
| Tier 1 (gloves) | $3.65 \times 10^{-3}$ | 2.8* | 0.028 | 100 | 13.0 | 767.1 |
| *In situ* spraying wooden structures for water-based formulation | | | | | | |
| Tier 1 (no PPE) | $5.19 \times 10^{-3}$ | 2.8* | 0.028 | 100 | 18.5 | 539.5 |
| *In situ* spraying wooden structures for solvent-based formulation | | | | | | |
| Tier 1 (no PPE) | $1.04 \times 10^{-2}$ | 2.8* | 0.028 | 100 | 37.1 | 269.2 |
| Small scale dipping for water-based formulation (pouring liquid) | | | | | | |
| Tier 1 (gloves, coverall, no RPE) | $1.70 \times 10^{-3}$ | 2.8* | 0.028 | 100 | 6.1 | 1647.1 |
| Small scale dipping for water-based formulation (pumping liquid) | | | | | | |
| Tier 1 (gloves, coverall, no RPE) | $1.48 \times 10^{-3}$ | 2.8* | 0.028 | 100 | 5.3 | 1891.9 |
| Small scale dipping for solvent-based formulation | | | | | | |
| Tier 1 (gloves) | $2.31 \times 10^{-3}$ | 2.8* | 0.028 | 100 | 8.3 | 1212.1 |

*Internal NOAEL based on an 80% oral absorption rate: NOAEL = 3.5 x 0.8 = 2.8 mg/kg bw/d

Conclusions:

For industrial applications, double-vacuum pressure (also covering simple vacuum impregnation process) and dipping/automated spraying, the risks are acceptable with solvent-based formulation with gloves (Tier 1) and with water-based formulation, with gloves, coverall and respiratory protection (Tier 2).

*In situ* applications of water-based and solvent-based formulations by spraying (covering brushing and injection) or small-scale dipping by professional users are acceptable in Tier 1:

- spraying/brushing/injection: the risks are acceptable without PPE,
- small-scale dipping: the risks are acceptable for water-based formulation considering the wearing of gloves and coverall and for solvent-based formulation with gloves only.

Table 2.2.1.3.2-2: Summary of exposure and risk assessment for non-professional users.

| Exposure Scenario | Systemic dose (mg/kg bw/d) | Relevant NOAEL (mg/kg bw/d) | AEL (mg/kg bw/d) | $MOE_{ref}$ | % AEL | MOE |
|---|---|---|---|---|---|---|
| Overhead indoor brushing (model 1) | | | | | | |
| Tier 1 | $1.55 \times 10^{-2}$ | 40* | 0.4 | 100 | 3.9 | 2581 |
| Outdoor brushing of sheds and fences (model 2) | | | | | | |
| Tier 1 | $1.16 \times 10^{-2}$ | 40* | 0.4 | 100 | 2.9 | 3448 |
| Outdoor brushing of sheds and fences (model 3) | | | | | | |
| Tier 1 | $6.52 \times 10^{-3}$ | 40* | 0.4 | 100 | 1.6 | 6135 |
| | | | | | | |
| Spraying indoor/outdoor (model 2) | | | | | | |
| Tier 1 | $8.55 \times 10^{-3}$ | 40* | 0.4 | 100 | 2.1 | 4678 |
| Trigger spray indoor/outdoor (model 2) | | | | | | |
| Tier 1 | $3.42 \times 10^{-3}$ | 40* | 0.4 | 100 | 0.9 | 11696 |
| Hand held pressurised sprayer indoor/outdoor (model 3) | | | | | | |
| Tier 1 | $5.39 \times 10^{-3}$ | 40* | 0.4 | 100 | 1.3 | 7421 |
| Electric powered sprayer outdoor (model 3) | | | | | | |
| Tier 1 | $3.15 \times 10^{-3}$ | 40* | 0.4 | 100 | 0.8 | 12698 |

*Internal NOAEL based on an 80% oral absorption rate: NOAEL = 49 x 0.8 = 40 mg/kg bw/d

Conclusion:

For scenarios of brushing and spraying, indoor and outdoor, % of AEL are below the trigger value of 100 and MOE are higher than MOE ref, the risks for non-professional users under the specified conditions are then acceptable.

#### *2.2.1.3.3 Risk characterisation for secondary exposure scenarios*

Secondary exposure during processing of treated wood (professionals), during manual handling of treated, wet wood (professional other than the operator in the industrial facility) and inhalation exposure in presence of treated wood in a room have been compared to the long-term AEL whereas exposure during processing of treated wood (amateurs) has been compared to the acute AEL.

The unintended scenario “chewing preserved timber off-cuts” has been compared to acute AEL whereas exposure for children playing on preserved timber has been compared to long-term AEL. Exposure during cleaning work wear at home was considered as a medium-term scenario and has been compared to the medium-term AEL (equivalent to the long term AEL).

Using the AEL and MOE approaches, the results are summarised in Table 2.2.1.3.3.

Table 2.2.1.3.3: Summary of exposure and risk assessment for secondary exposures

| Exposure Scenario | Systemic dose (mg/kg bw/d) | Relevant NOAEL (mg/kg bw/d) | AEL (mg/kg bw/d) | $MOE_{ref}$ | % AEL | MOE |
|---|---|---|---|---|---|---|
| Professional manual handling of treated, wet wood (water-based formulation) | | | | | | |
| Tier 1 (no protective clothing except gloves and shoes) | $6.63 \times 10^{-3}$ | 2.8* | 0.028 | 100 | 23.7 | 422 |
| Professional manual handling of treated wet wood (solvent-based formulation) | | | | | | |
| Tier 1 (gloves and shoes) | $1.33 \times 10^{-2}$ | 2.8* | 0.028 | 100 | 47.5 | 211 |
| Processing of treated wood (professionals) | | | | | | |
| Tier 1 (no PPE) | $9.02 \times 10^{-4}$ | 2.8* | 0.028 | 100 | 3.22 | 3104 |
| Processing of treated wood (amateurs) | | | | | | |
| Tier 1 | $8.98 \times 10^{-4}$ | 40** | 0.4 | 100 | 0.22 | 44543 |
| Inhalation exposure in presence of treated wood in a room (adults) | | | | | | |
| Tier 1 | $6.54 \times 10^{-10}$ | 2.8* | 0.028 | 100 | $2.34 \times 10^{-6}$ | $4.3 \times 10^{9}$ |
| Inhalation exposure in presence of treated wood in a room (children) | | | | | | |
| Tier 1 | $1.35 \times 10^{-8}$ | 2.8* | 0.028 | 100 | $4.8 \times 10^{-5}$ | $2.1 \times 10^{8}$ |
| | | | | | | |
| Cleaning work wear at home | | | | | | |
| Tier 1 | $2.3 \times 10^{-3}$ | 2.8* | 0.028 | 100 | 8.21 | 1217 |
| Playing on preserved timber (toddlers) | | | | | | |
| Tier 1 | $2.32 \times 10^{-2}$ | 2.8* | 0.028 | 100 | 82.9 | 121 |
| Playing on preserved timber (infants) | | | | | | |
| Tier 1 | $2.4 \times 10^{-2}$ | 2.8* | 0.028 | 100 | 85.7 | 117 |
| Chewing preserved timber off-cuts (double-vacuum impregnated timber) | | | | | | |
| Tier1 | $6.0 \times 10^{-4}$ | 40** | 0.4 | 100 | 0.2 | 66667 |
| Chewing preserved timber off-cuts (dipping) | | | | | | |
| Tier 1 | $2.84 \times 10^{-3}$ | 40** | 0.4 | 100 | 0.7 | 14085 |

*Internal NOAEL based on an 80% oral absorption rate: NOAEL = 3.5 x 0.8 = 2.8 mg/kg bw/d
**Internal NOAEL based on an 80% oral absorption rate: NOAEL = 49 x 0.8 = 40 mg/kg bw/d

**Conclusion:**

When exposure during processing activities on pre-treated wood (exposure to dust formation – amateur) and exposure consecutive to chewing of timber off cuts were compared to acute AEL, all the % of AEL are below 100 % and MOE are higher than MOEref, therefore, the risks are acceptable for the conditions specified above.

When the scenarios "manual handling of treated, wet wood" (professional other than the operator in the industrial facility) "processing activities on pre-treated wood" (exposure to dust formation - professional), "exposure in presence of treated wood in a room (inhalation)", "children playing on preserved timber" and "cleaning work wear at home" were compared to the medium/long-term AEL, all the % of AEL are below 100 % and MOE are higher than MOEref, therefore, the risks are acceptable for the conditions specified above.

#### *2.2.1.3.4 Combined exposure*

The potential for combined exposure for the different groups of risk has been calculated adding the indirect exposure to each user. Tier 1 exposure values have been considered when the risk was acceptable if not Tier 2 has been used, and always the worst case has been selected. The results are presented in the table 2.3.1-7.

**Table 2.3.1-7: Estimated total systemic combined exposure**

| User | Formulation | Total Systemic Exposure (mg a.s./kg bw/day) | | | | |
|---|---|---|---|---|---|---|
| | | | | Secondary | | |
| | | Professional application | Non-professional application | Handling and processing (amateur) | Cleaning of work wear | Combined |
| Industrial user (double-vacuum[1], dipping and automated spraying) | water-based | $8.87 \times 10^{-3}$ | $1.55 \times 10^{-2}$ | $8.98 \times 10^{-4}$ | $2.30 \times 10^{-3}$ | **$2.76 \times 10^{-2}$** |
| | solvent-based | $3.65 \times 10^{-3}$ | $1.55 \times 10^{-2}$ | $8.98 \times 10^{-4}$ | $2.30 \times 10^{-3}$ | **$2.24 \times 10^{-2}$** |
| Professional user (spraying) | water-based | $5.19 \times 10^{-3}$ | $1.55 \times 10^{-2}$ | $8.98 \times 10^{-4}$ | $2.30 \times 10^{-3}$ | **$2.39 \times 10^{-2}$** |
| | solvent-based | $1.04 \times 10^{-2}$ | $1.55 \times 10^{-2}$ | $8.98 \times 10^{-4}$ | $2.30 \times 10^{-3}$ | **$2.91 \times 10^{-2}$** |
| Professional user (small scale dipping) | water-based | $1.70 \times 10^{-3}$ | $1.55 \times 10^{-2}$ | $8.98 \times 10^{-4}$ | $2.30 \times 10^{-3}$ | **$2.04 \times 10^{-2}$** |
| | solvent-based | $2.31 \times 10^{-3}$ | $1.55 \times 10^{-2}$ | $8.98 \times 10^{-4}$ | $2.30 \times 10^{-3}$ | **$2.11 \times 10^{-2}$** |
| Non-professional user | | | $1.55 \times 10^{-2}$ | $8.98 \times 10^{-4}$ | $2.30 \times 10^{-3}$ | **$1.87 \times 10^{-2}$** |

[1)] Double-vacuum application is considered as a worst-case covering both vacuum and double-vacuum pressure. Exposures during vacuum applications are about twice lower than for double-vacuum applications.

**Table 12.5-2: Comparisons of AEL and combined exposure**

| User | Formulation | Total systemic exposure mg/kg/day | AEL mg/kg bw/day | % AEL | MOE |
|---|---|---|---|---|---|
| Industrial (double-vacuum, dipping and automated spraying) | water-based | **$2.76 \times 10^{-2}$** | 0.4 | 6.90 | 1449 |
| | solvent-based | **$2.24 \times 10^{-2}$** | 0.4 | 5.60 | 1786 |
| Professional (spraying) | water-based | **$2.39 \times 10^{-2}$** | 0.4 | 5.98 | 1674 |
| | solvent-based | **$2.91 \times 10^{-2}$** | 0.4 | 7.28 | 1375 |
| Professional (small scale dipping) | water-based | **$2.04 \times 10^{-2}$** | 0.4 | 5.10 | 1961 |
| | solvent-based | **$2.11 \times 10^{-2}$** | 0.4 | 5.28 | 1896 |
| Non-Professional | | **$1.87 \times 10^{-2}$** | 0.4 | 4.68 | 2139 |

***Industrial users / Water-based formulation***

For an **industrial user**, the estimated worst total systemic exposure, corresponding to dipping process, automated spraying, vacuum pressure and double vacuum pressure with **water-based formulation**, is $8.87 \times 10^{-3}$ mg a.s./kg bw/day (Tier 2). If, as an amateur (i.e. non professional user) he or she applies flufenoxuron by brushing indoor, which is the worst case among the non-professional techniques, a total systemic exposure of $1.55 \times 10^{-2}$ mg a.s./kg bw/day has to be added. Then, the potential secondary exposure has to be considered as a result of inhalation of residues in air places where the wood preservative has been used and / or as the result of dermal contact with treated wood. This amount ($8.98 \times 10^{-4}$ mg a.s./kg bw/day corresponding to the handling and processing of dry treated wood), is considered as the worst case among all the intended secondary exposure scenarios for adults. Finally, the cleaning of work wear is a task that may be carried out by the same person, and it entails a total systemic exposure of 0.0023 mg a.s./kg bw/day. Adding up all this figures, a combined exposure of **0.0276 mg a.s./kg bw/day** is obtained for an industrial user, giving a % of **AEL of 6.90% and a MOE of 1449. Therefore, risks for industrial applicators using water-based formulation are acceptable in the specified conditions.**

***Industrial users / Solvent-based formulation***

Acceptable risks were found for the industrial applicator using **solvent-based flufenoxuron containing formulation**. The estimated total systemic exposure, corresponding to dipping process/automated spraying and double vacuum pressure (covering vacuum pressure) with solvent-based formulation, is $3.65 \times 10^{-3}$ mg/kg bw/d (Tier 1). If, as an amateur (i.e. non professional user) he or she applies

flufenoxuron by brushing indoor, which is the worst case among the non-professional techniques, a total systemic exposure of $1.55x10^{-2}$ mg a.s./kg bw/day has to be added. Then, the potential secondary exposure has to be considered as a result of inhalation of residues in air places where the wood preservative has been used and / or as the result of dermal contact with treated wood. This amount ($8.98x10^{-4}$ mg a.s./kg bw/day, corresponding to the handling and processing of dry treated wood), is considered the worst case among all the intended secondary exposure scenarios for adults. Finally, the cleaning of work wear is a task that may be carried out by the same person, and it entails a total systemic exposure of 0.0023 mg a.s./kg bw/day. Adding up all this figures, a combined exposure of **$2.24x10^{-2}$ mg a.s./kg bw/day** is obtained for an industrial user, giving a % of **AEL of 5.60% and a MOE of 1786. The industrial combined exposures to solvent-based formulation are then considered acceptable.**

***Professional users / Water-based formulation***

For **professional**, the ***in situ* spraying (indoor/outdoor)** of water-based formulation leads to a total systemic exposure of 0.00519 mg a.s./kg bw/day. If this user is supposed to fulfil a non-professional application as well as the handling/processing of dry treated wood and the washing of contaminated clothes, the total combined exposure amounts **0.0239 mg a.s./kg bw/day**, giving a % of AEL of **5.98 % and a MOE of 1674**.

The exposure calculated for the professional using **small scale dipping**, also indicates that the risk is acceptable in first approach. With a total combined systemic exposure of **$2.04\ x10^{-2}$ mg/kg bw/day, the %AEL is 5.10 and the MOE is 1961.**

*In situ* brushing and injection are covered by the *in situ* spraying evaluation.

***Professional users / Solvent-based formulation***

Regarding the **professional user**, the ***in situ* spraying (indoor/outdoor)** of solvent-based formulation supposes a total systemic exposure of 0.0104 mg a.s./kg bw/day. If this user is supposed to fulfil a non-professional application as well as the handling/processing of dry treated wood and the washing of contaminated clothes, the total combined exposure amounts **0.0291 mg a.s./kg bw/day, giving a % of AEL of 7.28 and the MOE is 1375.**

The exposure calculated for the professional using **small scale dipping**, also indicates that the risk is acceptable in first approach. With a total combined systemic exposure of **$2.11x10^{-2}$ mg a.s./kg bw/day, the %AEL is 5.28 and the MOE is 1896.**

*In situ* brushing and injection are covered by the *in situ* spraying evaluation.

**In conclusion, acceptable combined risks for the professional exposed through *in situ* spray application**, **small scale dipping, *in situ* brushing and injection were found in the specified conditions.**

***Non-professional users / Solvent-based formulation (only intended use)***

The last scenario for combined exposure is for a **non-professional user**, who applies the product by brushing indoor and has a total systemic exposure of $1.55x10^{-2}$ mg a.s./kg bw/day. Secondarily, this user may be exposed after handling and processing of treated wood and cleaning work wear, and therefore

the combined exposure experienced is of **0.0187 mg a.s./kg bw/day,** giving a % of AEL of **4.68 % and a MOE of 2139. The risk is then considered as acceptable.**

***Overall conclusion of the risk characterisation for human health***

No unacceptable risk was identified for industrials, professionals and amateurs applying flufenoxuron as a wood protective. For the industrial/professional treatments considered, the operators must wear the appropriate personal protective equipment, except for *in situ* spraying (also covering brushing and injection) where the risk was acceptable without PPE. No PPE was considered for non professionals.

The indirect exposure to infants, toddlers, children or adults by inhalation, ingestion or dermal contact did not lead to any unacceptable risk.

No dietary risk assessment was performed for the annex I inclusion of flufenoxuron as no uses of treated wood in animal housing or in contact with food was intended.

## 2.2.2 Environmental risk assessment

### 2.2.2.1 Effect Assessment

#### 2.2.2.1.1 Fate and distribution in the environment

**Hydrolysis as a function of pH**

Flufenoxuron is stable to hydrolysis in buffer solutions at pH 5 and 7 at 25 C, while hydrolysis takes place to a certain but very low extent ($DT_{50}$ = 88-94 days, studies conducted with two different labels) in buffered solution at pH 9, forming one major metabolite Reg.No. 206925 (A 7.1.1.1.1/02).

**Photolysis in water**

Photolysis contributes to degradation of the active substance in water and several studies conducted under the following conditions confirm its UV-instability. One major metabolite (Reg.No. 102719) was identified. In study A 7.1.1.1.2/04, the calculated half-life of flufenoxuron for the top layer of aqueous systems in Spring and Summer varied from 39.2 days in April to 21.7 days in June.

**Photolysis in air**

Based on the vapour pressure ($6.52 \times 10^{-12}$ Pa at 20°C) and the Henry's constant ($7.46 \times 10^{-6}$ Pa × $m^3$/mol at 25°C), volatilisation of flufenoxuron is negligible. Calculations of the chemical lifetime in the troposphere (A 7.3.1) resulted in a half life of 1.12 days or 27 hours (QSAR estimates).

According to these results ($t_{1/2}$ < 2 days), flufenoxuron is rapidly degraded by photochemical processes and no accumulation of flufenoxuron in the air is to be expected.

**Biodegradation**

Flufenoxuron is not readily biodegradable according to OECD 301B and D guidelines .

A water/sediment simulation test conducted in the dark with two different water/sediment systems (A 7.1.2.2.2/01) showed that flufenoxuron moved rapidly from water into sediment with a $DT_{50}$ in the water of 0.3 to 0.4 days and was degraded with a $DT_{50}$ in the whole system of 85 to 116 days at a reference temperature of 12°C (45 to 61 days at 20°C). The $DT_{50}$ for the molecule in the sediment was 87 to 123 days at a reference temperature of 12°C (46 to 65 days at 20°C), which underlines the risk of persistence and accumulation of the molecule in sediment compartment. One major metabolite (Reg.No. 4064702) was detected in water (up to 9.3%) and in sediment (up to 19%).

In laboratory experiments on the degradation of flufenoxuron in soil, the unextractable residues were at a level of 21 – 43.8% after 120 days in key studies. The $CO_2$ formation was 23 - 52% of applied radioactivity under aerobic conditions after 120 days for benzamide-$^{14}$C-labelled flufenoxuron . Under anaerobic conditions no degradation was detected. Flufenoxuron was aerobically degraded with half-lives of 36 to 124 days (at 20°C) with Reg. No.4064702 as the only significant metabolite, accounting for 8% of the dose Reg.No. 4064702 itself was degraded with a half-life of 47 to 59 days. These values were recalculated to a reference temperature of 12°C. The $DT_{50}$ for flufenoxuron were ranged between 68 and

235 days at 12°C (with a geometric mean value of 158 days used for risk assessment). The $DT_{50}$ for Reg.No. 4064702 ranged from 89 to 112 days at 12°C. Carbon dioxide and bound residues were the major transformation products.

Field studies conducted in South regions only (A 7.2.2.2) revealed a moderate to fast dissipation of flufenoxuron in soils; the $DT_{50f}$ values varied between 6 and 67 days (n = 4).

**Mobility**

Based on reliable adsorption/desorption data (A 7.2.3.1/01 and A 7.2.3.1/02) it can be concluded that flufenoxuron is strongly adsorbed by soil components ($K_{OC}$ = 88240-289747, n = 5, mean value = 157643).
No potential for translocation into deeper soil layers or even groundwater is given.

**Bioaccumulation**

Different studies have been carried out in order to assess the bioaccumulation process of flufenoxuron in organisms. Bioconcentration factors were therefore 25920 and 24187 for the Fluoroaniline label and the Difluorobenzamide label, respectively (mean value = 25000) in the first study A 7.4.3.3.1/02. In the second study A 7.4.3.3.1/01, BCF value obtained varied from 15700 and 16130. Flufenoxuron is considered to be a very bioaccumulable substance with a BCF > 5000. The BCF value of 16130 has been used for the risk assessment.

An earthworm bioaccumulation study (A7.5) was also submitted. Earthworms were exposed to the active ingredient at 0.04 mg/kg dry soil distributed in soil for 28 days followed by an eliminated phase of 28 days. The plateau levels were reached after 16 days. The $BCF_{earthworms}$ relative to the concentration of $^{14}C$-flufenoxuron in dry weight soil was calculated to be 4.22.

### 2.2.2.1.2 Effects on environmental organisms (active substance)

**Aquatic compartment**

Long-term NOEC values are available for all three trophic levels in the aquatic compartment (fish, *Daphnia* and algae). Among the laboratory derived data, the result obtained in a chronic laboratory toxicity study with *Daphnia magna* was by far the lowest (21 d-NOEC = 0.00449 µg a.s./L, based on mean measured concentrations corrected for adsorption to glass and algae) and was therefore taken as the basis for the PNEC derivation. An assessment factor of 10 was applied, resulting in a $PNEC_{water}$ of 0.449 ng a.s./L for flufenoxuron.
Information on metabolites has been provided. The risk assessment concluded that the flufenoxuron is the only relevant residue.

Flufenoxuron showed no effect on the respiration of activated sludge micro-organisms up to the concentration of 1000 mg/L. Flufenoxuron is not expected to have any influence on sewage treatment plants. The $EC_{50}$ obtained divided by an assessment factor of 100 would have led to a $PNEC_{STP}$ of 10 mg/L. As the concentration tested is much higher than the solubility limit of the molecule, it is therefore proposed to set the PNEC value at the solubility limit; $PNEC_{stp}$ = 1.36 µg a.s./L.

As a conservative approach, it has been assumed that the $PNEC_{STP}$ = 1.36 µg/L is used for the risk assessment in first tier approach.

**Sediment**

The study considered relevant for the risk assessment has been conducted with *Chironomus riparius* exposed to flufenoxuron spiked sediment and provides a NOEC of 80 µg a.s./$kg_{dry\ sediment}$. An assessment factor of 50 was applied, resulting in a $PNEC_{sed}$ of 1.6 µg a.s./$kg_{dry\ sediment}$ (0.615 µg a.s./$kg_{wet\ sediment}$).

Information on metabolites has been provided. The risk assessment concluded that the flufenoxuron is the only relevant residue.

**Terrestrial compartment**

For the terrestrial compartment, NOEC values from long-term toxicity tests (earthworms, plants, microorganisms and soil dwelling arthropods) are available. According to the TGD for Risk Assessment (2003) an assessment factor of 10 is applied to the lowest NOEC, which was the result of chronic laboratory study on *Folsomia candida* (28-d) (NOEC = 0.117 mg/kg dry soil). The **$PNEC_{soil}$ was estimated to be 0.010 mg/$kg_{wet\ soil}$**

Information on metabolites has been provided. The risk assessment concluded that the flufenoxuron is the only relevant residue for aquatic compartment. In case of direct release to soil compartment, the terrestrial toxicity of the metabolite Reg. No. 4064702 must be investigated at the authorisation stage.

**PNECoral for secondary poisoning**

The NOEC in birds of 100 mg/kg feed is derived from a long-term study with the bobwhite quail (*Colinus virginianus*). The $PNEC_{oral/birds}$ of 3.33 mg a.s./$kg_{food}$ is derived taken into account of an $AF_{oral}$ of 30.

The $PNEC_{oral}$ of 1.67 mg a.s./$kg_{food}$ is calculated from the loewest oral toxicity data $NOAEL_{mammals}$ of 50 mg/$kg_{food}$ applying an assessment factor of 30.

**Summary of PNEC values**

| **ENVIRONMENTAL COMPARTMENT** | **PNEC** |
|---|---|
| $PNEC_{water}$ | 0.000449 µg a.s./L |
| $PNEC_{stp}$ | 1.36 µg a.s./L |
| $PNEC_{sediment}$ | 0.615 µg a.s./$kg_{wet\ sediment}$ |
| $PNEC_{soil}$ | 0.010 mg a.s./$kg_{wet\ soil}$ |
| $PNEC_{oral/birds}$ | 3.33 mg a.s./$kg_{food}$ |
| $PNEC_{oral/mammals}$ | 1.67 mg a.s./$kg_{food}$ |

#### 2.2.2.1.3 Environmental effect assessment (product)

No additional data on the environmental effects of the biocidal products were submitted. The risk assessment is based on the effect of the active substance flufenoxuron.

#### 2.2.2.1.4 PBT Assessment

In view of the characteristic of the substance and its PBT status, flufenoxuron has been sent for consideration by the ad hoc working group on PBT. Flufenoxuron has been discussed at the 10th and 11th meeting of the TC NES subgroup on identification of PBT and vPvB substances. At the 11th meeting, the group concluded that flufenoxuron fulfils the P, vP, B, vB and T criteria: flufenoxuron is a PBT/vPvB substance.

*Persistence criteria (P, vP)*

$DT_{50}$ (12°C) in soil degradation studies varies from 68 to 235 days (5 soils, 2 labels). P and vP criteria are fulfilled.

*Bioaccumulation criteria (B, vB)*

In the BCF key study done with *Oncorhynchus mykiss* according to OECD 305 guideline, the BCF value for uptake of flufenoxuron in fish from clean water based on the fitted steady state concentration at the exposure level of 40 ng/L is 25000 L/kg. Another study shows a BCF value comprise between 13700 and 16130 L/Kg with initial concentration of 40 ng/L and 31 ng/L respectively. B and vB criteria are fulfilled.

*Toxicity criteria (T)*

Based on ecotoxicity data on *Daphnia magna*, NOEC (21 d, reproduction) = 0.00449 µg/L (semi-static, mean measured concentrations corrected with adsorption to glass and algae), T criteria is fulfilled.

Flufenoxuron is a chitin synthesis inhibitor. Chitin is a structural component of insect cuticles. Chitin is a polymer of N-acetylglucosamine and is synthesized by a reaction catalyzed by chitin synthetase. Flufenoxuron disrupts normal development and molting by interfering with chitin synthetase thus preventing polymerization of N-acetylglucosamine and blocking formation of the cuticle at the molt. Immature insects exposed to chitin synthesis inhibitors develop malformed cuticles which cannot withstand internal pressure during molting or cannot give enough support to the muscles involved in molting. This results in failure of the insect to cast the old cuticle." Flufenoxuron is a benzoylurea and this group of chitin synthesis inhibitors are considered to have a non-endocrine mode of action (LeBlanc et al., 1999, Oetken et al., 2004).

Thus based on the human and ecological toxicity data currently available, flufenoxuron is considered not to have endocrine disrupting effects. It is also not listed in the document of the EU Commission on endocrine disrupting chemicals (Communication from the Commission to the council and the European parliament on the implementation of the Community Strategy for Endocrine Disrupters - a range of

substances suspected of interfering with the hormone systems of humans and wildlife (COM (1999) 706)). Considering the mode of action of flufenoxuron and the limited data on endocrine disruptive properties, these aspects should be re-assessed on the basis of new knowledge or information at the renewal of the annex I inclusion.

#### 2.2.2.2 Environmental exposure assessment

The applicant applied for an intended use of preventive and curative treatment of wood for use classes 1 to 3.

The environmental exposure assessment is calculated within the definitions of use sectors provided in the OECD Emission Scenario Document for Wood Preservatives, the EU Technical Guidance Document on Risk Assessment, and the EU Leaching Workshop on wood preservatives.

No exposure assessment has been performed for the life cycle stages “professional” and “private use of the biocidal product” intended for use classes 1 and 2 (indoor use) assuming negligible emissions to the environment.

The environmental exposure assessment for the “industrial application” was conducted for the treatment of wood by automatic spraying, dipping or vacuum-pressure impregnation and for the industrial storage of the treated wood prior to shipment. Industrial brushing was claimed by the applicant but no risk assessment was presented by the applicant. Since no scenario was specifically detailed in the OECD ESD and no information was available from applicant, RMS did not carry out any particular assessment. It is recommended that Member States pay attention to this application at the product authorisation stage.

As regards *in situ* treatments, emissions were estimated for application by brushing. For outdoor brushing treatment, final risk assessment was based on the concentrations after application associated with the concentrations resulting from the in-use phase. Outdoor application by spray was specified by the applicant as an intended use but not developed in the risk assessment by the applicant. Since no scenario was specifically detailed in the OECD ESD and no information was available from applicant, RMS did not carry out any particular assessment. It is recommended that Member States pay attention to this application at the product authorisation stage.

For “wood in service”, emissions according to the scenarios “Fence”, “House”, “Noise barrier”, and “Bridge over pond” have been estimated.

It has been considered that the claim for treatment by injection is limited to indoor application. No specific assessment was carried out for wood in service having received an outdoor injection treatment by the applicant. Since the corresponding scenario in the OECD ESD for wood preservatives was designed for wood used in class 4 and flufenoxuron is only intended to be used in class 3, no further assessment was

conducted by the RMS. It is therefore recommended that MS pay attention to this application at the product authorisation stage.

#### 2.2.2.3 Risk characterisation for the environment

The risk characterisation was conducted in accordance with the recommendations of the Technical Guidance Document on Risk Assessment (2003).

**Aquatic compartment (including sediment)**

Estimated risks from **industrial applications** of flufenoxuron by automatic spraying, dipping and vacuum pressure impregnation (simple or double) are unacceptable for the aquatic and/or sediment organisms. Further leaching from industrial treated wood (whatever the process) leads to unacceptable risks during **storage** for aquatic compartment. Releases via STP during industrial application should not be allowed. Wastes should be collected and treated appropriately (*e.g.* incineration).

For ***in situ*** **professional and amateur application** of flufenoxuron formulations the applicant has applied for brushing, spraying or injection, in use classes 1, 2, and 3. Use class 3 has a single aquatic exposure scenario, *viz*. the brushing bridge scenario. Risk ratios are very high, ranging from 1729 to 288 for application phase only, when removal is taken into account, indicating a high risk for aquatic organisms.

RMS therefore proposed that a label restriction would be included on flufenoxuron products for *in situ* uses, indicating that use of these products for wood in use class 3 should be restricted to wood not over or near water bodies.

The scenarios for **wood in service** indicate an acceptable risk for surface water when releases from wood treated by dipping/automatic spraying or impregnation are directed to the sewage treatment plant (noise barrier scenario) but show unacceptable risk when surface treated wood is located above a water body (bridge scenario). As previously stated, there should be a labelling against applications where direct losses to water are possible, thereby preventing use in these situations. In addition, wood installed over small ponds should therefore normally be protected with a topcoat to avoid leaching into water, provided this protection has shown sufficient efficacy.

**Sewage treatment plant organisms**

No risks are expected either from industrial or *in situ* applications, or from wood in service releases.

**Ground water**

Flufenoxuron is strongly adsorbed onto soil. Modelling using PEARL calculation using the maximum soil concentration indicates that flufenoxuron used as a wood preservative is not expected to pose a risk for groundwater contamination during in-use phase of the treated wood.

**Atmosphere**

No risks are expected due to extremely low volatility of flufenoxuron.

**Terrestrial compartment**

*Industrial application*

Automatic spraying, dipping and impregnation **application** scenarios consider the exposure of the soil compartment *via* the application of STP sludge to agricultural soil. No risk to terrestrial organisms is expected. However, due to the risk identified for surface water in these scenarios, releases via STP during industrial application should not be allowed.

The outdoor **storage** of treated wood (class 3) following automatic spraying, dipping or impregnation treatment on bare soil is expected to pose a risk to soil organisms. Storage on bare soil should not be allowed. The emissions from treated wood to soil should be substantially reduced by covering the storage area with impermeable coating e.g. concrete and, when relevant, a protective roof. Leachates should be collected and treated appropriately (*e.g.* incineration).

Industrial treatment for use class 1 and 2 and subsequent covered storage should not cause a risk to the terrestrial organisms. As above, however, due to the risk identified for surface water in these scenarios, releases via STP during industrial application should not be allowed.

*In situ application and wood in service – Brushing / Spraying*

The risk calculated for the *in situ* application and the following in-use phase of brushing treated wood shows unacceptable risk, whatever the type of applicator (professional or amateur) on fence and house at a distance of 50 cm from treated wood (depth and width), even when taking into account a degradation of the molecule in soil with time. Risk ratios ranged from 4 to 19 after 30 days and from 3 to 4 after 5 years (1825 days). Risks are also deemed unacceptable for in-use phase alone.

Due to the risk identified for soil in the scenarios, wood treated by *in situ* brushing should not be used outdoor (class 3).

Considering that wood treated by *in situ* spraying produce the same leaching rates than wood treated by brushing, spraying treatment and use of wood treated by *in situ* spraying should therefore not be used outdoor (class 3).

*Wood in service – dipping/spraying, vacuum pressure impregnation*

The risk calculated for the in-use phase of industrial treated wood (dipping/spraying, vacuum pressure impregnation) shows unacceptable risk on fence and house at a distance of 50 cm from treated wood (depth and width), even when taking into account a degradation of the molecule in soil with time. Concerning the risk assessment after direct release of the substance in the noise barrier scenario, the PEC/PNEC ratios are below 1 only in Time 2 and considering a degradation of the substance with time. The risk related to releases from noise barrier to agricultural soil *via* sludge application is expected to be low.

Due to the risk identified for soil in fence and house scenarios, wood treated by industrial application (dipping/spraying, vacuum pressure impregnation) should not be used outdoor (class 3).

**Secondary poisoning**

The risk characterisation of secondary poisoning to either fish-eating or worm-eating predators as calculated according to TGD recommendation indicates acceptable risks in environmental conditions where the risk would have been acceptable for aquatic and terrestrial organisms.

**Conclusions for the environmental risk assessment**

The industrial application of flufenoxuron by dipping, automatic spraying or impregnation (vacuum pressure or double vacuum pressure) and subsequent storage prior shipment and the releases from treated wood in service for uses classes 1 and 2 should allow an acceptable risk to the environment provided the following mitigation measures are applied:

- Releases to STP during industrial application should not be allowed; wastes should be collected and treated appropriately (*e.g.* incineration)
- The storage area should be covered with protective roof or the soil should be covered with impermeable coating e.g. concrete. Leachates should be collected and treated appropriately (*e.g.* incineration)

No safe use for the environment has been shown for *in situ* application in class 3. *In situ* application of flufenoxuron should be restricted to class 1 and 2.

No safe use for the environment has been shown for outdoor use of treated wood, whatever the treatment carried out (dipping/spraying, vacuum pressure impregnation, *in situ* brushing, *in situ* spraying). Treatment with flufenoxuron should be restricted to wood used in class 1 and 2.

No specific assessment was carried out for wood in service having received an injection treatment since the corresponding scenario in the OECD ESD for wood preservatives was design for wood used in class 4. As class 4 was not supported by the applicant, the injection will therefore be restricted to indoor applications (classes 1 and 2) with negligible emissions to the environment.

# 3 PROPOSAL FOR THE DECISION

## 3.1 BACKGROUND TO THE PROPOSED DECISION

On the basis of the proposed and supported uses and the evaluation conducted as summarised in the tables appended at the end of this document (Annexe II), it can be concluded that flufenoxuron fulfils under the conditions listed in 3.2 the requirements laid down in Article 5(1) (b), (c), and (d) of Directive 98/8/EC.

Article 10 of the Biocides Directive 98/8/EC addresses the inclusion of an active substance in the Annexes I, IA or IB. For the decision of inclusion or non-inclusion, it has to be examined if the criteria of article 10 (1) are fulfilled.

The physico-chemical properties of the flufenoxuron are deemed acceptable for the appropriate use, storage and transportation of the biocidal product.

With regard to efficacy, based on the assessment, flufenoxuron is efficient against wood borers in preventive applications (impregnation by double vacuum pressure impregnation, injection) and against Hylotrupes bajulus in curative application (brushing and spraying).

Regarding the development of resistance by wood boring insects, the risk is deemed very low.

With regard to human health exposure and effects, based on the risk assessments conducted, no unacceptable risk for professionals was identified for all treatment types considered in this report.

The risk for occasional non-professional users primarily exposed to flufenoxuron or consumers indirectly/secondarily exposed to flufenoxuron is also acceptable.

With regard to environmental exposure and effects, based on the risk assessments conducted, it is considered that safe use(s) can only be identified if the possibility of exposure of the environment is excluded. It is recommended that this should be a condition of Annex I inclusion.

The environmental risk assessment indicates that all mode of industrial process (dipping/automatic spraying and impregnation) result in unacceptable risk for the aquatic compartment after **application** and in unacceptable risk for the aquatic and terrestrial environment during **outdoor storage** whatever the industrial process.

All the intended treatments (dipping/automatic spraying, impregnation, *in situ* brushing or spraying) shows unacceptable risk for terrestrial organisms for fence and house scenarios and unacceptable risk for aquatic organisms in bridge scenario.

In view of its degradation, bioaccumulative and toxic properties, flufenoxuron should be considered as a PBT substance. Flufenoxuron has been discussed at the 10$^{th}$ and 11$^{th}$ meeting of the TC NES subgroup

on identification of PBT and vPvB substances. At the 11th meeting, the group concluded that flufenoxuron fulfils the P, vP, B, vB and T criteria: flufenoxuron is a PBT/vPvB substance.

Due to the properties of the active substance flufenoxuron and its PBT character, consideration for an inclusion into Annex IA of the Directive is not possible.

## 3.2 DECISION REGARDING INCLUSION IN ANNEX I

On the basis of the proposed and supported use, it is concluded that the proposed use of flufenoxuron in wood preservative products fulfils the safety requirements laid down in Article 5(1) of Directive 98/8/EC.

It is proposed that flufenoxuron (CAS-No. 101463-69-8) be included in Annex I of Council Directive 98/8/EC as an active substance in wood preservative products (product type 08), subject to the following specific provisions:

1. The active substance flufenoxuron, as manufactured, shall have a minimum of purity of ≥ 950 g/kg.
2. The identity and the maximum content of impurities have to comply with the confidential Annex of the IIA.
3. Flufenoxuron is efficient as a wood preservative (Product type 08) for preventive application by industrial techniques (double vacuum pressure impregnation and injection) in use class 1 to 3 against wood borers and in curative treatment (brushing and spraying) against Hylotrupes bajulus.
4. The following particular conditions also apply:
    a. When performing the industrial/professional treatments considered in this report, the operators must wear the appropriate personal protective equipment.
    b. When performing professional treatments indoor, the operator must secure the area and be sure of the absence of bystanders.
    c. During industrial wood pre-treatment, the emissions to surface water *via* STP must be forbidden. Appropriate mitigation measures such as waste recycling or incineration have to be performed.
    d. All timbers treated by industrial process must be stored on impermeable hard standing to prevent direct losses to soil and surface water and allow losses to be collected for disposal and, when relevant, a protective roof.
    e. The end life cycle of products containing flufenoxuron should be managed according to in force regulation.
    f. In view of the risks identified for the aquatic and soil compartments, products shall not be authorised for wood used outdoor or for wood that will be exposed to weathering and must be restricted to wood used in class 1 and 2. In view of the conclusions of the risk characterisation for the environment and of the PBT properties, application is restricted to industrial and professional applications. The use of flufenoxuron in a non-

industrial/professional context does not allow a sufficient control of the waste management.

g. The provisions in points a to d have to be reported on Labels/SDS

5. Although no resistance has been reported for chitin synthesis inhibitors in the field of treating wood in service, it is nevertheless recommended to watch out for the apparition of any resistance to flufenoxuron.

6. Taking into account the PBT intrinsic properties of the substance, flufenoxuron is a candidate for comparative assessment.

### 3.3 ELEMENTS TO BE TAKEN INTO ACCOUNT BY MEMBER STATES WHEN AUTHORISING PRODUCTS

1. Product containing flufenoxuron may only be used for industrial treatments by automatic spraying, dipping, vacuum pressure impregnation, double vacuum pressure impregnation and injection (class 1 to 2) and professional *in situ* application (class 1-2). The final product should be a liquid (no powder exposition) and it is not assumed that it will generate aerosol with mean droplet diameter < 50 µm, otherwise inhalation toxicity studies should be requested.
2. No dietary risk assessment was performed for the annex I inclusion as no uses of treated wood in animal housing or in contact with food was intended.
3. As the flufenoxuron concentration in the wood depends on the type of co-biocide used and its ratio to flufenoxuron, a full complete efficacy data package with the exact composition of a formulation will be required to support authorisation of products at the Member State level, for all claimed target organisms. Moreover, in the case of superficial treatment in preventive application, the efficiency of flufenoxuron will have to be completely demonstrated.
4. Before authorising products, Member States should ensure that the physical and chemical properties of the product, such as acidity/alkalinity, storage stability and shelf life, surface tension are appropriately described. Member States should also ensure that an analytical method allowing for the analysis of the active substance in the product is available.
5. Considering that the human health risk assessment was conducted for dummy products with a dermal absorption of 10% on the basis of a study with a low reliability (3)[4] and only on water based solution, a dermal absorption study will have to be submitted.
6. As a result of the environmental risk assessment, releases to surface water (via STP) during the industrial application of flufenoxuron either by dipping or impregnation will cause a risk to aquatic organisms. Effluents should not be allowed and therefore should be treated by an appropriate method (*e.g.* incineration).

[4] The results of this study on a wood preservative formulation were however comforted by the results of a valid study carried out with an insecticide (PT18) formulation.

Storage of timber treated with flufenoxuron wood preservative formulations on bare soil will pose a risk to soil. Therefore, during on-site storage of industrial pre-treated timber impermeable grounds (e.g. sealed flooring) are demanded as a condition of use.

Since unacceptable risks were identified where direct losses to water and soil are possible and considering the PBT character of the substance, the treatment with flufenoxuron should be restricted to wood used in classes 1 to 2.

7. Considering the growth regulator character of flufenoxuron, the possible endocrine disruptor activity of the parent compound and its metabolites must be kept in mind for further investigations.
8. If it is foreseen that use of a biocidal product containing flufenoxuron within a Member State entails significant risks to companion animals then – at the product authorisation stage – the Member State can introduce risk mitigation measures to alleviate the risk.

## 3.4 REQUIREMENT FOR FURTHER INFORMATION

The FR CA considers that the evaluation has shown that sufficient data have been provided to verify the outcome and conclusion of the risk assessment and permit the proposal for the inclusion of flufenoxuron on to Annex I of the Directive 98/8/CE.

The conditions and the restrictions proposed by the FR CA are considered appropriate. However, acceptable analytical method for monitoring of residues of flufenoxuron in water has to be provided before authorisation of products. It should be noted that a validated method has already been submitted but this study shown to be not sufficiently sensitive with respect to the levels of concern in surface water.

## 3.5 UPDATING THIS ASSESSMENT REPORT

This assessment report may need to be updated periodically in order to take into account of scientific developments and results from the examination of any of the information referred to in articles 7, 10.4 and 14 of directive 98/8/CE. Such adaptations will be examined and finalised in connection with any amendment of the conditions for the inclusion of flufenoxuron in Annex I to the Directive.

## 3.6 LIST OF END POINTS

In order to facilitate Member States, in granting or reviewing authorisations, to apply adequately the provisions of Article 5(1) of Directive 98/8/EC and the common principles laid down in Annex VI of that Directive, the most important endpoints as identified during the evaluation process are listed in document I.2a.

# APPENDIX I: LIST OF ENDPOINTS

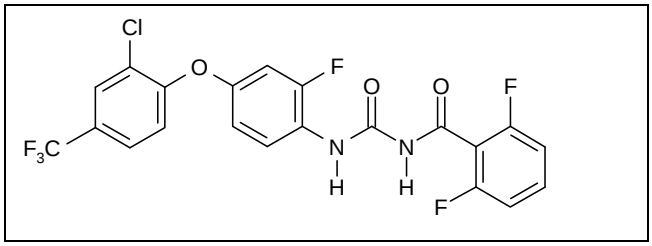
**Chapter 1: Identity, Physical and Chemical Properties, Details of Uses, Further Information, and Proposed Classification and Labelling**

| | |
|---|---|
| Active substance (ISO Common Name) | Flufenoxuron |
| Function (*e.g.* fungicide) | Insecticide (PT 8 – Wood Preservative) |
| Rapporteur Member State | France |

**Identity** (Annex IIA, point II.)

| | |
|---|---|
| Chemical name (IUPAC) | 1-[4-(2-chloro-alpha, alpha,alpha-trifluoro-para-tolyloxy)-2-fluorophenyl]-3-(2,6-difluorobenzoyl)urea |
| Chemical name (CA) | N-[[[4-[2-chloro-4-(trifluoromethyl)phenoxy]-2-fluorophenyl]amino]carbony]-2,6-difluorobenzamide |
| CAS No | 101463-69-8 |
| EC No | 417-680-3 |
| Other substance No. | CIPAC # 470 |
| Minimum purity of the active substance as manufactured (g/kg or g/l) | 960 g/kg |
| Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg) | Methanol : max 2g/kg (0,2 %)<br>Acetone : max 1 g/kg (0,1 %)<br>Cyclohexane : max 1 g/kg (0,1 %)<br>Ethyl acetate : max 1 g/kg (0,1 %)<br>Toluene : max 2 g/kg (0,2 %) |
| Molecular formula | $C_{21}H_{11}ClF_6N_2O_3$ |
| Molecular mass | 488.8 |

Structural formula



**Physical and chemical properties** (Annex IIA, point III., unless otherwise indicated)

| | |
|---|---|
| Melting point (state purity) | Melting under decomposition at 169-172°C (99%) |
| Boiling point (state purity) | Melting occurs under decomposition, therefore, no boiling point could be observed. |
| Temperature of decomposition | Not applicable |
| Appearance (state purity) | Flufenoxuron PAI[5] is a white crystalline solid; the TC[6] is a white, fine powder. |
| Relative density (state purity) | 1.649 (99.3%) |
| Surface tension | 49.4 mN/m at 1.0% w/w at 20°C |
| Vapour pressure (in Pa, state temperature) | 6.52 x $10^{-12}$ Pa at 20°C. |
| Henry's law constant (Pa $m^3$ $mol^{-1}$) | H = 7.46 x$10^{-6}$ (Pa x $m^3$/mol) at 25°C |
| Solubility in water (g/l or mg/l, state temperature) | pH 4: 1.86 µg/l at 25°C |
| | pH 7: 1.36 µg/l at 25°C |
| | pH 9: 3.69 µg/l at 25°C |
| Solubility in organic solvents (in g/l or mg/l, state temperature) (Annex IIIA, point III.1) | The a.i. is rather insoluble in unpolar solvents and of moderate to good solubility in several organic solvents. |
| | The various solubilities (in g/100 ml solvent) are:<br>n-heptane: < 0.001<br>toluene: 0. 35<br>dichloromethane: 1.6<br>methanol: 0.35<br>acetone: 8.3<br>ethyl acetate 5.5 |
| Stability in organic solvents used in biocidal products including relevant breakdown products (IIIA, point III.2) | Not requested |

5 PAI = Pure Active Ingredient

6 TC = Technical Concentrate

| | |
|---|---|
| Partition coefficient (log $P_{OW}$) (state temperature) | 5.6 (estimation) |
| Hydrolytic stability ($DT_{50}$) (state pH and temperature) (point VII.7.6.2.1) | pH 4, 5 and 7: stable at 25°C<br>pH 9: 88-94 days at 25°C |
| Dissociation constant (not stated in Annex IIA or IIIA; additional data requirement from TNsG) | pKa : 10.2 at 25°C |
| UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength) | The structure of Flufenoxuron is confirmed by all spectra: UV, IR, $^{1}$H-NMR, $^{13}$C-NMR and MS.<br>The UV spectrum in methanol shows three main peaks at 220, 235 and 254 nm with molar extinction coefficient of 19983 x $mol^{-1}$ x $cm^{-1}$, 17880 x $mol^{-1}$ x $cm^{-1}$, 19330 x $mol^{-1}$ x $cm^{-1,}$, respectively.<br>IR-spectroscopy:<br>3248 $cm^{-1}$ and 3108 $cm^{-1}$: amide N-H stretch<br>1710 $cm^{-1}$ and 1676 $cm^{-1}$ :amide C=O stretch<br>1542 $cm^{-1}$ and 1505 $cm^{-1}$ : amide N-H bending<br>1324 $cm^{-1}$ and 1297 $cm^{-1}$: trifluoromethyl C-F stretch<br>1135 $cm^{-1}$ :fluoroaromatics C-F stretch<br>797 $cm^{-1}$: aromatic C-H „out of plane“ → 1,2,3- tri-substitution .<br>For all hydrogens als well as for all carbons in the molecule, signals in the NMR spectra could be assigned. The presence and positions of the fluorine atoms on the aromatic rings are also confirmed by their couplings visible in the proton and carbon signals, respectively. |
| Photostability ($DT_{50}$) (aqueous, sunlight, state pH)<br>(point VII.7.6.2.2) | Less 7 days (pH 5-7) at 22°C, continuous irradiation at light intensity of 3mW $cm^2$ |
| Quantum yield of direct phototransformation in water at Σ > 290 nm (point VII.7.6.2.2) | 1.75 x $10^{-3}$ (mean value) |
| Flammability | Not highly flammable |
| Explosive properties | No explosive properties |

## Summary of intended uses[7]

| Object and/or situation | Member State or Country | Product name | Organisms controlled | Formulation | | Application | | | Applied amount per treatment | | | Remarks: |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Type | Conc. of as | method kind | number min max | interval between applications (min) | g as/L min max | water L/m$^2$ min max | g as/m$^2$ min max | |
| (a) | | | I | (d-f) | (i) | (f-h) | (k) | | | | | (m) |
| Preventive impregnation | EU | Wocosen 100 | Wood borers | SL | 0.75 g/l | Impregnation (vacuum pressure, double vacuum pressure, injection) | 1 | N/A | | | 0.75 g/m$^3$ | |
| Curative Superficial | EU | Basiment Holzwurm BV Konzentrat | *Hylotrupes bajulus* | EC | 1.0 g/l | Superficial treatment (Spray or brush) | 1 | N/A | | | 0.064 g/m$^2$ | |
| Curative Superficial | EU | Basiment Holzwurm BV U 1551 | *Hylotrupes bajulus* | SL | 0.2 g/l | Superficial treatment (Spray or brush) | 1 | N/A | | | 0.064 g/m$^2$ | |

a) *e.g.* biting and suckling insects, fungi, molds; (b) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(c) GCPF Codes – GIFAP Technical Monograph No 2, 1989 ISBN 3-8263-3152-4); (d) All abbreviations used must be explained
(e) g/kg or g/l;(f) Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench;
(g) Kind, *e.g.* overall, broadcast, aerial spraying, row, bait, crack and crevice equipment used must be indicated;

[7] The intended uses below are the one which are supported by valid efficacy data. The applicant has also supported intended use for superficial preventive treatment against woodborers. Superficial preventive application will have to be demonstrated when authorizing product

(h) Indicate the minimum and maximum number of application possible under practical conditions of use;
(i) Remarks may include: Extent of use/economic importance/restrictions

**Classification and proposed labelling** (Annex IIA, point IX.)

**Under directive 67/548/EEC**

| | |
|---|---|
| with regard to physical/chemical data | None |
| with regard to toxicological data | R33 Danger of cumulative effects<br>R64 May cause harm to breastfed babies |
| with regard to fate and behaviour data | R53 May cause long term adverse effects in the aquatic environment |
| with regard to ecotoxicological data | N, R50/53 Very toxic to aquatic organisms, may cause long term adverse effects in the aquatic environment |

**Under Regulation 1272/2008**

| | |
|---|---|
| with regard to physical/chemical data | None |
| with regard to toxicological data | Lact. H362 - May cause harm to breast-fed children |
| with regard to fate and behaviour data and ecotoxicological data | Aquatic acute 1 /H400 - Very toxic to aquatic life<br>Aquatic chronic 1 /H410 - Very toxic to aquatic life with long lasting effect<br>M- factor =10 000 |

## Chapter 2: Methods of Analysis

### Analytical methods for the active substance

| | |
|---|---|
| Technical active substance (principle of method) (Annex IIA, point 4.1) | HPLC-UV |
| Impurities in technical active substance (principle of method) (Annex IIA, point 4.1) | HPLC-UV; GC-FID |

### Analytical methods for residues

| | |
|---|---|
| Soil (principle of method and LOQ) (Annex | HPLC-MS/MS (method RLA 12637), LOQ: 0.001 |

| | |
|---|---|
| IIA, point 4.2) | mg/kg for flufenoxuron and CL 932338 |
| Air (principle of method and LOQ) (Annex IIA, point 4.2) | LC-MS/MS, LOQ : 0.0001 µg/l |
| Water (principle of method and LOQ) (Annex IIA, point 4.2) | Drinking water: HPLC-MS/MS (method RLA 12680), LOQ: 0.01 µg/l for flufenoxuron and CL 932338 |
| Body fluids and tissues (principle of method and LOQ) (Annex IIA, point 4.2) | Not relevant |
| Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes) (Annex IIIA, point IV.1) | Not applicable as PT8 (Wood Preservative) |
| Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes) (Annex IIIA, point IV.1) | Not applicable as PT8 (Wood Preservative) |

**Chapter 3: Impact on Human Health**

**Absorption, distribution, metabolism and excretion in mammals** (Annex IIA, point 6.2)

| | |
|---|---|
| Rate and extent of oral absorption: | Between 79.76 % (males) and 92.15 % (females), for low doses (3.5 mg/kg bw).<br>An oral absorption rate of 80% was used for the risk characterisation. |
| Rate and extent of dermal absorption: | Default value of 10 % (physicochemical properties and studies on different formulations) |
| Distribution: | Well distributed in the whole organism, mainly in gastro-intestinal tract, fat tissue, bone marrow and skin. |
| Potential for accumulation: | Mean $t_{1/2}$ (depuration) = 34 days with liver 48d; carcass and fat 28 d |
| Rate and extent of excretion: | Urine: between 3 to 14 % depending on the study (low dose: 3.5 mg/kg bw, cannulated-rats) and < 1 % (high dose: 350 mg/kg bw)<br>Faeces: between 4 to 24% TRR♠ depending on the study (low dose) and 85% TRR (high dose) |
| Toxicologically significant metabolite | WL 115096/Reg. Nos. 241208 (free base)/4064703 (hydrochloride salt)<br>WL 129183/Reg. No. 4064702 |

**Acute toxicity** (Annex IIA, point 6.1)

| | |
|---|---|
| Rat $LD_{50}$ oral | > 3000 mg/kg bw |
| Rat $LD_{50}$ dermal | > 2000 mg/kg bw |
| Rat $LC_{50}$ inhalation | > 5.1 mg/l (4-h dust aerosol, nose-only) |
| Skin irritation | Non irritant |
| Eye irritation | Non irritant |
| Skin sensitization (test method used and result) | Non skin sensitiser (M&K method) |

**Repeated dose toxicity** (Annex IIA, point 6.3)

| | |
|---|---|
| Species/ target / critical effect | Dog and rat / blood / anemia (rat & dog); methemoglobinemia (dog) |
| Lowest relevant oral NOAEL / LOAEL | NOAEL (28-day rat): 49 mg/kg bw/day (M); 1067 mg/kg bw/day (F)<br>NOAEL (90-day rat) = 35 mg/kg bw/d (M); 4.1 mg/kg bw/day (F)<br>NOAEL (1-year dog) = 3.5 mg/kg bw/d (M); 3.7 mg/kg bw/d (F) |
| Lowest relevant dermal NOAEL / LOAEL | Not required |
| Lowest relevant inhalation NOAEL / LOAEL | Not required |

| | |
|---|---|
| **Genotoxicity** (Annex IIA, point 6.6) | Not genotoxic *in vivo* (rat bone marrow chromosomal aberration assay, mouse bone marrow micronucleus assay and *in vivo/in vitro* UDS test, with rat liver cells). |

**Carcinogenicity** (Annex IIA, point 6.4)

| | |
|---|---|
| Species/type of tumour | Mice/ hemangiosarcoma in the spleen of females observed in a toxic context (dose higher than the maximum tolerated dose) |
| Lowest dose with tumours | LOAEL = 50,000 ppm (7,780 mg/kg bw/d) for female mice |

**Reproductive toxicity** (Annex IIA, point 6.8)

| | |
|---|---|
| Species/ Reproduction target / critical effect | 2-gen, rat: decreased lactation index and decreased pup survival and weight |
| Lowest relevant reproductive NOAEL / LOAEL | $NOAEL_{fertility}$ > 10,000 ppm (≈ 875 mg/kg bw/day). |
| Species/Developmental target / critical effect | No evidence of developmental or foetal toxicity in rat and rabbit studies |
| Lowest relevant developmental NOAEL / LOAEL | NOAEL (rat & rabbit): >1,000 mg/kg bw/d (highest dose tested) |

**Neurotoxicity / Delayed neurotoxicity** (Annex IIIA, point VI.1)

| | |
|---|---|
| Species/ target/critical effect | No evidence of neurotoxicity from rat 28-day oral neurotoxicity study, no concern from other studies |
| Lowest relevant NOAEL / LOAEL for neurotoxicity. | NOAEL (Rat 28-day oral neurotox.): > 20,000 ppm (>1,775 mg/kg bw/d) |

**Other toxicological studies** (Annex IIIA, VI/XI)

| | |
|---|---|
| Reg. No. 241208<br>(rat minor metabolite, co-tested in all Flufenoxuron studies)<br>[* = Reg No. 241208; ** = Reg. No 4064703 (=Reg No. 241208 hydrochloric acid salt)] | * Mouse oral $LD_{50}$ = 2372 mg/kg bw (m&f)<br>* Ames: weak mutagen with S9-mix (TA98, 100)<br>* Gene mutation test (HPRT test, CHO cells) negative<br>* UDS hepatocytes rats negative<br>* Cellular transformation assay on SHE cells negative<br><br>**Rat oral $LD_{50}$ = 612 mg/kg bw (m&f)<br>**Rat dermal $LD_{50}$ > 2,000 mg/kg bw<br>**Rat 28-d oral gavage: NOAEL < 10 mg/kg bw/d (anemia /methemoglobinemia, liver and kidney toxicity)<br>** Ames: weak mutagen with S9-mix (TA98, 100)<br>** *In vitro* test in CHO cells: negative<br>** *In vivo* micronucleus assay: negative.<br><br>Reg. No. 241208 binds readily to hemoglobin (Hb), but only minimal Reg. No. 241208 - Hb adducts were detected after high-dose flufenoxuron treatment |
| Reg. No 4064702 (soil metabolite) | Rat oral $LD_{50}$ = 367 mg/kg bw<br>No evidence of mutagenicity (Ames test) |
| Mechanistic studies | No evidence of replicative DNA synthesis (RDS) induction in hepatocytes of rats administered up to 4,000 mg/kg bw flufenoxuron via single oral gavage |

**Medical data** (Annex IIA, point 6.9)

| |
|---|
| No poisoning incidents reported, no concern from medical surveillance of manufacturing plant personnel. |

| **Summary** (Annex IIA, point 6.10) | Value | Study | Safety factor |
|---|---|---|---|
| Medium to long-term AEL | 0.028 mg/kg bw/d | 1-yr dog | 100 |
| Acute AEL | 0.4 mg/kg bw/d | 28 days rat | 100 |

**Chapter 4: Fate and Behaviour in the Environment**

**Route and rate of degradation in water** (Annex IIA, point 7.6, IIIA, point XII.2.1, 2.2)

| | |
|---|---|
| Hydrolysis of active substance and relevant metabolites ($DT_{50}$) (state pH and temperature) | pH 4, 5, and 7 (25°C): no hydrolysis over 30 days<br><br>pH 9 (25°C): slow hydrolysis;<br>benzamide label DT50 94 days<br>fluoroaniline label DT50 88 days |
| | Formation of difluorobenzoic acid (CL 245508, max. 16% after 30 days) and "urea" metabolite (CL 932338, max. 21% after 30 days) |
| Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites | **Flufenoxuron**:<br>direct photolysis, Suntest apparatus, 22 °C, 15 d continuous irradiation, pH 7with xenon lamp:<br>$DT_{50}$ 1.9 d (benzamide label)<br>$DT_{50}$ 7.2 d (fluoroaniline label)<br>$DT_{50}$ 4.6 d (mean of both labels)<br>Estimated half-lives in top layer of aqueous systems: 39.2 d (April) and 21.7 d (June). |
| Readily biodegradable (yes/no) | No |
| Biodegradation in seawater | Not relevant, as hazard wood class 1, 2, 3 |
| Degradation in water/sediment at 12°C<br>- $DT_{50}$ water<br>- $DT_{90}$ water | Flufenoxuron:<br>$DT_{50,water}$ (first order) at 12°C (no degradation, therefore no temperature correction)<br>system A: 0.3 d; system B: 0.4 d<br>$DT_{90,water}$ (first order) at 12°C<br>system A: 0.9 d; system B: 1.2 d |
| - $DT_{50}$ whole system | $DT_{50,system}$ (first order) corrected at 12°C<br>system A: 116 d; system B: 85 d |
| - $DT_{90}$ whole system | $DT_{90,system}$ (first order) corrected at 12°C<br>system A: 385 d; system B: 285 d |
| - $DT_{50}$sediment | $DT_{50,sediment}$ (first order) corrected at 12°C<br>system A: 87 d; system B: 123 d |
| - $DT_{90}$sediment | $DT_{90,sediment}$ (first order) corrected at 12°C<br>system A: 288 d; system B: 410 d |

| | |
|---|---|
| Mineralisation | System A*: 30.2 % after 100 d (benzamide label)<br>0.9 % after 100 d (fluoroaniline label)<br><br>System B#: 29.2 % after 100 d (benzamide label)<br>6.5 % after 100 d (fluoroaniline label) |
| Non-extractable residues | System A: 32.5 % after 100 d (benzamide label)<br>37.1 % after 100 d (fluoroaniline label)<br><br>System B: 39.7 % after 100 d (benzamide label)<br>57.3 % after 100 d (fluoroaniline label) |
| Distribution in water / sediment systems (active substance) | Water: System A: 0.5 % after 100 d<br>System B: 0.0 % after 100 d<br><br>Sediment: System A: 19 - 37 % after 100 d<br>System B: 15 - 28 % after 100 d |
| Distribution in water / sediment systems (metabolites) | "**urea" (CL 932338, Reg. No. 4064702), water**:<br>System A: max. 4.2% after 57 d (2.5% after 100 d)<br>System B: max. 1.8% after 14 d (0 % after 100 d)<br><br>"**urea" (CL 932338, Reg. No. 4064702), sediment**:<br>System A: max. 19.3% after 57 d (16.9% after 100 d)<br>System B: max. 13.0% after 30 d (2.3 % after 100 d)<br>System A: $DT_{50}$ 40 d, $DT_{90}$ 135 d (12°C)<br>System B: $DT_{50}$ 19 d, $DT_{90}$ 61 d (12°C)<br><br>**2,6-difluorobenzamide (CL 211558, Reg. No. 102719), water**:<br>System A: max. 4.1% after 100d<br>System B: max. 2.8% after 57 d (0.9 % after 100 d)<br><br>**2,6-difluorobenzamide (CL 211558, Reg. No. 102719), sediment**: not detected<br>Sum of all other metabolite always < 4% |

♠ TRR: Tissues Radioactive Residues

* System A (loamy sand sediment)

**Route and rate of degradation in soil** (Annex IIIA, point VII.4, XII.1.1, XII.1.4; Annex VI, para. 85)

| | |
|---|---|
| Mineralization (aerobic) | fluoroaniline-label: 3.7 - 5.1% after ~120 days<br>toluyl-label: 6.7% after 120 days<br>benzamide-label: 23.2 - 52.5% after 120 days |
| Laboratory studies (range or median, with number of measurements, with regression coefficient) | Method: graphical estimation; ModelMaker 3.0.4 or 4.0 (first order) |
| | $DT_{50lab}$ aerobic, 40-45% MWC:<br>**Flufenoxuron (20-22°C)**<br>36 - 124 days (ModelMaker, $r^2 \geq 0.95$, n=5)<br>~90 - 140 days (graphical estimation, no $r^2$ given, n=3)<br>**"urea"metabolite** (ModelMaker, $r^2 \geq 0.97$, n=4) **(CL 932338, Reg.No. 4064702) (20-22°C)**<br>47 - 59 days<br><br>**Flufenoxuron (12°C, recalculated from 20-22°C results)**<br>68 - 235 days (geometric mean : 158 days used for the risk assessment)<br><br>**"urea"metabolite (12°C, recalculated from 20-22°C results) (CL 932338, Reg.No. 4064702)**<br>89 - 112 days |
| | $DT_{90lab}$ aerobic, 40-45% MWC<br>**Flufenoxuron (20-22°C)**<br>191 - 449 days (ModelMaker, $r^2 \geq 0.95$, n=5)<br><br>**"urea"metabolite** (ModelMaker, $r^2 \geq 0.97$, n=4) **(CL 932338, Reg.No. 4064702) (20-22°C)**<br>156-196 days<br>**Flufenoxuron (12°C, recalculated from 20-22°C results)**<br>362 - 852 days |

| | |
|---|---|
| | **"urea"metabolite (12°C, recalculated from 20-22°C results) (CL 932338, Reg.No. 4064702)**<br>296-372 days |
| | |
| | $DT_{50lab}$ (20°C, anaerobic): no degradation observed |
| Degradation in the saturated zone: | not relevant |
| Field studies (state location, range or median with number of measurements) | $DT_{50f}$ (South region) : 6-67 days |
| | $DT_{90f}$: 20-222 days |
| Anaerobic degradation | No significant degradation under anaerobic conditions |
| Soil photolysis | After 16 d: > 80% Flufenoxuron remained;<br>mineralization 4% (benzamide-label),<br>bound residues 6.4%, all metabolites <3% |
| Non-extractable residues | In all soils tested 17.5 - 31 % after 90 days<br>21 – 43.8% after 120 days |
| Relevant metabolites - name and/or code, % of applied a.i. (range and maximum) | "urea" metabolite (CL 932338, Reg.No. 4064702)<br>–8.3% after 30 days |

| | |
|---|---|
| Soil accumulation and plateau concentration | Based on degradation studies, no accumulation is expected |

**Adsorption/desorption** (Annex IIA, point XII.7.7; Annex IIIA, point XII.1.2)

| | | | |
|---|---|---|---|
| Ka , Kd<br>$Ka_{oc}$ , $Kd_{oc}$ | Range | $K_a$ | $K_{a,oc}$ |
| | Flufenoxuron | 1738-4250<br>5 soils | 88240-289747<br>mean value 157643 |
| | | $K_F$ | $K_{F,oc}$ |
| | "urea" CL932338 | 37.5-118.5<br>5 soils | 3711-8467 |
| pH dependence (yes / no) (if yes type of dependence) | No | | |

**Fate and behaviour in air** (Annex IIIA, point VII.3, VII.5)

| | |
|---|---|
| Direct photolysis in air | See photochemical oxidative degradation |
| | |
| Photo-oxidative degradation in air | Tropospheric half life of Flufenoxuron: 1.12 days (Atkinson) |
| Volatilization | $V_p$ 6.52 x $10^{-12}$ Pa at 20 °C |

**Monitoring data, if available** (Annex VI, para. 44)

| | |
|---|---|
| Soil (indicate location and type of study) | Not available |
| Surface water (indicate location and type of study) | Not available |
| Ground water (indicate location and type of study) | Not available |
| Air (indicate location and type of study) | Not available |

## Chapter 5: Effects on Non-target Species

**Toxicity data for aquatic species (most sensitive species of each group)**
(Annex IIA, point 8.2, Annex IIIA, point 10.2)

| Test Species | Test System<br>Time-Scale | Endpoints (µg a.s./L) | |
|---|---|---|---|
| | | $LC_{50}/EC_{50}$ | NOEC |
| **Flufenoxuron** | | | |
| *Danio rerio* | Flow-through – 96 h | > 5.19 | 5.19 |
| *Pimephales promelas* | Flow-through 34-d<br>(early life stage) | n.d. | ≥ 0.82 |
| *Daphnia magna* | Static – 48 h | 0.0429 | 0.01 |
| *Daphnia magna* | Semi-Static – 21 d | n.d. | **0.00449** |
| *Pseudokirchneriella subcapitata* | Static – 96 h | $E_bC_{50}$: 19 228<br>$E_rC_{50}$: 1940 | $E_bC_{10}$ = 600<br>$E_rC_{10}$ : 9500 |
| *Activated sludge* | Respiration ihibition -180 min | >1000 mg/ | >1000 mg/L<br>(above water solubility limit) |
| *Lumbriculus variegatus*<br>Spiked-sediment | Static – 28 d | n.d. | ≥ 306 µg/kg dry sediment |
| *Chironomus riparius*<br>spiked-sediment | Static – 28 d | 142.7 µg/kg dry sediment | 80 µg/kg<br>dry sediment |
| **"urea", Reg No 4064702** | | | |
| *O.myki s* | Static – 96 h | 570 | 200 |
| *Daphnia magna* | Static – 48 h | 1030 | n.d. |
| *Pseudokirchneriella subcapitata* | Static – 72 h | 90 | **$E_bC_{10}$** = 66<br>**$E_rC_{10}$** = 70 |
| **2,6-difluorobenzamide, Reg. No. 102719** | | | |
| *O. mykiss* | Static – 96 h | > 100 000 | 100 000 |
| *Daphnia magna* | Static – 48 h | > 100 000 | 25000 |
| *Pseudokirchneriella subcapitata* | Static – 72 h | > 100 000 | n.d |

| | | | |
|---|---|---|---|
| **4-amino-3-fluorophenol, Reg. No. 4108386** | | | |
| *O. mykiss* | Static – 96 h | 2096 | |
| *Daphnia magna* | Static – 48 h | 3361<br>(9700 based on aged residues) | 1060 |
| **Reg.No.4064703** | | | |
| *O. mykiss* | Static – 96 h | 462 | |
| *Daphnia magna* | Static – 48 h | 5.45 | |
| **Reg.No.241208** | | | |
| *Daphnia magna* | Static – 48 h | 654 | 500 |
| **Reg.No.206925** | | | |
| *Daphnia magna* | Static – 48 h | >100 000 | 100 000 |

**Effects on earthworms or other soil non-target organisms**

| | |
|---|---|
| Acute toxicity to earthworms<br>(Annex IIIA, point XIII.3.2) | $LC_{50}$ (parent): 1000 mg/kg soil dry weight<br>$LC_{50}$ (degradate, Reg. No. 4064702) > 1000 mg/kg soil dry weight |
| Reproductive toxicity to earthworms (Annex IIIA, point XIII.3.2) | NOEC> 5 mg/kg soil dry weight<br>$NOEC_{standard}$ > 1.7 mg/kg soil dry weight |
| Chronic toxicity on other soil macro-organisms | *Folsomia candida*<br>NOEC : 0.117 mg/kg soil dry weight |
| Acute toxicity to terrestrial plants<br>(Annex IIIA, point XIII.3.4) | $LC_{50}$: > 0.11 mg a.s./kg |

**Effects on soil micro-organisms** (Annex IIA, point 7.4)

| | |
|---|---|
| Nitrogen mineralization | (parent) : < 25% at rate 1.7 mg a.s./kg soil<br>NOEC standard : 3.7 mg/kg soil dry weight<br>(degradate, Reg. No. 4064702) : < 25% at rate 0.076 mg/kg soil |
| Carbon mineralization | (parent) : < 25% at rate 1.7 mg a.s./kg soil<br>NOEC standard : 3.7 mg/kg soil dry weight<br>(degradate, Reg. No. 4064702): < 25% at rate 0.076 mg/kg soil |

**Effects on terrestrial vertebrates**

| | |
|---|---|
| Acute toxicity to mammals (Annex IIIA, point XIII.3.3) | LD50 (oral): > 5000 mg/kg (rat; male and female) |
| | LD50 (dermal): > 2000 mg/kg (rat; male and female) |
| | LC50 (inhalation): > 5.1 mg/kg (rat; male and female) |
| Acute toxicity to birds (Annex IIIA, point XIII.1.1) | LD50 > 2000 mg/kg bw |
| Dietary toxicity to birds (Annex IIIA, point XIII.1.2) | LC50 > 5243 mg/kg feed |
| Reproductive toxicity to birds (Annex IIIA, point XIII.1.3) | NOEC = 100 mg/kg feed |

**Effects on honeybees** (Annex IIIA, point XIII.3.1)

| | |
|---|---|
| Acute oral toxicity | $LD_{50}$ (48 h) > 109 µg a.s. per bee |
| Acute contact toxicity | $LD_{50}$ (48 h) > 100 µg a.s. per bee |

**Effects on other beneficial arthropods** (Annex IIIA, point XIII.3.1)

| | |
|---|---|
| Acute oral toxicity | Not relevant for PT 8 uses |
| Acute contact toxicity | Not relevant for PT 8 uses |

**Bioconcentration** (Annex IIA, point 7.5)

| | |
|---|---|
| Bioconcentration factor (BCF) | BCF: ≈ 25000 L/kg (kinetic / whole fish) |
| Depuration time ($DT_{50}$)<br>($DT_{90}$) | 21 days<br>70 days<br>Based on kinetic study/whole fish study |
| Level of metabolites (%) in organisms accounting for > 10 % of residues | Metabolically stable in fish, based on kinetic study/whole fish study |

## Chapter 6: Other Endpoints

All required end points required for risk assessment are presented here above.

# APPENDIX II: LIST OF USES SUPPORTED BY AVAILABLE DATA

Intended uses (initial dossier):

- Industrial: automatic spraying, dipping vacuum pressure and double vacuum pressure impregnation,
- Professional: brushing, spraying or injecting in wood
- General public: brushing, spraying

Flufenoxuron is intended to be used as a preventive wood preservative for wood and construction timbers in Use Classes 1, 2, and 3 according to CEN TC 38 standard and curative wood preservative according to CEN TC 38 standard.

Indirect/secondary exposures correspond to cutting and sanding wood, manual handling of treated, wet wood, processing of treated wood, inhalation in presence of treated wood in a room, cleaning work ware at home, playing on preserved timber, chewing preserved timber off-cuts.

The following tables summarise the assessment of the intended uses, but don't take into account all the risk mitigation measures proposed in document I.3 "Proposal for Decision".

**In the following tables, the "water based formulation" refers to the Basiment Holzwurm BV Konzentrat which is a solvent based formulation diluted in water for using and solvent based formulation refers to the Basiment Holzwurm BV U 1551.**

| Intended uses | Scenario | | Risk assessment conclusion |
|---|---|---|---|
| **INDUSTRIAL APPLICATIONS** | | | |
| ***Industrial application by double vacuum pressure and service life*** | HUMAN EXPOSURE ASSESSMENT | | |
| | Water-based and solvent-based formulations | Primary exp. - Mixing and loading: No exposure<br>- Application: TNG handling model 1<br>- Post application and disposal: TNG handling model 1 | *Acceptable* |
| | | Secondary exposure (prof.) | *Acceptable* |
| | | Secondary exposure (public.) | *Acceptable* |
| | | Combined exposure | *Acceptable* |
| | ENVIRONMENTAL EXPOSURE ASSESSMENT | | |
| | Double-vacuum pressure *application* (solvent and water based formulations) | Double Vacuum pressure application | *Recommendation needed* |
| | | Double Vacuum pressure storage | *Recommendation needed* |
| | | Double Vacuum application + storage | *Recommendation needed* |
| | Double-vacuum pressure *service life* (solvent and water based formulations) | Surface treated wood – indoor (use class 1-2): | *Negligible risk* |
| | | Surface treated wood – outdoor (use class 3):<br>- Fence scenario (soil)<br>- House construction material (soil)<br>- Noise barrier (soil and surface water)<br>- Bridge (surface water) | <br>*Not acceptable*<br>*Not acceptable*<br>*Not acceptable*<br>*Not acceptable* |
| | ***OVERALL CONCLUSION:*** *Industrial application by double-vacuum pressure and further uses of wood up to class 2 are acceptable provided that the following risk mitigation apply :*<br>• *During industrial treatments, collective protective equipment shall be ensured when appropriate, and the operators must wear the appropriate personal protective equipments.*<br>• *During industrial application the emissions to surface water have to be forbidden. Appropriate mitigation measures such as waste recycling or incineration have to be performed.*<br>• *All timbers treated by industrial process will have to be stored on impermeable hard standing or under a protective roof to prevent direct losses to soil and surface water and to allow losses to be collected and treated appropriately (e.g. incineration)* | | ***Acceptable (class 1-2) with restrictions*** |

| Intended uses | Scenario | | Risk assessment conclusion |
|---|---|---|---|
| ***Industrial application by dipping and service life*** | HUMAN EXPOSURE ASSESSMENT | | |
| | Water-based and solvent-based formulations | Primary exp. - Mixing and loading: No exposure<br>- Application: TNG handling model 1<br>- Post application and disposal: TNG handling model 1 | *Acceptable* |
| | | Secondary exposure (prof.) | *Acceptable* |
| | | Secondary exposure (public.) | *Acceptable* |
| | | Combined exposure | *Acceptable* |
| | ENVIRONMENTAL EXPOSURE ASSESSMENT | | |
| | Dipping application and storage (solvent and water based formulations) | Dipping application | *Recommendation needed* |
| | | Dipping storage | *Recommendation needed* |
| | | Dipping Application + storage | *Recommendation needed* |
| | Dipping service life (solvent and water based formulations) | Surface treated wood – indoor (use class 1-2): | *Negligible risk* |
| | | Surface treated wood – outdoor (use class 3):<br>- Fence scenario (soil)<br>- House construction material (soil)<br>- Noise barrier (soil and surface water)<br>- Bridge (surface water) | <br>*Not acceptable*<br>*Not acceptable*<br>*Not acceptable*<br>*Not acceptable* |
| | ***OVERALL CONCLUSION:*** *Industrial application by dipping and further uses of wood up to class 2 are acceptable provided that the following risk mitigation apply :*<br>• *During industrial treatments, collective protective equipment shall be ensured when appropriate, and the operators must wear the appropriate personal protective equipments.*<br>• *During industrial application the emissions to surface water have to be forbidden. Appropriate mitigation measures such as waste recycling or incineration have to be performed.*<br>• *All timbers treated by industrial process will have to be stored on impermeable hard standing or under a protective roof to prevent direct losses to soil and surface water and to allow losses to be collected and treated appropriately (e.g. incineration)* | | ***Acceptable (class 1-2) with restrictions*** |

| Intended uses | Scenario | | Risk assessment conclusion |
|---|---|---|---|
| ***Industrial application by vacuum pressure and service life*** | HUMAN EXPOSURE ASSESSMENT | | |
| | Water-based and solvent-based formulations | Primary exp. - Mixing and loading: No exposure<br>- Application: TNG handling model 1<br>- Post application and disposal: TNG handling model 1 | *Acceptable* |
| | | Secondary exposure (prof.) | *Acceptable* |
| | | Secondary exposure (public.) | *Acceptable* |
| | | Combined exposure | *Acceptable* |
| | ENVIRONMENTAL EXPOSURE ASSESSMENT | | |
| | Vacuum pressure *application* (solvent and water based formulations) | Vacuum pressure application | *Recommendation needed* |
| | | Vacuum pressure storage | *Recommendation needed* |
| | | Vacuum application + storage | *Recommendation needed* |
| | Vacuum pressure *service life* (solvent and water based formulations) | Surface treated wood – indoor (use class 1-2): | *Negligible risk* |
| | | Surface treated wood – outdoor (use class 3):<br>- Fence scenario (soil)<br>- House construction material (soil)<br>- Noise barrier (soil and surface water)<br>- Bridge (surface water) | <br>*Not acceptable*<br>*Not acceptable*<br>*Not acceptable*<br>*Not acceptable* |
| | ***OVERALL CONCLUSION:*** *Industrial application by vacuum pressure and further uses of wood up to class 2 are acceptable provided that the following risk mitigation apply :*<br>• *During industrial treatments, collective protective equipment shall be ensured when appropriate, and the operators must wear the appropriate personal protective equipments.*<br>• *During industrial application the emissions to surface water have to be forbidden. Appropriate mitigation measures such as waste recycling or incineration have to be performed.*<br>• *All timbers treated by industrial process will have to be stored on impermeable hard standing or under a protective roof to prevent direct losses to soil and surface water and to allow losses to be collected and treated appropriately (e.g. incineration)* | | ***Acceptable (class 1-2) with restrictions*** |

| Intended uses | Scenario | | Risk assessment conclusion |
|---|---|---|---|
| ***Industrial application by automated spraying and service life*** | HUMAN EXPOSURE ASSESSMENT | | |
| | Water-based and solvent-based formulations | Primary exp. - Mixing and loading: No exposure<br>- Application: TNG handling model 1<br>- Post application and disposal: TNG handling model 1 | *Acceptable* |
| | | Secondary exposure (prof.) | *Acceptable* |
| | | Secondary exposure (public.) | *Acceptable* |
| | | Combined exposure | *Acceptable* |
| | ENVIRONMENTAL EXPOSURE ASSESSMENT | | |
| | *Automatic spraying application and storage* | Automatic spraying application | *Recommendation needed* |
| | | Automatic spraying storage | *Recommendation needed* |
| | | Automatic spraying Application + storage | *Recommendation needed* |
| | *Automatic spraying service life* | Surface treated wood – indoor (use class 1-2): | *Negligible risk* |
| | | Surface treated wood – outdoor (use class 3):<br>- Fence scenario (soil)<br>- House construction material (soil)<br>- Noise barrier (soil and surface water)<br>- Bridge (surface water) | <br>*Not acceptable*<br>*Not acceptable*<br>*Not acceptable*<br>*Not acceptable* |
| | *OVERALL CONCLUSION: Industrial application by automatic spraying and further uses of wood up to class 2 are acceptable provided that the following risk mitigation apply :*<br>• *During industrial treatments, collective protective equipment shall be ensured when appropriate, and the operators must wear the appropriate personal protective equipments.*<br>• *During industrial application the emissions to surface water have to be forbidden. Appropriate mitigation measures such as waste recycling or incineration have to be performed.*<br>• *All timbers treated by industrial process will have to be stored on impermeable hard standing or under a protective roof to prevent direct losses to soil and surface water and to allow losses to be collected and treated appropriately (e.g. incineration).*<br>*Human and environmental exposures were estimated from dipping scenario.* | | ***Acceptable (class 1- 2) with restrictions.*** |

| Intended uses | Scenario | | | Risk assessment conclusion |
|---|---|---|---|---|
| ***IN SITU PROFESSIONAL APPLICATION*** | | | | |
| ***In situ indoor spraying and service life*** | HUMAN EXPOSURE ASSESSMENT | | | |
| | Water-based and solvent-based formulations | Primary exp. - Mixing and loading:<br>- Application:<br>- Post application and disposal: | TNG spray model 2<br>TNG spray model 2<br>Internal calculation | *Acceptable* |
| | | Secondary exposure (prof.) | | *Acceptable* |
| | | Secondary exposure (public.) | | *Acceptable* |
| | | Combined exposure | | *Acceptable* |
| | ENVIRONMENTAL EXPOSURE ASSESSMENT | | | |
| | *In situ* indoor spraying *application* (solvent and water based formulation) | Indoor application (use class 1-2): | | *Negligible risk* |
| | *In situ* indoor spraying *service life* (solvent and water based formulation) | Surface treated wood – indoor (use class 1-2): | | *Negligible risk* |
| | ***OVERALL CONCLUSION:*** *in situ indoor application by spraying and further uses of wood up to class 2 are acceptable.* | | | ***Acceptable*** |

| Intended uses | Scenario | | Risk assessment conclusion |
|---|---|---|---|
| ***In situ outdoor spraying and service life*** | HUMAN EXPOSURE ASSESSMENT | | |
| | Water-based and solvent-based formulations | Primary exp. - Mixing and loading: TNG spray model 2<br>- Application: TNG spray model 2<br>- Post application and disposal: Internal calculation | *Acceptable* |
| | | Secondary exposure (prof.) | *Acceptable* |
| | | Secondary exposure (public.) | *Acceptable* |
| | | Combined exposure | *Acceptable* |
| | ENVIRONMENTAL EXPOSURE ASSESSMENT | | |
| | *In situ* outdoor spraying *application* (solvent and water based formulation) | Outdoor application (use class 1-3): | *Not relevant (cumulated exposure)* |
| | *In situ* outdoor spraying *service life* (solvent and water based formulation) | *In situ* outdoor spraying application and wood in service (use class 3): | |
| | | - Fence scenario (soil)<br>- House scenario (soil)<br>- Bridge scenario (surface water) | - *Not acceptable*<br>- *Not acceptable*<br>- *Not acceptable* |
| | ***OVERALL CONCLUSION:*** *in situ application by spray and further uses of wood up to class 2 are not acceptable.*<br>***Application and use of wood in use class 3 should not be allowed.*** | | ***Not acceptable*** |

| Intended uses | Scenario | | Risk assessment conclusion |
|---|---|---|---|
| ***Small scale dipping and service life*** | HUMAN EXPOSURE ASSESSMENT | | |
| | Water-based and solvent-based formulations | Primary exp. - Mixing and loading: TNG Mix/Load - model 7<br>- Application: TNG, dipping - model 1<br>- Post application and disposal: TNG, handling - model 1 | *Acceptable* |
| | | Secondary exposure (prof.) | *Acceptable* |
| | | Secondary exposure (public.) | *Acceptable* |
| | | Combined exposure | *Acceptable* |
| | ENVIRONMENTAL EXPOSURE ASSESSMENT | | |
| | *In situ* outdoor small scale dipping *application* (solvent and water based formulation) | Outdoor application (use class 1-3): Application is made under a roof and is considered as an indoor application from an environmental point of view. | *Negligible risks* |
| | *In situ* small scale dipping *service life* (solvent and water based formulation) | Surface treated wood – indoor (use class 1-2): | *Negligible risk* |
| | | Surface treated wood – outdoor (use class 3):<br>- Fence scenario (soil)<br>- House construction material (soil)<br>- Noise barrier (soil and surface water)<br>- Bridge (surface water) | <br>*Not acceptable*<br>*Not acceptable*<br>*Not acceptable*<br>*Not acceptable* |
| | ***OVERALL CONCLUSION:*** *small-scale dipping application and further uses of wood up to class 2 are acceptable.*<br>*Application and use for wood in use class 3 should not be allowed.* | | ***Acceptable (class 1 – 2)*** |

| Intended uses | Scenario | | Risk assessment conclusion |
|---|---|---|---|
| ***In situ outdoor/indoor brushing application by professional and service life*** | HUMAN EXPOSURE ASSESSMENT | | |
| | Water-based and solvent-based formulations (Indoor and Outdoor) | Primary exp. - Mixing and loading: TNG Mix/Load - model 7<br>- Application: TNG, dipping - model 1<br>- Post application and disposal: TNG, handling - model 1 | *Acceptable* |
| | | Secondary exposure (prof.) | *Acceptable* |
| | | Secondary exposure (public.) | *Acceptable* |
| | | Combined exposure | *Acceptable* |
| | ENVIRONMENTAL EXPOSURE ASSESSMENT | | |
| | *In situ* brushing application (solvent and water based formulation) | *Brushing* indoor application (use class 1-2)*: no scenario available* | *Negligible risk* |
| | | *Brushing* outdoor application (use class 3)*:* | *Not relevant (cumulated exposure)* |
| | *In situ* brushing service life (solvent and water based formulation) | *Brushing* indoor application (use class 1-2)*: no scenario available* | *Negligible risk* |
| | | *Brushing* outdoor application and wood in service (use class 3)*:* | |
| | | - Fence scenario (soil) | *- Not acceptable* |
| | | - House scenario (soil) | *- Not acceptable* |
| | | - Bridge scenario (surface water) | *- Not acceptable* |
| | ***OVERALL CONCLUSION:***<br>*In situ application by brushing and further uses of wood up to class 2 are acceptable.*<br>*Application and use for wood in use class 3 should not be allowed.* | | ***Acceptable (class 1-2)*** |

| **Intended uses** | **Scenario** | | **Risk assessment conclusion** |
|---|---|---|---|
| *IN SITU NON-PROFESSIONAL APPLICATION* | | | |
| ***In situ outdoor/indoor brushing application by non-professional and service life*** | HUMAN EXPOSURE ASSESSMENT | | |
| | Water-based and solvent-based formulations (Indoor and Outdoor) | Primary exp. - Mixing and loading: No exposure<br>- Application: TNG, consumer product painting, indoor, model 1, and outdoor models 2,3<br>- Post application and disposal: internal calculation | *Acceptable* |
| | | Secondary exposure (prof.) | *Acceptable* |
| | | Secondary exposure (public.) | *Acceptable* |
| | | Combined exposure | *Acceptable* |
| | ENVIRONMENTAL EXPOSURE ASSESSMENT | | |
| | *In situ* brushing application (solvent based formulation) | *Brushing* indoor application (use class 1-2)*: no scenario available* | *Negligible risk* |
| | | *Brushing* outdoor application (use class 3)*:* | *Not relevant (cumulated exposure)* |
| | *In situ* brushing service life (solvent based formulation) | *Brushing* indoor application (use class 1-2)*: no scenario available* | *Negligible risk* |
| | | *Brushing* outdoor application (use class 3)*:*<br>- Fence scenario (soil)<br>- House scenario (soil)<br>- Bridge scenario (surface water) | <br>*- Not acceptable*<br>*- Not acceptable*<br>*- Not acceptable* |
| | ***OVERALL CONCLUSION:*** *in situ application by non professionals by brushing and further uses of wood up to class 2 are acceptable. The risk was assessed for solvent-based formulation only.*<br>*Application and use for wood in use class 3 should not be allowed.* | | ***Acceptable (class 1-2)*** |

| Intended uses | Scenario | | Risk assessment conclusion |
|---|---|---|---|
| ***In situ outdoor/indoor spraying application by non-professional and service life*** | HUMAN EXPOSURE ASSESSMENT | | |
| | Water-based and solvent-based formulations (Indoor and Outdoor) | Primary exp. - Mixing and loading: No exposure<br>- Application: TNG consumer product spraying, model 2<br>- Post application and disposal: internal calculation | *Acceptable* |
| | | Secondary exposure (prof.) | *Acceptable* |
| | | Secondary exposure (public.) | *Acceptable* |
| | | Combined exposure | *Acceptable* |
| | ENVIRONMENTAL EXPOSURE ASSESSMENT | | |
| | *In situ* brushing application (solvent based formulation) | *Spraying* indoor application (use class 1-2)*: no scenario available* | *Negligible risk* |
| | | *Spraying* outdoor application (use class 3)*:* | *Not relevant (cumulated exposure)* |
| | *In situ* brushing service life (solvent based formulation) | *Spraying* indoor application (use class 1-2)*: no scenario available* | *Negligible risk* |
| | | *Spraying* outdoor application (use class 3)*:*<br>- Fence scenario (soil)<br>- House scenario (soil)<br>- Bridge scenario (surface water) | <br>*- Not acceptable*<br>*- Not acceptable*<br>*- Not acceptable* |
| | ***OVERALL CONCLUSION:*** *in situ application by non professionals by spraying and further uses of wood up to class 2 are acceptable The risk was assessed for solvent-based formulation only.*<br>*Application and use for wood in use class 3 should not be allowed.* | | ***Acceptable (class 1-2)*** |
| | | | |

[8] When writing the assessment report, please ensure that the following formatting is respected

***Text of the report (other than titles and headings):***

Font: Times New Roman, 12 pt, English (U.K.), Justified, Line spacing: single, Space After: 12 pt, Widow/Orphan control

***Content of tables of the report:***

Font: Times New Roman, 11 pt, English (U.K.), Justified, Line spacing: single, Widow/Orphan control

[#] System B (loamy silt sediment)

# APPENDIX III: LIST OF STUDIES

| Annex point(s) | Author(s) | Date Year / Month / Day | Title<br>Source<br>BASF DocID<br>GLP or GEP status<br>Published or not | Data Protection Y/N | Owner |
|---|---|---|---|---|---|
| IV 3.1.1/1 | A Camilleri P. et al. | 1986 | Melting point and differential thermal analysis of WL115110<br>XXXX No<br>unpublished | N | BASF |
| IV 3.1.1/2 | A 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<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV 3.1.2/1 | A Camilleri P. et al. | 1986 | Melting point and differential thermal analysis of WL115110<br>XXXX<br>No<br>unpublished | N | BASF |
| IV 3.1.2/2 | A 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<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV 3.1.3/1 | A Kaestel R. | 2001 | Density determination of the technical material of Flufenoxuron<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV A 3.2/1 | Langner E.J. | 1988 | Physico-chemical properties of WL115110<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV 3.2.1/1 | A Rice P. | 2000 | Flufenoxuron (BAS 307 I): Calculation of Henry's law constant<br>XXXX<br>No, not subject to GLP regulations<br>unpublished | Y | BASF |
| IV A 3.3/1 | Kaestel R. | 2001 | Physical properties of Flufenoxuron (TC)<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV A 3.3/2 | Kaestel R. | 2001 | Physical properties of Flufenoxuron (PAI)<br>XXXX<br>Yes<br>unpublished | Y | BASF |

| Annex point(s) | Author(s) | Date Year / Month / Day | Title<br>Source<br>BASF DocID<br>GLP or GEP status<br>Published or not | Data Protection<br>Y/N | Owner |
|---|---|---|---|---|---|
| IV A 3.4/1 | Fang L.Y. | 1996 | CL 811678 (Flufenoxuron) spectral database<br>XXXX<br>No<br>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<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV A 3.5/1 | Langner E.J. | 1988 | Physico-chemical properties of WL115110<br>XXXX<br>Yes<br>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<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV A 3.6/1 | Camilleri P., Langner E.J. | 1986 | Solubility and pKa of WL115110 in water<br>XXXX<br>No<br>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))<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV A 3.9/1 | Langner E.J. | 1988 | Physico-chemical properties of WL115110<br>XXXX<br>Yes<br>unpublished | N | BASF |
| 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<br>XXXX<br>Yes<br>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<br>XXXX<br>Yes<br>unpublished | Y | BASF |

| Annex point(s) | Author(s) | Date Year / Month / Day | Title<br>Source<br>BASF DocID<br>GLP or GEP status<br>Published or not | Data Protection<br>Y/N | Owner |
|---|---|---|---|---|---|
| IV A 3.11/1 | Van Helvoirt J.A.M.W. | 1990 | Determination of the flammability of Flufenoxuron<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV A 3.11/2 | Van Helvoirt J.A.M.W. | 1990 | Determination of the auto-flammability of Flufenoxuron<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV A 3.13/1 | Kaestel R. | 2001 | Physical properties of Flufenoxuron (TC)<br>XXXX<br>Yes<br>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<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV A 3.16/1 | Van Helvoirt J.A.M.W. | 1990 | Determination of the oxidizing properties of Flufenoxuron<br>XXXX<br>Yes<br>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)<br>XXXX<br>Yes<br>unpublished | N | 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<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV A 4.2/2 | Anonymous | 1996 | Determination of residues of WL115110 in soil - Liquid chromatographic method<br>XXXX<br>No<br>unpublished | N | BASF |
| IV A 4.2/3 | Anonymous | 1989 | Determination of residues of WL 129183 in soil - liquid chromatographic method<br>XXXX<br>No<br>unpublished | N | BASF |

| Annex point(s) | Author(s) | Date Year / Month / Day | Title<br>Source<br>BASF DocID<br>GLP or GEP status<br>Published or not | Data Protection Y/N | Owner |
|---|---|---|---|---|---|
| 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<br>XXXX<br>Yes<br>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<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV A 4.2/6 | Anonymous | 1986 | Determination of residues of WL115110 in water - Liquid chromatographic method<br>XXXX<br>No<br>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<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| 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<br>XXXX<br>Yes<br>unpublished | Y | BASF |

| Annex point(s) | Author(s) | Date Year / Month / Day | Title<br>Source<br>BASF DocID<br>GLP or GEP status<br>Published or not | Data Protection<br>Y/N | Owner |
|---|---|---|---|---|---|
| IV 6.1.1/1 | A XXXX | XXXX | WL115110 (Cascade): Acute oral toxicity<br>XXXX<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV 6.1.1/2 | A XXXX | XXXX | Toxicology of insecticides (acyl ureas): The acute oral and percutaneous toxicity, skin and eye irritancy and skin sensitizing potential of WL115110<br>XXXX<br>No<br>unpublished | N | BASF |
| IV 6.1.1/3 | A 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<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV 6.1.2/1 | A XXXX | XXXX | Toxicology of insecticides (acyl ureas): The acute oral and percutaneous toxicity, skin and eye irritancy and skin sensitizing potential of WL115110<br>XXXX<br>No<br>unpublished | N | BASF |
| IV 6.1.2/2 | A 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<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV 6.1.3/1 | A XXXX | XXXX | WL 115110: Acute inhalation toxicity study in rats<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV 6.1.3/2 | A XXXX | XXXX | Addendum to XXXX: WL 115110: Acute inhalation toxicity study in rats<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV 6.1.4/1 | A XXXX | XXXX | Toxicology of insecticides (acyl ureas): The acute oral and percutaneous toxicity, skin and eye irritancy and skin sensitizing potential of WL115110<br>XXXX<br>No<br>unpublished | N | BASF |

| Annex point(s) | Author(s) | Date Year / Month / Day | Title<br>Source<br>BASF DocID<br>GLP or GEP status<br>Published or not | Data Protection<br>Y/N | Owner |
|---|---|---|---|---|---|
| IV 6.1.4/2 | A 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<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV 6.1.5/1 | A XXXX | XXXX | Toxicology of insecticides (acyl ureas): The acute oral and percutaneous toxicity, skin and eye irritancy and skin sensitizing potential of WL115110<br>XXXX<br>No, studies were conducted prior to the implementation of GLP but are scientifically valid<br>unpublished | N | BASF |
| IV 6.1.5/2 | A 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<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV 6.1.5/3 | A XXXX | XXXX | BAS 307 I (Flufenoxuron) – Maximization Test in Guinea pigs.<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV A 6.2/1 | Huckle K.R. | 1988 | The fate of (14C-aniline)-WL115110 in the fischer 344 rat following a single low oral dose of 3.5 mg per kg bodyweight<br>XXXX<br>Yes<br>unpublished | N | BASF |
| 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<br>XXXX<br>Yes<br>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<br>XXXX<br>Yes<br>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<br>XXXX<br>Yes<br>unpublished | N | BASF |

| Annex point(s) | Author(s) | Date Year / Month / Day | Title<br>Source<br>BASF DocID<br>GLP or GEP status<br>Published or not | Data Protection<br>Y/N | Owner |
|---|---|---|---|---|---|
| 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<br>XXXX<br>Yes<br>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<br>XXXX<br>Yes<br>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<br>XXXX<br>Yes<br>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<br>XXXX<br>Yes<br>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<br>XXXX<br>Yes<br>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<br>XXXX<br>Yes<br>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<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV A 6.2/12 | XXXX | XXXX | The metabolism of 14C-WL115110 in rats<br>XXXX<br>Yes<br>unpublished | N | BASF |

| Annex point(s) | Author(s) | Date Year / Month / Day | Title<br>Source<br>BASF DocID<br>GLP or GEP status<br>Published or not | Data Protection<br>Y/N | Owner |
|---|---|---|---|---|---|
| IV A 6.2/13 | XXXX | XXXX | Report amendment no. 1: The metabolism of 14C-WL115110 in rats<br>XXXX<br>Yes<br>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<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV A 6.2/15 | XXXX | XXXX | The absorption and disposition of 14C-WL 115110 in the dog after a single oral administration<br>XXXX<br>Yes<br>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<br>XXXX<br>Yes<br>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<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV A 6.2/18 | XXXX | XXXX | WL115110 kinetic accumulation and elimination study in the dog<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV A 6.2/19 | XXXX | XXXX | WL115110: Percutaneous penetration of the 10 DC formulation in the rat in vivo<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV A 6.3.1/1 | XXXX | XXXX | WL115110: A 28 day feeding study in rats<br>XXXX No<br>unpublished | N | BASF |
| IV A 6.3.1/2 | XXXX | XXXX | Corrigendum 1 WL115110: A 28 day feeding study in rats<br>XXXX No<br>unpublished | N | BASF |

| Annex point(s) | Author(s) | Date Year / Month / Day | Title<br>Source<br>BASF DocID<br>GLP or GEP status<br>Published or not | Data Protection<br>Y/N | Owner |
|---|---|---|---|---|---|
| IV 6.3.1/3 | A XXXX | XXXX | Flufenoxuron (WL115110): A 28 day range-finding feeding study in mice<br>XXXX<br>No<br>unpublished | N | BASF |
| IV 6.4.1/1 | A XXXX | XXXX | WL115110: A 90 day feeding study in rats<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV 6.4.1/2 | A XXXX | XXXX | Corrigenda/Addenda to XXXX: WL115110: A 90 day feeding study in rats<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV 6.4.1/3 | A XXXX | XXXX | Corrigenda/Addenda to XXXX: WL115110: A 90 day feeding study in rats<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV 6.4.1/4 | A XXXX | XXXX | WL115110: A 90 day feeding study in mice<br>XXXX<br>No<br>unpublished | N | BASF |
| IV 6.4.1/5 | A XXXX | XXXX | Corrigenda/Addenda to XXXX: WL115110: A 90 day feeding study in mice<br>XXXX<br>No<br>unpublished | N | BASF |
| IV 6.4.1/6 | A XXXX | XXXX | Corrigenda/Addenda to XXXX: WL115110: A 90 day feeding study in mice<br>XXXX<br>No<br>unpublished | N | BASF |
| IV 6.4.1/7 | A XXXX | XXXX | WL115110: A 13 week oral toxicity study in dogs<br>XXXX<br>No<br>unpublished | N | BASF |
| IV 6.4.1/8 | A XXXX | XXXX | Addendum to XXXX - WL115110: A 13 week oral toxicity study in dogs<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV 6.4.1/9 | A XXXX | XXXX | Supplement to XXXX (WL115110: 13 week oral toxicity study in dogs). A 13 week no effect level<br>XXXX No<br>unpublished | N | BASF |

| Annex point(s) | Author(s) | Date Year / Month / Day | Title<br>Source<br>BASF DocID<br>GLP or GEP status<br>Published or not | Data Protection<br>Y/N | Owner |
|---|---|---|---|---|---|
| IV 6.4.1/10 | A XXXX | XXXX | Supplement to XXXX (WL115110 : 13 week oral toxicity study in dogs)<br>XXXX<br>No<br>unpublished | N | BASF |
| IV 6.4.1/11 | A XXXX | XXXX | WL 115110: 52 week oral toxicity study in dogs<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV 6.4.1/12 | A XXXX | XXXX | Addendum to XXXX - WL 115110: 52 week oral toxicity study in dogs<br>XXXX<br>No<br>unpublished | N | BASF |
| IV A 6.5/1 | XXXX | XXXX | WL115110: A two year chronic toxicity feeding study in rats<br>XXXX<br>Yes<br>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<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV A 6.5/3 | XXXX | XXXX | Corrigenda/addenda to XXXX - WL115110: A 2 year chronic toxicity feeding study in rats<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV 6.6.1/1 | A Brooks T.M. | 1986 | Microbial mutagenicity studies with WL115110<br>XXXX<br>No<br>unpublished | N | BASF |
| IV 6.6.1/2 | A Brooks T.M. | 1991 | Addendum to XXXX: Microbial mutagenicity of WL115110<br>XXXX<br>No<br>unpublished | N | BASF |
| IV 6.6.1/3 | A Engelhardt G., Le bold E. | 2005 | Salmonella typhimurium / Escherichia coli - Reverse mutation assay (standard plate test and preincubation test) with BAS 307 I (Flufenoxuron)<br>XXXX<br>Yes<br>unpublished | Y | BASF |

| Annex point(s) | Author(s) | Date Year / Month / Day | Title<br>Source<br>BASF DocID<br>GLP or GEP status<br>Published or not | Data Protection Y/N | Owner |
|---|---|---|---|---|---|
| IV 6.6.2/1 | A Meyer A.L. | 1987 | Genotoxicity studies with WL115110 : in vitro chromosome studies with WL115110<br>XXXX<br>No<br>unpublished | N | BASF |
| IV 6.6.2/2 | A Meyer A.L. | 1991 | Addendum to XXXX: Genotoxicity studies with WL115110 : in vitro chromosome studies with WL115110<br>XXXX<br>No<br>unpublished | N | BASF |
| IV 6.6.2/3 | A Meyer A.L. | 1988 | Genotoxicity studies with WL115110: in vitro chromosome studies with WL115110 and glutathione using chinese hamster ovary (CHO) cells<br>XXXX<br>No<br>unpublished | N | BASF |
| IV 6.6.2/4 | A 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<br>XXXX<br>No<br>unpublished | N | BASF |
| IV 6.6.2/5 | A Meyer A.L. | 1988 | Genotoxicity studies with WL115110: in vitro chromosome studies with WL115110 using a rat liver (RL4) cell line<br>XXXX<br>No<br>unpublished | N | BASF |
| IV 6.6.2/6 | A 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<br>XXXX<br>No<br>unpublished | N | BASF |
| IV 6.6.2/7 | A 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<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV 6.6.3/1 | A Clare M.G. | 1986 | In vitro mutagenicity studies with WL115110 (insecticide) using cultured chinese hamster V79 cells<br>XXXX<br>No<br>unpublished | N | BASF |

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| IV 6.6.3/2 | A Brooks T.M. | 1991 | Addendum 1 in vitro mutagenicity studies with WL115110 (insecticide) using cultured Chinese hamster V79 cells<br>XXXX<br>No<br>unpublished | N | BASF |
| IV 6.6.4/1 | A XXXX | XXXX | Genotoxicity studies with WL115110 : In vivo chromosome studies with rat bone marrow cells<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV 6.6.4/2 | A XXXX | XXXX | Report amendment no. 1 - Genotoxicity studies with WL115110 : In vivo chromosome studies with rat bone marrow cells<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV 6.6.4/3 | A XXXX | XXXX | Report amendment no.2 - Genotoxicity studies with WL115110: In vivo chromosome studies with rat bone marrow cells<br>XXXX)<br>Yes<br>unpublished | N | BASF |
| IV 6.6.4/4 | A XXXX | XXXX | Micronucleus test on WL115110 in mice<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV 6.6.5/1 | A XXXX | XXXX | Mutagenicity test on WL115110 in the in vivo/in vitro rat primary hepatocyte unscheduled DNA synthesis assay - Revised final report<br>XXXX<br>No<br>unpublished | N | BASF |
| IV A 6.7/1 | XXXX | XXXX | WL115110: A two year oncogenicity feeding study in rats<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV A 6.7/2 | XXXX | XXXX | Addendum to XXXX - WL115110: A two year oncogenicity feeding study in rats<br>XXXX<br>Yes<br>unpublished | N | BASF |

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|---|---|---|---|---|---|
| IV A 6.7/3 | XXXX | XXXX | Corrigenda/addenda to XXXX - WL115110: A 2 year oncogenicity feeding study in rats<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV A 6.7/4 | XXXX | XXXX | WL115110: A 2 year oncogenicity feeding study in mice<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV A 6.7/5 | XXXX | XXXX | Corrigenda/addenda to XXXX - WL115110: A 2 year oncogenicity feeding study in mice<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV A 6.7/6 | XXXX | XXXX | Corrigenda/addenda to XXXX - WL115110: A 2 year oncogenicity feeding study in mice<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV A 6.7/7 | XXXX | XXXX | Corrigenda/addenda to XXXX - WL115110: A 2 year oncogenicity feeding study in mice<br>XXXX<br>Yes<br>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<br>Literature<br>XXXX<br>No<br>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<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV A 6.8.1/1 | XXXX | XXXX | Reissued report XXXX: WL115110 teratogenicity study in rats<br>XXXX<br>Yes<br>unpublished | N | BASF |

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|---|---|---|---|---|---|
| IV 6.8.1/2 | A XXXX | XXXX | Addendum to XXXX - WL115110: Teratogenicity study in rats<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV 6.8.1/3 | A XXXX | XXXX | Response to BGVV concern regarding variations in branching of the great vessels of the heart in rat fetuses<br>XXXX<br>No, not subject to GLP regulations<br>unpublished | N | BASF |
| IV 6.8.1/4 | A XXXX | XXXX | Reissued report XXXX - WL115110: Teratogenicity study in rabbits<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV 6.8.1/5 | A XXXX | XXXX | Addendum to XXXX - WL115110: Teratogenicity study in rabbits<br>XXXX<br>Yes<br>Unpublished | N | BASF |
| IV 6.8.2/1 | A XXXX | XXXX | The effect of WL115110 on the reproductive function of two generations in the rat<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV 6.8.2/2 | A XXXX | XXXX | Addendum to SLL 138/891394: The effects of WL115110 on the reproductive function of two generations in the rat<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV 6.8.2/3 | A XXXX | XXXX | Amendment no. one: The effects of WL115110 on the reproductive function of two generations in the rat<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV A 6.8.2/4 | XXXX | XXXX | Dietary investigative study in pregnant rats rearing young to weaning. Compound: WL 115110<br>XXXX<br>No<br>Unpublished | N | BASF |
| IV 6.8.2/5 | A XXXX | XXXX | WL115110: A cross-fostering study, supplementary to a previous two generation rat reproduction study<br>XXXX<br>Yes<br>unpublished | N | BASF |

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|---|---|---|---|---|---|
| IV A 6.8.2/6 | XXXX | XXXX | WL 115110: A CKA embryotoxicity study in rats<br>XXXX<br>No<br>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<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV A 6.10/1 | XXXX | XXXX | WL129183: Acute oral toxicity<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV A 6.10/2 | Brooks T.M., Wiggins D.E. | 1990 | Bacterial mutagenicity studies with WL129183<br>Sittingbourne Research Centre; Kent ME9 8AG; United Kingdom<br>FX-470-018<br>Yes<br>unpublished | N | BASF |
| IV A 6.10/3 | XXXX | XXXX | WL115096: Acute oral toxicity<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV A 6.10/4 | XXXX | XXXX | The acute oral and percutaneous toxicity WL125892<br>XXXX<br>No<br>unpublished | N | BASF |
| IV A 6.10/5 | XXXX | XXXX | WL125892: A 28 day oral toxicity study in Fischer 344 rats<br>XXXX<br>No<br>unpublished | N | BASF |
| IV A 6.10/6 | Brooks T.M., Wiggins D.E. | 1990 | Bacterial mutagenicity studies with WL115096<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV A 6.10/7 | Brooks T.M., Wiggins D.E. | 1987 | Bacterial mutagenicity studies with WL125892<br>XXXX<br>No<br>unpublished | N | BASF |

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| IV A 6.10/8 | Engelhardt G., Le bold E. | 2005 | In vitro gene mutation test with Reg. No. 241208 (Metabolite of BAS 307 I, Flufenoxuron) in CHO cells (HPRT locus assay)<br>XXXX<br>Yes<br>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)<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV 6.10/10 | A Brooks T.M., Wiggins D.E. | 1992 | WL115096: In vitro chromosome studies with cultured chinese hamster ovary (CHO) cells<br>XXXX Yes<br>unpublished | N | BASF |
| IV 6.10/11 | A 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<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV 6.10/12 | A 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<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV 6.10/13 | A Brooker P. et al. | 1987 | Analysis of metaphase chromosomes obtained from CHO cells cultured in vitro and treated with WL125892<br>XXXX<br>No<br>unpublished | N | BASF |
| IV 6.10/14 | A XXXX | XXXX | WL125892 (95-06-0752): Micronucleus test in the mouse<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV 6.10/15 | A Engelhardt G., Le bold 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)<br>XXXX<br>Yes<br>unpublished | Y | BASF |

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| IV 6.10/16 | A 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)<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV 6.10/20 | A Evelyn K.A., Malloy H.T. | 1938 | Microdetermination of oxyhemoglobin, methemoglobin, and sulfhemoglobin in a single sample of blood<br>Literature<br>XXXX<br>No<br>Published in The Journal of Biological Chemistry, Volume 126, 655-662 | N | Not Applicable |
| IV 6.10/21 | A XXXX | XXXX | Haemoglobin binding of WL 115110 (Cascade) and its precursor WL 125892: A pilot study in the rat<br>XXXX<br>No<br>unpublished | N | BASF |
| IV 6.10/22 | A XXXX | XXXX | Replicative DNA synthesis (RDS) test using rat livers on WL115110<br>XXXX<br>No<br>unpublished | N | BASF |
| IV A 6.12.1/1 | Deweerdt J., Mommee J.C. | 1997 | SNPE Chimie - Health surveillance program in Flufenoxuron production plant<br>XXXX No<br>unpublished | N | SNPE |
| IV A 6.12.1/2 | Flynn A. | 2003 | Medical information (Great Lakes)<br>XXXX<br>No<br>unpublished | N | Great Lakes |
| IV A 6.12.1/3 | Evrard P. | 2004 | Medical information (Isochem)<br>XXXX<br>No<br>unpublished | N | Isochem |

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| IV 7.1.1.1.1/1 | A Langner E.J., Camilleri P. | 1987 | Hydrolysis of WL115110 in aqueous media<br>XXXX<br>No<br>unpublished | N | BASF |
| IV 7.1.1.1.1/2 | A Hassink J. | 2003 | Hydrolysis of BAS 307 I<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV 7.1.1.1.2/1 | A Camilleri P., Langner E.J. | 1987 | Photodecomposition of aqueous solutions of Flufenoxuron by sunlight<br>XXXX<br>No<br>unpublished | N | BASF |
| IV 7.1.1.1.2/2 | A Langner E.J. | 1991 | Corrigendum to SBGR.87.150: Photodecomposition of aqueous solutions of Flufenoxuron by sunlight<br>XXXX<br>No<br>unpublished | N | BASF |
| IV 7.1.1.1.2/3 | A Burgener A. | 2001 | 14C-Flufenoxuron (BAS 307 I): Quantum yield of direct phototransformation in water<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV 7.1.1.1.2/4 | A Hassink J. | 2003 | Aqueous photolysis of BAS 307 I<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV 7.1.1.1.2/5 | A Mamouni A., van der Gaauw A. | 2001 | 14C-Flufenoxuron (BAS 307 I): Photolysis in natural water<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV 7.1.1.1.2/6 | A Mamouni A., van der Gaauw A. | 2001 | Amendment no.1: 14C-Flufenoxuron (BAS 307 I): Photolysis in natural water<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV 7.1.1.2.1/1 | A Turner S.J., Watkinson R.J. | 1986 | WL115110: An assessment of the ready biodegradability<br>XXXX<br>No<br>unpublished | N | BASF |

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| IV A 7.1.2.2.2/1 | Ebert D. | 2003 | Degradation of BAS 307 I (Flufenoxuron) in water/sedimentsystems under aerobic conditions<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV A 7.1.2.2.2/2 | Fent G. | 2003 | Degradation and distr bution of BAS 307 I in a water-sediment system under outdoor conditions<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV A 7.2.1/1 | Richardson K.A. | 1987 | The effect of soil pH on the degradation of 14C-WL115110<br>XXXX<br>No<br>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<br>XXXX<br>Yes<br>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<br>XXXX<br>Yes<br>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<br>XXXX<br>Yes<br>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<br>XXXX<br>Yes<br>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)<br>XXXX<br>Yes<br>unpublished | Y | 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<br>XXXX<br>No, not subject to GLP regulations<br>unpublished | Y | BASF |
| IV 7.2.2.2/1 | A 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<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV 7.2.2.3/1 | A 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<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV 7.2.2.3/2 | A Goodyear A., Gross R. | 2001 | 14C-Flufenoxuron (BAS 307 I): Aerobic soil rate of degradation in three soils<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV 7.2.2.4/1 | A Richardson K.A. | 1990 | A comparison of the degradation of (aniline-14C)-WL115110 in soil under aerobic and anaerobic conditions<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV 7.2.2.4/2 | A Richardson K.A. | 1991 | A comparison of the degradation of (aniline-14C)-WL115110 in soil under aerobic and anaerobic conditions<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV 7.2.2.4/3 | A 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<br>Sittingbourne Research Centre; Kent ME9 8AG; United Kingdom<br>FX-620-037<br>Yes<br>unpublished | N | BASF |
| IV 7.2.2.4/4 | A Lewis C.J., Gross R. | 2001 | 14C-Flufenoxuron (BAS 307 I): Soil photolysis under artificial sunlight<br>XXXX<br>Yes<br>unpublished | Y | BASF |

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| IV 7.2.3.1/1 | A Hill A.D., Standen M.E. | 1993 | [Carbonyl-14C] WL115110 (Cascade): Adsorption/desorption in three soils<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV 7.2.3.1/2 | A Rosenwald J. | 2002 | Adsorption/desorption of 14C-Flufenoxuron (BAS 307 I) in three soils<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV 7.2.3.1/3 | A Zirnstein M. | 2003 | Adsorption/desorption - Study of BAS 307 I metabolite (Reg.No. 406 4702) on five European soils<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV 7.3.1/1 | A Hassink J. | 2003 | Photochemical oxidative degradation of Flufenoxuron BAS 307 I (QSAR estimates)<br>XXXX<br>No, not subject to GLP regulations<br>unpublished | Y | BASF |
| IV 7.3.2/1 | A Hassink J. | 2003 | Volatilisation of BAS 307 I after application of BAS 307 10 I on soil and on plant surfaces<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV 7.4.1.1/1 | A XXXX | XXXX | WL115110: Acute toxicity to Salmo gairdneri, Daphnia magna and Selenastrum capricornutum<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV 7.4.1.1/2 | A XXXX | XXXX | Acute toxicity of Flufenoxuron (AC 811678) technical to zebra fish (Brachydanio rerio) under flow-through test conditions<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV 7.4.1.1/3 | A XXXX | XXXX | Acute toxicity of SKI-8503 to Cyprinus carpio<br>XXXX<br>No<br>unpublished | N | BASF |
| IV 7.4.1.1/4 | A XXXX | XXXX | 4-Amino-3-Fluorophenol: Acute toxicity to Daphnia magna and Salmo gairdneri<br>XXXX<br>Yes<br>unpublished | N | BASF |

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| IV 7.4.1.1/5 | A XXXX | XXXX | 4-Amino-3-Fluorophenol : Acute toxicity to Daphnia magna and Salmo gairdneri<br>XXXX )<br>Yes<br>unpublished | N | BASF |
| IV 7.4.1.1/6 | A XXXX | XXXX | WL125892: Acute toxicity to Salmo gairdneri and Daphnia magna<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV 7.4.1.1/7 | A 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<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV 7.4.1.1/8 | A 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<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV 7.4.1.2/1 | A Funk M. | 2003 | Effect of radiolabelled BAS 307 I on the immobility of Daphnia magna STRAUS in a 48 hours static, acute toxicity test<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV 7.4.1.2/2 | A XXXX | XXXX | WL115110: Acute toxicity to Salmo gairdneri, Daphnia magna and Selenastrum capricornutum<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV 7.4.1.2/3 | A Shumei W. | 1987 | Acute toxicity of SKI-8503 on Daphnia carinata<br>XXXX<br>No<br>unpublished | N | BASF |
| IV 7.4.1.2/4 | A Pearson N., Girling A.E. | 1989 | Flufenoxuron (WL115110): Acute toxicity to Gammarus pulex, Lymnaea stagnalis, Tubifex tubifex and chiromonus lugubris<br>XXXX Yes<br>unpublished | N | BASF |
| IV 7.4.1.2/5 | A XXXX | XXXX | 4-Amino-3-Fluorophenol: Acute toxicity to Daphnia magna and Salmo gairdneri<br>XXXX<br>Yes<br>unpublished | N | BASF |

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| IV 7.4.1.2/6 | A XXXX | XXXX | 4-Amino-3-Fluorophenol : Acute toxicity to Daphnia magna and Salmo gairdneri<br>XXXX)<br>Yes<br>unpublished | N | BASF |
| IV 7.4.1.2/7 | A XXXX | XXXX | WL125892: Acute toxicity to Salmo gairdneri and Daphnia magna<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV 7.4.1.2/8 | A 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<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV 7.4.1.2/9 | A 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<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV 7.4.1.2/10 | A 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<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV 7.4.1.2/11 | A 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<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV 7.4.1.3/1 | A Kubitza J. | 2003 | Effect of BAS 307 I (Flufenoxuron) on the growth of the green alga Pseudokirchneriella subcapitata<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV 7.4.1.3/2 | A XXXX | XXXX | WL115110: Acute toxicity to Salmo gairdneri, Daphnia magna and Selenastrum capricornutum<br>XXXX<br>Yes<br>unpublished | N | BASF |

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| IV 7.4.1.3/3 | A Hanstveit A.O., Oldersma H. | 1993 | Effect of WL 125892 on the growth of alga Selenastrum capricornutum (OECD 201)<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV 7.4.1.3/4 | A Jatzek H.-J. | 2003 | Reg.No. 102 719 (metabolite of BAS 307 I) - Determination of the inh bitory effect on the cell multiplication of unicellular green algae<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV 7.4.1.3/5 | A 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<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV 7.4.1.4/1 | A Lebertz H., Yan Z. | 2001 | Flufenoxuron (BAS 307I): Activated sludge, respiration inhibition test<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV 7.4.3.1/1 | A XXXX | XXXX | Flufenoxuron (Cascade): An early life stage test with the fathead minnow Pimephales promelas (Rafinesque)<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV 7.4.3.2/1 | A XXXX | XXXX | Flufenoxuron 100 DC (BAS 307 10 I): Zebrafish (Danio rerio), static full life cycle test with sediment<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV 7.4.3.3.1/1 | A XXXX | XXXX | Flufenoxuron: The accumulation and elimination by rainbow trout (Oncorhynchus mykiss) in a continuous flow test<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV 7.4.3.3.1/2 | A XXXX | XXXX | Bioaccumulation and metabolism of 14C-BAS 307 I (Flufenoxuron) in rainbow trout<br>XXXX<br>Yes<br>unpublished | Y | BASF |

| Annex point(s) | Author(s) | Date Year / Month / Day | Title<br>Source<br>BASF DocID<br>GLP or GEP status<br>Published or not | Data Protection<br>Y/N | Owner |
|---|---|---|---|---|---|
| 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<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV A 7.4.3.4/1 | Pearson N., Girling A. | 1989 | Flufenoxuron: Chronic toxicity to Daphnia magna<br>XXXX<br>Yes<br>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<br>XXXX<br>Yes<br>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<br>XXXX<br>Yes<br>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<br>XXXX<br>Yes<br>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<br>XXXX<br>Yes<br>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 sp ked sediment in a 28 d study.<br>XXXX<br>Yes<br>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.<br>XXXX<br>Yes<br>unpublished | Y | BASF |

| Annex point(s) | Author(s) | Date Year / Month / Day | Title<br>Source<br>BASF DocID<br>GLP or GEP status<br>Published or not | Data Protection Y/N | Owner |
|---|---|---|---|---|---|
| IV 7.5.1.1/1 | A Koelzer U. | 2003 | Assessment of the side effects of BAS 307 QA I on the activity of the soil microflora, nitrogen turnover<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV 7.5.1.1/2 | A Koelzer U. | 2003 | Assessment of the side effects of BAS 307 QA I on the activity of the soil microflora, short-term respiration<br>XXXX<br>Yes<br>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<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV 7.5.1.2/1 | A Hillaby J.M. | 1987 | The toxicity of WL115110 to the earthworm, Eisenia foetida L. (Oligocheata: Lumbriculidae) in laboratory tests<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV 7.5.1.3/1 | A Sack D. | 2003 | BAS 307 QA I: Effects on non-target plants in the greenhouse - A limit test<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV 7.5.1.2/2 | A Staebler D. | 2003 | Acute toxicity of CL 932 338 (metabolite of BAS 307 I) on earthworms, Eisenia fetida using an artificial soil test<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV 7.5.2.1/1 | A Luehrs U. | 2001 | Effects of Flufenoxuron technical (AC 811678) on reproduction and growth of earthworms Eisenia fetida (Savigny 1826) in artificial soil<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV 7.5.3.1.1/1 | A XXXX | XXXX | The acute oral toxicity (LD50) of WL 115110 to the bobwhite quail<br>XXXX<br>Yes<br>unpublished | N | BASF |
| IV 7.5.3.1.2/1 | A XXXX | XXXX | The subacute dietary toxicity (LC50) ofWL 115110 to the bobwhite quail<br>XXXX<br>Yes<br>Unpublished | N | BASF |

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|---|---|---|---|---|---|
| IV A 7.5.3.1.2/2 | XXXX | XXXX | The subacute dietary toxicity (LC50) of WL 115110 to the mallard duck<br>XXXX<br>Yes<br>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<br>XXXX<br>Yes<br>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)<br>XXXX<br>No, not subject to GLP regulations<br>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<br>XXXX<br>Yes<br>unpublished | Y | BASF |
| IV A 8.4/1 | Schenk W. | 2001 | Possible procedures for the decontamination of water from Flufenoxuron<br>XXXX<br>No<br>unpublished | Y | BASF |