Section A6.9 (02) **Delayed Neurotoxicity**

Annex Point IIA6.9

5. APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

Groups of 30 time-mated Alpk:APfSD (Wistar-derived) rats were given diets containing 0, 25, 60 or 150 ppm lambda-cyhalothrin from day 7 of pregnancy through parturition and lactation to day 23 post partum. On days 10 and 17 of pregnancy, dams were subjected to a functional observation battery of tests outside the cage including assessment of signs of autonomic function e.g. lachrymation, ptosis, papillary function, exophthalmus, salivation, piloerection, urination and defecation. Any convulsions, tremors or abnormal behaviours or movements, posture or gait were noted.
Litters were examined after completion of parturition, and on days 1 and 5, sex, weight and clinical condition each pup was recorded. Litters were culled to 8 pups on day 5. Offspring were separated from the dam on day 29 post partum, caged in fours by sex and maintained to 63 days of age. The F1 animals were not given test diet after separation from the dam. F1 animals were examined to determine the day of either vaginal opening or preputial separation. Animals were supplied with environmental enrichment items (including paper, and „fun tunnels").

Offspring were assessed using the same functional observation battery as for their dams on days 5, 12, 22, 36, 46 and 61 post partum. On days 14, 18, 22 and 60, selected offspring were also assessed for effects on motor activity, on days 23 and 61 for response to auditory startle, assessment of learning and memory (Y-shaped swimming maze) on either days 21 or 59, and retested 3 days later. At termination, animals were subject to gross necropsy and neuropathological evaluation including morphometry and brain weights. On day 12 post partum and at termination on day 63, ten animals per sex per group were killed by over-exposure to carbon dioxide and the brain weighed after fixation (to prevent damage). On day 63 a further ten rats/sex/group were perfused with formol saline, and various neural tissues taken and preserved, including brain, eye, spinal cord, spinal nerve roots, root ganglia, sciatic and tibial nerves. The brains from control and high dose level were then processed and examined by light microscopy.

X

Section A6.9 (02) **Delayed Neurotoxicity**

Annex Point IIA6.9

5.2	**Results and discussion**	Test material in the diet was shown to be homogenous, and stable for up to 29 days. Mean maternal food intake during gestation at 25, 60 or 150 ppm was 2.1, 4.9 or 11.4 mg/kg bw/day. Post partum equivalents were 4.6, 10.7 or 26.3 mg/kg bw/day. The report assumes that all post partum food was consumed by the dam.	
		Maternal bodyweight and food intake was lower than controls at 60 and 150 ppm. Pup survival and mean pup weight were slightly lower at 150 ppm, but there were no other adverse effects, on duration of gestation, parturition, and numbers and type of macroscopically abnormal offspring. There were no treatment-related effects on clinical observations, gross neurological and behavioural abnormalities or adverse effects on motor activity, response to auditory startle, assessment of learning and memory as either young pups (age 21-24 days) or young adults (age 59-62 days).	X9 X10 X11 X12
		Day 21 swimming speeds of females at 150 ppm were slightly lower than controls, although this was considered to reflect a difference in swimming performance rather than an effect on learning or memory.	X13
		Maternal treatment at 150 ppm was associated with slightly lower group mean bodyweights of the F1 animals in the post-lactation period. There were no adverse effects on the neuropathological evaluation including morphometry and brain weights.	X14
5.3	**Conclusion**	Maternal treatment with up to 150 ppm lambda-cyhalothrin produced no evidence of developmental neurotoxicity in F1 animals. The NOEL for developmental neurotoxicity is >150 ppm (11.4 mg/kg bw/day), and the NOEL for maternal toxicity is 25 ppm (2.1 mg/kg bw/day), as a consequence of lower maternal bodyweight gain and food intake during pregnancy at 150 ppm and to a lesser extent also at 60 ppm.	
5.3.1	LOAEL	Lower maternal bodyweight gain and food intake during pregnancy at 150 ppm and to a lesser extent also at 60 ppm. Pup survival and mean pup weight slightly lower at 150 ppm	
5.3.2	NOAEL	NOEL for developmental neurotoxicity >150 ppm (11.4 mg/kg bw/day) NOEL for maternal toxicity 25 ppm (2.1 mg/kg bw/day), LEL: Maternal: 600 ppm; Developmental >150 ppm	
5.3.3	Reliability	1	
5.3.4	Deficiencies	No	

Borttaget: September

Borttaget: 0

Section A6.9 (02) Delayed Neurotoxicity

Annex Point IIA6.9

	Evaluation by Competent Authorities
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	April 2007
Materials and Methods	[redacted]
Results and discussion	[redacted]

Borttaget: September

Borttaget: 0

Section A6.9 (02) Delayed Neurotoxicity

Annex Point IIA6.9

[redacted]

Section A6.9 (02) **Delayed Neurotoxicity**

Annex Point IIA6.9

[redacted]

[redacted]			

[redacted]

Conclusion

[redacted]

Reliability

Borttaget: September

Borttaget: 0

Section A6.9 (02) Delayed Neurotoxicity

Annex Point IIA6.9

Acceptability	[redacted]
Remarks	[redacted]

6. MECHANISTIC DATA

98/8 Doc IIIA section No. 6.10	Mechanistic study	Official use only
Section 6.10 Annex Point IIA 6.10	**Mechanistic study**	Official use only
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	
Other existing data [ ]	Technically not feasible [ ] Scientifically unjustified [X]	
Limited exposure [ ]	Other justification [ ]	
Detailed justification:	[redacted]	

	Evaluation by Competent Authorities
98/8 Doc IIIA Section No. 6.10	Mechanistic study
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	April 2007
Conclusion	[redacted]

[redacted]

7. STUDIES ON OTHER ROUTES OF ADMINISTRATION

98/8 Doc IIIA section No. 6.11	Other routes of administration	Official use only
Section 6.11 Annex Point IIA 6.6.5	**Other routes of administration**	Official use only
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	
Other existing data [ ]	Technically not feasible [ ] Scientifically unjustified [X]	
Limited exposure [ ]	Other justification [ ]	
Detailed justification:	[redacted]	

	Evaluation by Competent Authorities
98/8 Doc IIIA Section No. 6.11	Other routes of adminstration
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	April 2007
Results and discussion	
Conclusion	[redacted]

8. MEDICAL DATA IN ANONYMOUS FORM

98/8 Doc IIIA section No.	6.12.1	Medical surveillance data on manufacturing plant personnel if available.	Official use only
91/414 Annex Point addressed	II 5.9.1	Medical Surveillance data on manufacturing plant personnel	
		A computer database of adverse reactions to chemicals is maintained within Stewardship and Safety department at Syngenta, Fernhurst. This records formal reports of clinical symptoms arising from chemical exposure at [redacted] This database contains information from 1983 to the present and includes field trials workers. This system is currently being extended to provide coverage of manufacturing and formulation operations world-wide. Cases of subjective facial sensation (also known as 'SFS' or paraesthesia) have occurred at all stages of *lambda*-cyhalothrin handling, from small-scale laboratory work to commercial synthesis and formulation operations. Subjective facial sensation is a collection of skin-associated symptoms, including itching, tingling, burning, cold or numbness due to skin contact with *lambda*-cyhalothrin. The face is most commonly affected. These symptoms can cause discomfort and may in some individuals last for up to 24 hours after exposure. Recovery is apparently complete and there is no evidence of lasting damage. The production plant design aims to contain, as far as is possible, chemical exposure by use of total or partial enclosure. Suitable PPE is worn by operators where there is potential for skin exposure. The results from the database reveal 223 cases of subjective facial sensation from *lambda*-cyhalothrin, 30 of these were associated with eye irritation and 6 with headaches. Investigations of these reports indicate that the majority are caused during plant breakdown, maintenance work or failure of the individual to wear the appropriate protective clothing. Reports are individually investigated by the site.	

98/8 Doc IIIA section No.	**6.12.1**	**Medical surveillance data on manufacturing plant personnel if available.**	**Official use only**
91/414 Annex Point addressed	**II 5.9.1**	Medical Surveillance data on manufacturing plant personnel	
		These investigations have led to many modifications to plant operating procedures, protective equipment worn and plant cleaning which have all improved hygiene standards and reduced operator exposure. As only a very small amount of skin contamination with the active ingredient can lead to the development of subjective facial sensation, monitoring of these reports is a very sensitive indicator of general plant hygiene. During the last few years the general trend has been a reduction in reporting which would indicate improvements in plant hygiene overall. When cases now occur rapid investigation ensures that the cause is identified and a solution found.	

	Evaluation by Competent Authorities
98/8 Doc IIIA Section No. 6.12.1	Medical surveillance data on manufacturing plant personnel if available.
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	April 2007
Conclusion	[redacted]
Remark	[redacted]

98/8 Doc IIIA section No.	6.12.2	Direct observation e.g. clinical cases, poisoning incidents if available	Official use only
91/414 Annex Point addressed	II 5.9.2	Direct observations, e.g.: clinical cases and poisoning incidents	
		No cases of poisoning have been reported from use and application of *lambda*-cyhalothrin. Cases of subjective facial sensation (also known as 'SFS' or paraesthesia) have occurred at all stages of *lambda*-cyhalothrin handling, from small-scale laboratory work to commercial synthesis and formulation operations. Subjective facial sensation is a collection of skin-associated symptoms, including itching, tingling, burning, cold or numbness due to skin contact with *lambda*-cyhalothrin. The face is most commonly affected. These symptoms can cause discomfort and may in some individuals last for up to 24 hours after exposure. Recovery is apparently complete and there is no evidence of lasting damage. The production plant design aims to contain, as far as is possible, chemical exposure by use of total or partial enclosure. Suitable PPE is worn by operators where there is potential for skin exposure. The results from the database reveal 223 cases of subjective facial sensation from *lambda*-cyhalothrin, 30 of these were associated with eye irritation and 6 with headaches. Investigations of these reports indicate that the majority are caused during plant breakdown, maintenance work or failure of the individual to wear the appropriate protective clothing. Reports are individually investigated by the site. During the last few years the general trend has been a reduction in reporting which would indicate improvements in plant hygiene overall. When cases now occur rapid investigation ensures that the cause is identified and a solution found.	

	Evaluation by Competent Authorities
98/8 Doc IIIA Section No. 6.12.2	Direct observation e.g. clinical cases, poisoning incidents if available
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	April 2007
Conclusion	[redacted]
Remark	[redacted]

98/8 Doc IIIA section No.	6.12.3	Health records, both from industry and other available sources	Official use only
91/414 Annex Point addressed	No corresponding Annex point		
		No cases of poisoning have been reported from use and application of *lambda*-cyhalothrin. Cases of subjective facial sensation (also known as 'SFS' or paraesthesia) have occurred at all stages of *lambda*-cyhalothrin handling, from small-scale laboratory work to commercial synthesis and formulation operations. Subjective facial sensation is a collection of skin-associated symptoms, including itching, tingling, burning, cold or numbness due to skin contact with *lambda*-cyhalothrin. The face is most commonly affected. These symptoms can cause discomfort and may in some individuals last for up to 24 hours after exposure. Recovery is apparently complete and there is no evidence of lasting damage. The production plant design aims to contain, as far as is possible, chemical exposure by use of total or partial enclosure. Suitable PPE is worn by operators where there is potential for skin exposure. The results from the database reveal 223 cases of subjective facial sensation from *lambda*-cyhalothrin, 30 of these were associated with eye irritation and 6 with headaches. Investigations of these reports indicate that the majority are caused during plant breakdown, maintenance work or failure of the individual to wear the appropriate protective clothing. Reports are individually investigated by the site. During the last few years the general trend has been a reduction in reporting which would indicate improvements in plant hygiene overall. When cases now occur rapid investigation ensures that the cause is identified and a solution found.	

	Evaluation by Competent Authorities
98/8 Doc IIIA Section No. 6.12.3	Health records, both from industry and other available sources
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	April 2007
Conclusion	[redacted]
Remark	[redacted]

98/8 Doc IIIA section No.	6.12.4	Epidemiological studies on the general population, if available.	Official use only
91/414 Annex Point addressed	II 5.9.3	Observations on exposure of the general population and epidemiological studies if appropriate	
		No epidemiological study has been performed by the company. The public literature since 1990 does not report on investigations indicating health effects on the general population due to exposure to *lambda*-cyhalothrin.	

	Evaluation by Competent Authorities
98/8 Doc IIIA Section No. 6.12.3	Health records, both from industry and other available sources
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	April 2007
Conclusion	[redacted]

98/8 Doc IIIA section No.	6.12.5	Diagnosis of poisoning including specific signs of poisoning and clinical tests, if available	Official use only
91/414 Annex Point addressed	**II 5.9.4**	Diagnosis of poisoning (determination of active substance, metabolites) including specific signs of poisoning and clinical tests, if available	
		Cases of subjective facial sensation (also known as 'SFS' or paraesthesia) have occurred at all stages of lambda-cyhalothrin handling, from small-scale laboratory work to commercial synthesis and formulation operations. Subjective facial sensation is a collection of skin-associated symptoms, including itching, tingling, burning, cold or numbness due to skin contact with lambda-cyhalothrin. The face is most commonly affected. These symptoms can cause discomfort and may in some individuals last for up to 24 hours after exposure. Recovery is apparently complete and there is no evidence of lasting damage. There are no reported cases of systemic poisoning. The most likely route of exposure is from skin contact, and the consequences of this are well documented. No reports have been found, either in the scientific literature or in Company records, on poisoning associated with *lambda*-cyhalothrin. Signs and symptoms of systemic poisoning are therefore described by analogy with other pyrethroids for which information is available (He F, Wang S, Liu L, Chen S, Zhang Z, Sun J, 1989; Poulos L, Athanaselis S, Loutyselinis A 1982). The following signs and symptoms have been described following poisoning incidents with several other pyrethroids and are presented here as possible effects in the eventuality that a poisoning incident occurred with *lambda*-cyhalothrin. Following ingestion of pyrethroids, numbness of the lips and tongue can occur, followed by epigastric pain, nausea, vomiting and diarrhoea. Systemic effects can include dizziness, headache, fatigue, weakness, increased stomal secretion, palpitations, blurred vision, increased sweating and low grade pyrexia. In severe cases there may be loss of consciousness, coarse muscular fasciculations, convulsions, pulmonary oedema and cardiorespiratory failure. There are no specific symptoms indicative of pyrethroid poisoning.	

Lambda-cyhalothrin is a synthetic α-cyano pyrethroid insecticide. Pyrethroids are nervous system stimulants, especially on sensorial nerves and toxicity in mammals, including man, is generally low. Because of its poor solubility in water, liquid formulations of *lambda*-cyhalothrin are usually hydrocarbon solvent-based. These solvents may account for more effects than the active ingredient itself. Depending on the formulation, skin or eye irritancy may occur, as with other pyrethroids.. Nose and throat irritation, sometimes associated with coughing or sneezing have been described by spray operators.

Diagnosis of acute pyrethroid poisoning should be made on the basis of verified exposure within 2 days before onset, corresponding symptoms and reasonable exclusion of other diseases. The following criteria have been proposed for occupational acute pyrethroid poisoning, graded by severity, based on findings with pyrethroids other than *lambda*-cyhalothrin.

Suspicious cases: Abnormal facial sensation (paraesthesia), miliary papules or contact dermatitis, no significant systemic symptoms

Mild acute poisoning: In addition to above mentioned skin symptoms: systemic symptoms, e.g. dizziness, headache, nausea, anorexia, fatigue.

Moderate acute poisoning: Aggravation of above mentioned systemic symptoms, occurrence of disturbance of consciousness, or muscular fasciculations in limbs.

Severe acute poisoning: In addition to above mentioned systemic symptoms, convulsions, coma or pulmonary oedema.

Ultimately, diagnosis can only be confirmed by measurement of pyrethroids or, more likely, their metabolites in body fluids or secreta.

For lambda-cyhalothrin, analytical methods have been established for the three major metabolites :

trifluoro-methylchloro-vinylcyclopropyl carboxylic acid (also known as TFMCVA, or Compound Ia);

3-ph noxybenzoic acid (also known as 3-PBA, or Compound V); and 4-hydroxy-3-phenoxybenzoic acid (also known as 4-OH-3PBA, or Compound XIII).

These involve simultaneous measurement of the metabolites by gas chromatography-mass spectrometry with a limit of quantitative determination of 0.01 µg/ml.

98/8 Doc IIIA section No.	6.12.6	Sensitization/allergenicity observations, if available	Official use only
91/414 Annex Point addressed	No corresponding Annex point		

	No cases of poisoning have been reported to the company: No reports from the open medical literature are on record. Refer to information presented in 6.10.1 on subjective facial sensation.	

	Evaluation by Competent Authorities
98/8 Doc IIIA Section No. 6.12.5 Section No. 6.12.6	Diagnosis of poisoning including specific signs of poisoning and clinical tests, if available Sensitization/allergenicity observations, if available
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	April 2007
Conclusion	[redacted].
Remark	[redacted]

98/8 Doc IIIA section No.	6.12.7	Specific treatment in case of accident or poisoning; first aid measures, antidotes and medical treatment, if known.	Official use only
91/414 Annex Point addressed	II 5.9.5	Proposed treatment: first aid measures, antidotes, medical treatment	
		First Aid Terminate exposure and then remove person from scene of spillage or other contamination. Following eye contact: Rinse thoroughly with running water for 10-15 mins and cover with a sterile pad. Seek medical advice. Following skin contact: Remove contaminated clothing immediately and wash affected parts of the skin thoroughly with soap and water. Clean all contaminated clothing before re-use. Following ingestion: Do not induce vomiting if the formulation is hydrocarbon solvent- based, or if the patient is unconscious, or if the formulation is either not acutely toxic or a dose unlikely to be fatal has been ingested, or if medical assistance is readily available. Induce vomiting if the formulation is acutely toxic and medical assistance is not readily available (unless contraindicated as above). **Further Treatment** Solvent-based formulations: If the amount of chemical is judged to be less than a potentially lethal dose, observe the patient and employ general supportive measures only. If gastric lavage is considered necessary prevent aspiration. Administer activated charcoal and a laxative. For other formulations: Perform gastric lavage. Administer activated charcoal and a laxative. General supportive measures: Give oxygen if the patient is cyanosed or in respiratory distress. Suction and positive-pressure ventilatory equipment should be readily available. Avoid the use of respiratory depressants unless otherwise indicated, e.g.barbiturates, opiates. If fits occur, use anticonvulsants. Monitor and maintain fluid and electrolyte balance. Treatment of paraesthesia: It has been advocated that the use of vitamin E-containing creams or oils alleviates the symptoms of paraesthesia. However, there is no conclusive evidence that such treatment is effective. In most people, symptoms will be mild and in all cases they will subside spontaneously, generally within 24 hours.	

98/8 Doc IIIA section No.	6.12.8	Prognosis following poisoning	Official use only
91/414 Annex Point addressed	II 5.9.6	Expected effects of poisoning Human case report	

	Prognosis There is no specific antidote available for pyrethroid poisoning. The following proposed treatment is general to all pyrethoids. Unless a fatal dose has been ingested, the prognosis of acute pyrethroid poisoning is generally favourable. For the 100g/L *lambda*-cyhalothrin formulation the median lethal dose for a 70 kg man would be estimated to be around 25 ml (by extrapolation from animal data). In a review of 573 cases of acute pyrethroid poisoning (mainly deltamethrin, fenvalerate and cypermethrin), He F, Wang S, Liu L, Chen S, Zhang Z, Sun J, (1989), found complete recovery in the vast majority of cases within 1-6 days of hospital admission. There were only 7 fatal outcomes in the reviewed cases, one of which was due to inappropriate treatment with atropine and another involving a pyrethroid-organophosphate mixture. 15 cases were followed up and no long-standing or residual symptoms were found.	

	Evaluation by Competent Authorities
98/8 Doc IIIA Section No. 6.12.7 Section No. 6.12.8	Specific treatment in case of accident or poisoning; first aid measures, antidotes and medical treatment, if known. Prognosis following poisoning
Date	**EVALUATION BY RAPPORTEUR MEMBER STATE** April 2007
Conclusion	[redacted]

98/8 Doc IIIA section No.	6.12.9	Other data provided by the Notifier	Official use only
91/414 Annex Point addressed	**No corresponding Annex point**		

WORKER EXPERIENCE/ SURVEILLANCE DURING MANUFACTURE, FORMULATION, FILLING AND PACKING	PRODUCTION OUTLINE **Synthesis:** *Lambda*-cyhalothrin is currently synthesised at the [redacted]. Thirty workers are involved working on a twelve hour shift system. [redacted]

:	worldwide. The recent tonnages produced are around X *(this information has been moved to the confidential section by the RMS)* per year (crop Protection use). **Formulation:** The active ingredient is formulated into a wide range of solid and liquid formulations handled at many locations worldwide. Approximately one hundred workers are involved in formulation of the active ingredient, filling and packing into sales packs.	
	CONTROL STRATEGY The principles of good occupational hygiene practice set a clear hierarchy of control which places primacy to removing the hazard or controlling it by engineering or procedural means, before the use of personal protective equipment (PPE) and respiratory protective equipment (RPE). This hierarchy of control is clearly followed in Syngenta and includes consideration of aspects such as design and construction of the plant, the cleanliness of the workplace and equipment, working practices and personal hygiene. For exposure to any substance which can be hazardous by ingestion, absorption or inhalation control must be to a standard that eliminates any health effects. **Ingestion:** Eating and drinking are forbidden in areas where chemical handling takes place. **Skin contact:** The plant design aims to contain, as far as is possible, chemical exposure by use of total or partial enclosure. Suitable PPE is worn by operators where there is potential for skin exposure. In vitro studies with human epidermis indicate a low intrinsic permeability to *lambda*-cyhalothrin: the material was very poorly absorbed (<1% at 24 hours) though a large proportion of the applied dose did remain with the skin after washing. Cases of subjective facial sensation (also known as 'SFS' or paraesthesia) have occurred at all stages of *lambda*-cyhalothrin handling, from small-scale laboratory work to commercial synthesis and formulation operations. Subjective facial sensation is a collection of skin-associated symptoms, including itching, tingling, burning, cold or numbness due to skin contact with *lambda*-cyhalothrin. The face is most commonly affected. These symptoms can cause discomfort and may in some individuals last for up to 24 hours after exposure. Recovery is apparently complete and there is no evidence of lasting damage.	

	Inhalation: The plant design aims to contain chemical exposure, as far as is possible, by use of total or partial enclosure and appropriate extraction systems. The plant is designed using the Occupational Exposure Standards (OES) (see below). The material is practically non-volatile according to data sheet classification (i.e. 1.5 x 10^{-9} mm Hg at 20°C, Henry's Law Constant 2 x 10^{-2} Pa m^3/mol).	
	ATMOSPHERIC EXPOSURE STANDARD Occupational Exposure Standards are used in pesticide manufacture as a means of monitoring and controlling atmospheric exposure to chemicals during active ingredient synthesis and formulation. These standards are set by the Syngenta Occupational Exposure Standards Panel as a primary mechanism of control. These are acceptable concentrations in work-place air based on available toxicology data with the application of a suitable safety factor when making the extrapolation from animal data to a human standard. The Occupational Exposure Panel consists of the Principal Medical Officer (an occupational physician), the Business Occupational Hygienist and the Occupational Toxicology Manager. The panel considers the toxicology data available from the package of registration studies together with worker experience during the research, development and commercial manufacturing operations. The standard value is kept under review and may be amended in the light of significant new toxicology or hygiene information. The current OES value for *lambda*-cyhalothrin is 0.04 mg/m^3 for an 8-hour time weighted average (TWA) exposure. This value is based on the no-observed adverse effect level (NOAEL) in the 1 year feeding study in dogs of 0.5 mg/kg/day assuming a body weight of 70 kg for an adult worker and a shift inhalation volume of 10 m^3.	X1 X2
	HYGIENE MONITORING As highlighted above in Control Strategy, the aim is to achieve containment by engineering or procedural means. Hygiene monitoring is used as a method of assessing the success of control measures and also for highlighting specific problem areas if particular pieces of equipment are leading to loss of containment. The need for atmospheric monitoring is decided by the site hygienist and will usually be identified as part of an annual site programme of work. The need for additional monitoring	

	may be determined by a walk-through survey or formal risk assessment but may be prompted by changes in standards, complaints from the workforce, or evidence of adverse effects in the workplace. A monitoring campaign would usually include personal samples i.e. the use of pumps attached to individuals for a specific time period or full shift to give operator exposure data, and static samples i.e. pumps placed at particular points of interest within the plant to give data on the performance of control systems, again for a measured time period. The samples obtained are then analysed and the results adjusted to establish the exposure expected over an 8-hour working period i.e. the Time Weighted Average (TWA). The aim is to show acceptable workplace conditions by demonstrating more than 90% of exposure limits within the published occupational exposure standard. This requires at least 10 and preferably 20 measurements under normal working conditions to prove acceptability. An example of hygiene monitoring data carried out at our Yalding plant is shown in tabular form below: As can be seen 99% of fixed readings and 100% of personal readings are recorded as being less than the occupational exposure standard which indicates good compliance and verifies minimal exposure of the workforce. Additional monitoring for *lambda*-cyhalothrin is carried out in the form of 'wipe-testing' of contaminated surfaces. This is a semi-quantitative way of assessing plant cleanliness and consists of analysis of swabs taken over a specific surface area at various points in the plant. The use of this test has been most helpful in assessing plant cleanliness prior to maintenance work. Positive swab tests have allowed further cleaning to be carried out thus reducing the possibility of operator exposure. In addition the test has been used following routine plant cleaning to assess adequacy and to highlight areas of contamination. This has led to rewriting of clean-down procedures and general improvement in plant hygiene.	

	BIOLOGICAL MONITORING Analytical procedures have been established for measurement of *lambda*-cyhalothrin concentrations in human body fluids during human volunteer studies. The techniques are technologically demanding and do not provide a cost-effective method for routine worker surveillance. As a general principle in good occupational health practice biological monitoring is seen as the last resort within the hierarchy of control. In addition it is necessary to demonstrate an adverse effect within the individual which would be prevented by maintaining levels below a certain limit. This is not the case with *lambda*-cyhalothrin and this form of health monitoring is therefore not used.	

Data for hygiene monitoring carried out at Yalding plant

Measured Levels (mg/m^3) for 8hr -TWA	<0.004	<0.01	<0.02	<0.04	Mean
Fixed	73%	78%	95%	99%	0.006
Personal	30%	83%	100%	100%	0.005

	Evaluation by Competent Authorities
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	April 2007
Conclusion	[redacted]
Remarks	[redacted]

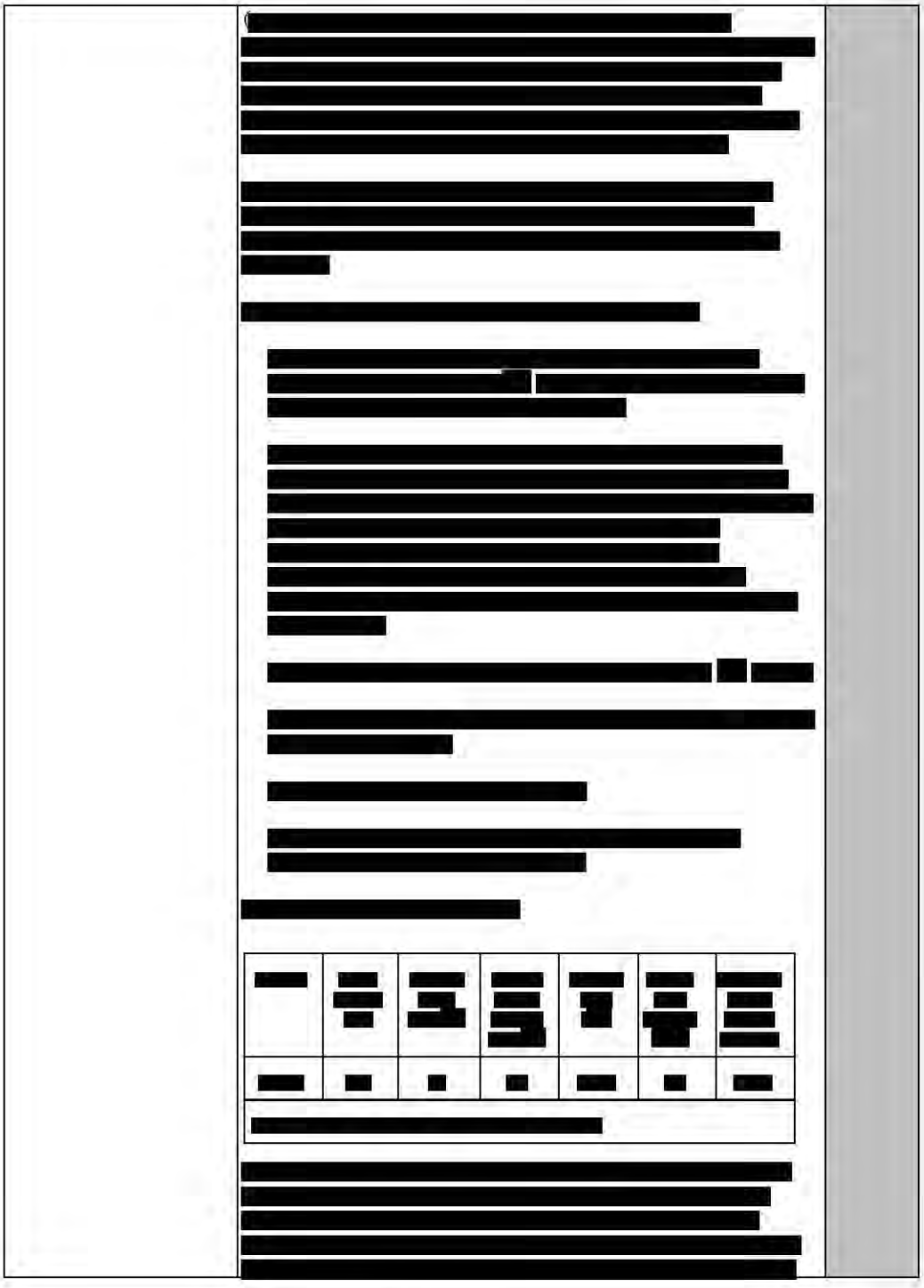
98/8 Doc IIIA section No.	**6.13**	**Toxic effects on livestock and pets**	**Official use only**
91/414 Annex Point addressed	**NA**		

Section 6.13 Annex Point IIA 6.13	**Toxic effects on livestock and pets**		**Official use only**
	JUSTIFICATION FOR NON-SUBMISSION OF DATA		
Other existing data [ ]	**Technically not feasible** [ ]	**Scientifically unjustified** [ ]	

Section 6.13 Annex Point IIA 6.13	**Toxic effects on livestock and pets**	Official use only
Limited exposure [X]	Other justification [ ]	
Detailed justification:	[redacted]	

Borttaget: September

Borttaget: 0



Borttaget: September

Borttaget: 0

	[redacted]	X1

	Evaluation by Competent Authorities
98/8 Doc IIIA Section No. 6.12.13	Toxic effects on livestock and pets
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	April 2007
Discussion	[redacted]
Conclusion	[redacted]

Borttaget: The data requirement is fulfilled.

98/8 Doc IIIA section No.	6.14	Other tests related to the exposure of humans

Section 6.14 Annex Point IIA 6.14	Other tests related to the exposure of humans	Official use only
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	
Other existing data [ ]	Technically not feasible [ ] Scientifically unjustified [ ]	
Limited exposure [ ]	Other justification [X]	
Detailed justification:	[redacted]	

	Evaluation by Competent Authorities
98/8 Doc IIIA Section No. 6.12.13	Other tests related to the exposure of humans
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	June 2007
Results and discussion	[redacted]
Conclusion	[redacted]

98/8 Doc IIIA section No.	6.15	Food and feedingstuffs	Official use only

Section 6.15 Annex Point IIA 6.15	Food and feedingstuffs	Official use only
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	
Other existing data [ ]	Technically not feasible [ ] Scientifically unjustified [ ]	

Borttaget: September

Borttaget: 0

Section 6.15 Annex Point IIA 6.15	**Food and feedingstuffs**	Official use only
Limited exposure [ ]	Other justification [X]	
Detailed justification:	[redacted]	

	Evaluation by Competent Authorities
98/8 Doc IIIA Section No. 6.12.15	Food and feedingstuffs
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	June 2007
Discussion	[redacted]
Conclusion	[redacted]

98/8 Doc IIIA section No. 6.16	Other tests related to the exposure of humans in the products	Official use only

Section 6.16 Annex Point IIA 6.16	Other tests related to the exposure of humans in the products	Official use only
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	
Other existing data [ ]	Technically not feasible [ ] Scientifically unjustified [ ]	
Limited exposure [ ]	Other justification [X]	
Detailed justification:	[redacted]	

	Evaluation by Competent Authorities
98/8 Doc IIIA Section No. 6.12.16	Other tests related to the exposure of humans in the products
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	June 2007
Conclusion	[redacted]

98/8 Doc IIIA section No. 6.17	Effects of metabolites from treated plants	Official use only
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	
Other existing data [ ]	Technically not feasible [ ] Scientifically unjustified [ ]	

98/8 Doc IIIA section No.	6.17	Effects of metabolites from treated plants	Official use only
Limited exposure [ ]		Other justification [X]	
Detailed justification:		[redacted]	

	Evaluation by Competent Authorities
98/8 Doc IIIA Section No. 6.12.17	Effects of metabolites from treated plants
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	June 2007
Conclusion	[redacted]

98/8 Doc IIIA section No.	6.18	Summary of mammalian toxicology and conclusions (refer to IIA)	Official use only

CONCLUSIONS, MAMMALIAN TOXICOLOGY

An acceptable daily intake is not strictly valid for a biocide insecticide, used in and around buildings, as there is no potential to contaminate food, feedingstuffs or livestock.

The acceptable daily intake (ADI) for humans is normally derived from the NO(A)EL in the most susceptible species in long-term toxicity studies, and an appropriate safety factor.

Considering all available long-term toxicity data, summarised below, the no observed effect level which best meets the criteria to calculate an acceptable daily intake is the NOEL of 0.05 mg/kg bw/day from the one year dog study.

Species	Study	NO(A)EL (mg/kg bw/day)
Rat	2-year oral toxicity & carcinogenicity	50 ppm (= 2.5 mg/kg bw/day)*
Mouse	2-year oral carcinogenicity	20 ppm (= 1.9 mg/kg bw/day)*
Dog	6-month oral toxicity	NOAEL 2.5 mg/kg bw/day*
Dog	12-month oral toxicity	NOEL 0.5 mg/kg bw/day
Rat	3-generation oral reproduction	30 ppm (= 2 mg/kg bw/day)*

*Study on cyhalothrin

Lambda-cyhalothrin is not carcinogenic mutagenic or toxic to reproduction. Accordingly, a safety factor (SF) of 100 is appropriate. The ADI for humans is calculated as follows:

$$ADI = \frac{NOAEL_{2-generationrat}}{SF} = \frac{0.5mg/kgbw/day}{100} = \underline{\underline{0.005mg/kgbw/day}}$$

The ADI for *lambda*-cyhalothrin has been set by the EU at 0.005 mg/kg bw/day based upon the NOAEL value of 0.5 mg/kg bw/day from the 1 year dog study and the application of a 100 fold safety factor.

ACCEPTABLE OPERATOR EXPOSURE LEVEL (AOEL)

The AOEL is defined on the basis of short-term toxicity studies and the application of an appropriate safety factor. The use of short-term studies of up to 13 weeks duration for operator risk assessment is appropriate but conservative. Results of the applicable short-term toxicity studies are summarized below.

Species	Study	Lowest NO(A)EL (mg/kg bw/day)
Rat	**90-day dietary toxicity**	50 ppm (approx 3 mg/kg bw/day)*
Rat	90-day dietary toxicity*	50 ppm (approx 3 mg/kg bw/day)
Dog	6-week capsule toxicity*	
Dog	26-week capsule toxicity*	2.5 mg/kg bw/day*
Dog	52-week capsule toxicity	0.5 mg/kg bw/day
Rat	Oral embryotoxicity study*	10 mg/kg bw/day (maternal)*
Rat	Developmental neurotoxicity study	2.1 mg/kg bw/day (maternal)
Rabbit	Oral embryotoxicity study*	10 mg/kg bw/day (maternal)*

The $AOEL_{systemic}$ for *lambda*-cyhalothrin has been set by the EU at 0.0025 mg/kg bw/day based upon the NOAEL value of 0.5 mg/kg bw/day from the 1 year dog study, the assumption of 50% oral absorption and the application of a 100 fold safety factor.

PARAMETRIC VALUE FOR DRINKING WATER

On the basis that exposure through drinking water should not account for more than 10% of the ADI, and assuming an average consumption of 2 litres of water per person per day and a bodyweight of 60 kg, a Parametric Value for drinking water of 0.015 mg/l is proposed for *lambda*-cyhalothrin.

The parametric value is calculated as:

$$\frac{ADI \times 0.1 \times 60}{2} = 0.015$$

In practice, on the basis of the data on the fate of *lambda*-cyhalothrin in the environment, it is unlikely that *lambda*-cyhalothrin will be present in water abstracted for drinking water following normal use of the insecticide.

	Evaluation by Competent Authorities
	Conclusions
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	March 2008
Conclusion	[redacted]

Competent Authority Report
According to Directive 98/8/EC

lambda-Cyhalothrin

CAS 91465-08-6
Active substance in Biocidal Products, Product Type 18 (Insecticide)

Notifier: Syngenta European Center

DOCUMENT III-A

Section 7.1-7.3: Environmental Fate and Behaviour

Rapporteur Member State: Sweden

Final CAR, September 2010

Borttaget: Draft

KEMI
Kemikalieinspektionen
Swedish Chemicals Agency

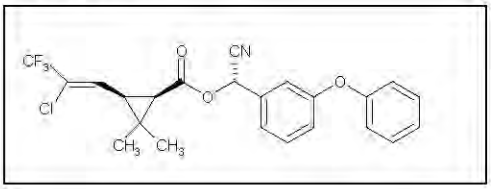
INFORMATION FROM THE RMS:

Format

Lambda-cyhalothrin has previously been evaluated as a plant protection product and was included in the Annex I of the Council Directive of 15 July 1991 concerning placing of plant protection products on the market (91/414/EEC) in 2002. Syngenta has used the possibility to utilise the PPP dossier for the BP dossier preparation in agreement with the EU document "Guidance Document on How to utilize PPP Dossiers/Monographs and Existing Substances (ESR) Dossiers/Risk Assessments for the Preparation of BP dossiers/ CAs' reports" thus study summaries in this dossier does not follow the standard BPD format. The study summaries are from Tier I sections 5 and 6 for Annex II of 91/414/EEC dossier. For studies which were not part of the original PPP-dossier and for studies which were submitted to supplement the original BP-dossier (e.g., at the stage of completeness check) more complete study summaries were provided.

Stereoisomers

Lambda-cyhalothrin (code PP321), α-cyano-3-phenoxybenzyl 3-(2-chloro-3,3,3-trifluoropropenyl)-2,2-dimethylcyclopropanecarboxylate, is a 1:1 mixture of the (Z)-(1R,3R),S-ester and the (Z)-(1S,3S),R-ester:



The molecule "cis, trans-ZE-cyhalothrin" (PP564) contains three asymmetric carbon atoms and a centre for geometrical isomerism about the double bond (either an E or Z configuration). Therefore 2^4 structures (eight enantiomeric pairs) are possible. Eight of these isomers have a cis-configuration about the 1,3-bond of the cyclopropane ring and the other eight a trans-configuration:

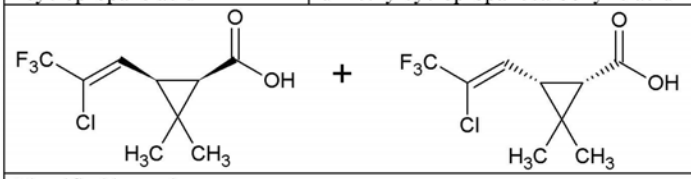
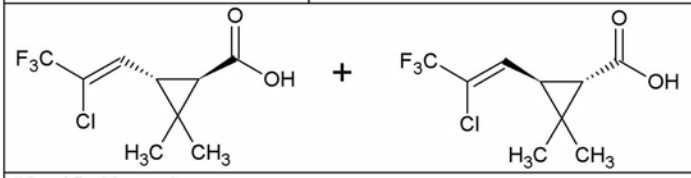
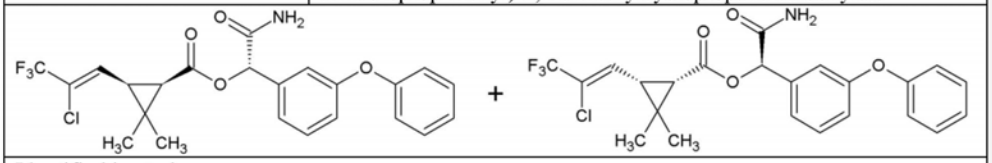
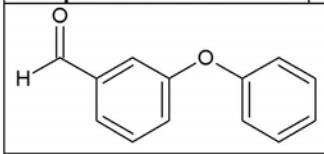
isomers with a cis-configuration about the 1,3-bond of the cyclopropane ring	A'	E(1R,3R,αR) and E(1S,3S,αS) enantiomer pair
	A	Z(1R,3R,αR) and Z(1S,3S,αS) enantiomer pair
	B'	E(1R,3R,αS) and E(1S,3S,αR) enantiomer pair
	B	Z(1R,3R,αS) and Z(1S,3S,αR) enantiomer pair
isomers with a trans-configuration about the 1,3-bond of the cyclopropane ring	C	Z(1R,3S,αR) and Z(1S,3R,αS) enantiomer pair
	C'	E(1R,3S,αR) and E(1S,3R,αS) enantiomer pair
	D	Z(1R,3S,αS) and Z(1S,3R,αR) enantiomer pair
	D'	E(1R,3S,αS) and E(1S,3R,αR) enantiomer pair

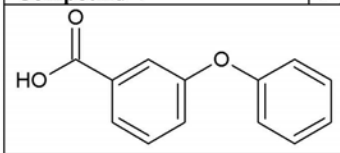
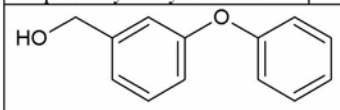
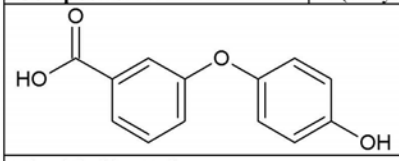
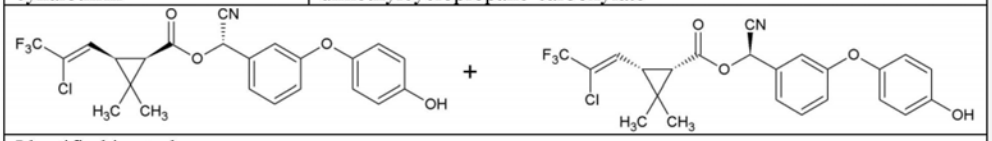
Lambda-cyhalothrin (PP321) consists of the enantiomeric pair cis B.
Cyhalothrin (PP563) consists of the enantiomeric pairs cis A and cis B.

Some of the studies on environmental fate and behaviour and ecotoxicology were conducted on Cyhalothrin, however, in all areas data were also available for *Lambda*-cyhalothrin. The information provided in studies carried out on Cyhalothrin is used as supportive information.

Metabolites and transformation products

The following table provides a overview of the metabolites and transformation products identified in different test systems investigating the degradation of *lambda*-cyhalothrin.

Code, trivial name	**Chemical/trivial name**
Compound Ia "cyclopropane acid"	(1RS)-cis-3-(Z-2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylic acid
	
Identified in study on: Hydrolysis pH 7: 2% at study end day 30, pH 9: 73% at study end day 30 Photolysis in water (pH 5; light simulating Florida autumn sunlight for 31 days): 14% at study end Water/sediment systems (dark, pH 7.2/7.8): max 29%, day 14 Water with aquatic plants (irradiated; pH not stated; large variation in temperature): max 50% at study end day 14 Microcosm with aquatic plants (irradiated; pH 9.8) 40% at study end by day 4 Sandy loam soil (dark, pH 6.7-6.8): max 6.2%, day 30, 6.0% day 90 Field study on silt (pH 6.0) and silty clay loam (pH 6.6): small amounts (max 5.5% day 14)	
Compound Ib *trans*-form of cyclopropane acid	(1RS)-trans-3-(Z-2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylic acid
	
Identified in study on: Photolysis in water (at pH 5, light simulating Florida autumn sunlight for 31 days): <10% at study end Was not always used as reference substance and could potentially have been present but not identified also in other test systems.	
Compound II	(RS)-α-amido-3-phenoxybenzyl (1RS)-cis, trans-3-(Z-2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropane-carboxylate
	
Identified in study on: Photolysis on soil (pH 6.45): ca 5% after 34/35 days irradiated samples; 17-18% 30 days dark controls	
Compound IV	3-phenoxybenzaldehyde
	

Identified in study on: Photolysis in water (at pH 5; light simulating Florida autumn sunlight for 31 days): <10% at study end	
Compound V	3-phenoxybenzoic acid
	
Identified in study on: Photolysis in water (at pH 5; light simulating Florida autumn sunlight for 31 days): 25% at study end Water/sediment systems (dark; pH 7.2/7.8): <1% Field study on silt (pH 6.0) and silty clay loam (pH 6.6): small amounts (max 2.5% day 28)	
Compound VI "3-phenoxybenzyl alcohol"	3-phenoxyphenylmethanol
	
Identified in study on: Water/sediment systems (dark; pH 7.2/7.8): <8%	
Compound VII	3-(4'-hydroxyphenoxy)benzoic acid
	
Identified in study on: Field study on silt (pH 6.0) and silty clay loam (pH 6.6): small amounts (max 1.0% day 124)	
Compound XV Hydroxylated *lambda*-cyhalothrin	(1R) cis α-(S) and (1S) cis α-(R) α-cyano-3-(4-hydroxyphenoxy) benzyl 3 (Z-2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropane-carboxylate
	
Identified in study on: Water/sediment systems (dark; pH 7.2/7.8): max 10.5%, day 14 Sandy loam soil (dark) (at pH 6.7-6.8 max 12.1%, day 60) Field study on silt (pH 6.0) and silty clay loam (pH 6.6): small amounts (max 3.9% day 14)	

98/8 Doc IIIA section No.	**7.1.1.1.1**	**Hydrolysis as a function of pH and identification of breakdown products**
91/414 Annex IIA point addressed	**7.2.1.1**	**Rate of hydrolysis**

		Official use only
Reference point in dossier	**7.1.1.1.1/01**	
Title:	PP321: Hydrolysis in water at pH 5, 7 and 9	
Project/Report number:	RJ0338B	
Author(s):	Collis, W.M.D and Leahey, J.P.	
Date of report:	1984	
Published:	No	
Testing facility:	Jealott's Hill Research Station, Bracknell, Berkshire, UK	
Test substance:	^{14}C-cyclopropane *lambda*-Cyhalothrin (PP321), radiochemical purity ■%	X1
Study dates	July 1983 to September 1983.	
GLP:	Yes	
Reliability indicator	1	

	Official use only
Materials and methods: Hydrolysis studies were carried out on ^{14}C-cyclopropane labelled *lambda*-Cyhalothrin, in the dark, at 25°C, over a period of 30 days and at pH 5, 7 and 9.	X2
Findings: The applied radioactivity did not remain completely in solution at any of the pHs tested. This is not surprising since *lambda*-Cyhalothrin is an extremely hydrophobic compound. It was therefore necessary to extract the aqueous solutions and the glass vessels containing these solutions with dichloromethane in order to recover most of the applied radioactivity.	X3
The results indicated that *lambda*-Cyhalothrin is stable to hydrolysis at pH 5, hydrolyses very slowly at pH 7 and rapidly at pH 9. Since *lambda*-Cyhalothrin does not remain completely in solution in water, it cannot be expected that good kinetic data can be obtained from this experiment. It is possible to make an estimate of the half-life in water, at pH 7 and 9, by linear regression analysis. Using this procedure, the half-lives for *lambda*-Cyhalothrin are 453 days at pH 7 and 7.3 days at pH 9.	X4
At both pH 7 and 9, the cyclopropane acid (Compound Ia) was the major product of hydrolysis (2% at pH 7 and 73% at pH 9). Polar compounds, which remained at the origin of thin layer chromatograms, were also formed, but were always less than 10% of the radioactivity recovered into dichloromethane.	X5

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	Not relevant
Materials and Methods	[redacted]
Results and discussion	[redacted]

	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	[redacted]

98/8 Doc IIIA section No.	**7.1.1.1.2**	**Photo-transformation in water including identity of products of transformation**
91/414 Annex IIA point addressed	**7.2.1.2**	**Direct photo-transformation**

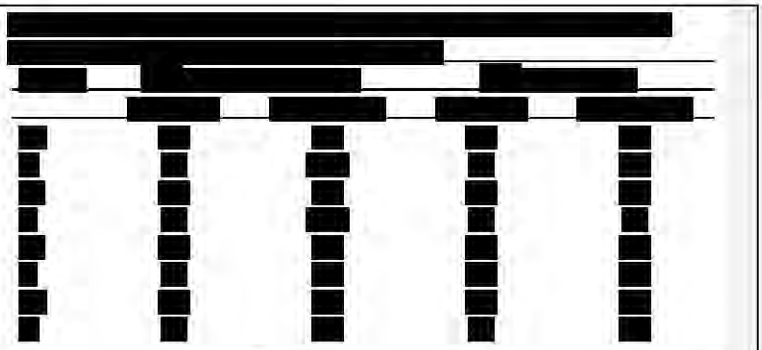
		Official use only
Reference point in dossier:	**7.1.1.1.2/01**	
Title:	PP321: Aqueous photolysis at pH 5	
Project/Report number:	RJ0605B	
Author(s):	Priestley, D.B. and Leahey, J.P.	
Date of report:	1988	
Published:	No	
Testing facility:	Jealott's Hill Research Station, Bracknell, Berkshire, UK	
Test substance:	^{14}C-phenyl and ^{14}C-cyclopropane *lambda*-Cyhalothrin (PP321), radiochemical purity [redacted] for each label.	X1
Study dates:	December 1986 to January 1987	
GLP:	Yes	
Reliability indicator:	1	

	Official use only
Materials and methods: Buffered photolysis test solutions of *lambda*-Cyhalothrin (radiolabelled in either the cyclopropane or the benzyl ring) were continuously irradiated at pH5 and 25°C with a Xenon arc light for a period equivalent to 31 days of natural autumn sunlight at 30°N.	X2
Findings: An average value taken from the data obtained can be used to estimate a half-life for *lambda*-Cyhalothrin at 30°N in autumn, by linear regression analysis and was 24 days. This value can only be an approximation because *lambda*-Cyhalothrin is so hydrophobic that it does not remain totally in solution during the irradiation, and therefore accurate kinetic data cannot be expected. However, measurement of the quantum yield for *lambda*-Cyhalothrin does supply data from which the half-life of *lambda*-Cyhalothrin under European conditions can be calculated. The photo-degradation products were characterised at each sampling interval and a summary of the data after 31 days irradiation is presented in the table below.	X3 X4 X5, X6

Radioactive Residue Compound	Recovery (as % of Applied)	
	Cyclopropane label	Phenyl label
Lambda-Cyhalothrin	37.9	43.6
Compound Ia	13.7	Not detectable using this label
Compound Ib	7.1	Not detectable using this label
Compound IV	Not detectable using this label	5.5
Compound V	Not detectable using this label	25.0
3 Unidentified Compounds	9.2	7.8
$^{14}CO_2$	18.2	1.6
Unidentified Volatilised Radioactivity	3.5	8.1
Unidentified Water Soluble Radioactivity	4.4	2.6

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	Not relevant
Materials and Methods	[redacted]

	followed the recommendations of US EPA guideline 161-2.
Results and discussion	[redacted]

	[redacted]  [redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	[redacted]

		Official use only
Reference point in dossier:	**7.1.1.1.2/02**	
Title:	*Lambda*-Cyhalothrin: environmental half-life and quantum yield for direct photo-transformation in aqueous solution	
Project/Report number:	RJ1617B	
Author(s):	Moffatt, F.	
Date of report:	1994	
Published:	No	
Testing facility:	Jealott's Hill Research Station, Bracknell, Berkshire, UK	
Test substance:	*Lambda*-Cyhalothrin (PP321), purity [redacted]	X1
Study dates:	August 1993 to February 1994	
GLP:	Yes	
Reliability indicator:	1	

	Official use only
Materials and methods: The method of Frank and Klöpffer was used to predict the half-life, by direct photo-degradation, of *lambda*-Cyhalothrin in natural water. This method uses the quantum yield and the extinction coefficients in the region of overlap with sunlight to estimate half-lives in a range of depths of water and at different seasons.	X2 X3
Findings: Quantum yields of 0.094 and 0.090 were obtained from the duplicate measurements. Predicted half-lives for photo-degradation in water were therefore calculated using an average value of 0.092. The half-lives obtained in 5 cm and 30 cm depths of water for the four seasons of the year in mid Europe are listed below.	X4 X5

Season	Half-life in 5 cm depth of water, days.	Half-life in 30 cm depth of water, days.
Spring	3.6	5.8
Summer	1.7	5.3
Autumn	3.3	8.2
Winter	31	75

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	Not relevant
Materials and Methods	[redacted]

	[redacted]
Results and discussion	[redacted]

	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	[redacted]

98/8 Doc IIIA section No.	7.1.1.2.1	Ready biodegradability

JUSTIFICATION FOR NON-SUBMISSION OF DATA		Official use only
Other existing data [X] Limited exposure [ ]	Technically not feasible [ ] Other justification [ ]	Scientifically unjustified [ ]
Detailed justification:	[redacted] 1.	
Undertaking of intended data submission [ ]		
Evaluation by Competent Authorities		
EVALUATION BY RAPPORTEUR MEMBER STATE		
Date	Not relevant	
Evaluation of applicant's justification	[redacted] t.	
Conclusion	[redacted] .	
Remarks		

98/8 Doc IIIA section No.	7.1.1.2.2	Inherent biodegradability, where appropriate

JUSTIFICATION FOR NON-SUBMISSION OF DATA		Official use only
Other existing data [X] Limited exposure [ ]	Technically not feasible [ ] Scientifically unjustified [ ] Other justification [ ]	
Detailed justification:	[redacted]	
Undertaking of intended data submission [ ]		
Evaluation by Competent Authorities		
EVALUATION BY RAPPORTEUR MEMBER STATE		
Date	Not relevant	
Evaluation of applicant's justification	[redacted]	
Conclusion	[redacted]	
Remarks		

98/8 Doc IIIA section No.	7.1.1.2.3	Biodegradation in seawater

	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ] Limited exposure [X]	Technically not feasible [ ] Scientifically unjustified [ ] Other justification [ ]	
Detailed justification:	[redacted]	
Undertaking of intended data submission [ ]		
	Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	Not relevant	
Evaluation of applicant's justification	[redacted]	
Conclusion	[redacted]	
Remarks		

98/8 Doc IIIA section No.	7.1.2.1.1	Aerobic biodegradation

JUSTIFICATION FOR NON-SUBMISSION OF DATA		Official use only
Other existing data [X] Limited exposure [ ]	Technically not feasible [ ] Scientifically unjustified [ ] Other justification [ ]	
Detailed justification:	[redacted]	
Undertaking of intended data submission [ ]		
Evaluation by Competent Authorities		
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	Not relevant	
Evaluation of applicant's justification	[redacted]	
Conclusion	[redacted]	
Remarks		

98/8 Doc IIIA section No.	7.1.2.1.2	Anaerobic biodegradation

	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [X] Limited exposure [ ]	Technically not feasible [ ] Scientifically unjustified [ ] Other justification [ ]	
Detailed justification:	[redacted]	
Undertaking of intended data submission [ ]		
	Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	Not relevant	
Evaluation of applicant's justification	[redacted]	
Conclusion	[redacted]	
Remarks		

98/8 Doc IIIA section No.	7.1.2.2.1	Aerobic aquatic degradation study

JUSTIFICATION FOR NON-SUBMISSION OF DATA		Official use only
Other existing data [X] Limited exposure [ ]	Technically not feasible [ ] Scientifically unjustified [ ] Other justification [ ]	
Detailed justification:	[redacted]	
Undertaking of intended data submission [ ]		
Evaluation by Competent Authorities		
EVALUATION BY RAPPORTEUR MEMBER STATE		
Date	Not relevant	
Evaluation of applicant's justification	[redacted]	
Conclusion	[redacted]	
Remarks		

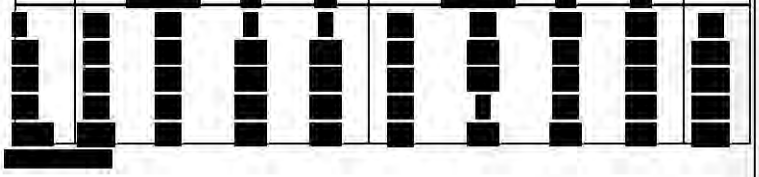
98/8 Doc IIIA section No.	**7.1.2.2.2**	**Water/sediment degradation study**
91/414 Annex IIA point addressed	**7.2.1.3.2**	**Water/sediment study**

		Official use only
Reference point in dossier	**7.1.2.2.2/01**	
Title:	Cyhalothrin : Fate in River Water	
Project/Report number:	RJ0320B	
Author(s):	Hall, J.S. and Leahey, J.P.	
Date of report:	1983	
Published:	No	
Testing facility:	Jealott's Hill Research Station, Bracknell, Berkshire, UK	
Test substance:	^{14}C-cyclopropane Cyhalothrin, radiochemical purity [redacted]	X1
Study dates	July 1982 to May 1983	
GLP:	Yes	
Reliability indicator	1	

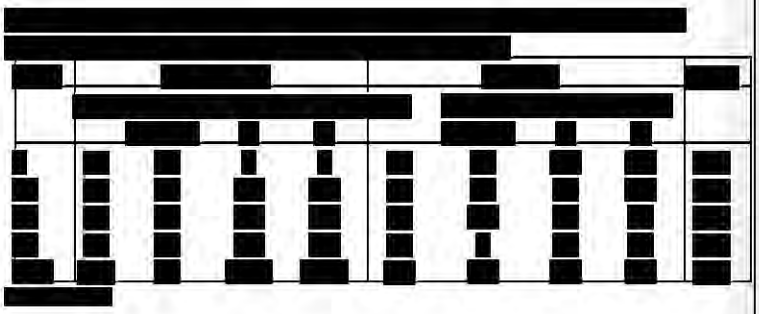
	Official use only
Materials and methods: ^{14}C-cyclopropane labelled Cyhalothrin was applied, at the nominal application rate of 0.9 mg/l, to two natural river water and associated sediment systems and exposed to daylight for up to 32 days. In order to distinguish between photo-degradation and other degradative processes, additional systems were prepared, in which light was totally excluded. The water:sediment test systems were set up in quartz flasks and a flow-through system enabled the trapping and quantification of volatile products. The water in each flask was aerated for 3 minutes each day, to ensure the longevity of the biological activity of the test systems. The sediment types used were Whitewater (pH 8.05, silty soil type) and Pang (pH 7.8, stoney soil type).	X2
Findings: Under dark conditions, degradation of Cyhalothrin was fairly slow (80% unchanged after 32 days), however, when exposed to sunlight, Cyhalothrin degraded more rapidly, with a half-life of approximately 20 days. Significantly, the rate at which the parent compound was lost from the aqueous phase, was much faster than its rate of degradation in the whole water:sediment system. Indeed this result is unsurprising, given the strong adsorption to soil. The primary route of degradation in light of the ^{14}C-cyclopropane-labelled Cyhalothrin proceeded by ester hydrolysis, yielding the corresponding acids (Compound Ia and Ib), which represented up to 47.3% of the applied material after 32 days. Unextracted radioactivity reached levels of approximately 12% after 32 days. The remainder of the radioactivity after 32 days consisted of two unidentified compounds (up to 1.2%), radioactivity remaining at the origin or "streaked" over the length of chromatograms (up to 7%) and radioactivity remaining in water after partition with dichloromethane (up to 7.8%).	X3

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	Not relevant
Materials and Methods	[redacted]
Results and discussion	[redacted]

[redacted]



[redacted]



[redacted]

Conclusion	[redacted]

	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	[redacted]

		Official use only
Reference point in dossier	**7.1.2.2.2/02**	
Title:	*Lambda*-Cyhalothrin: Degradation in Water-Sediment Systems Under Laboratory Conditions	
Project/Report number:	RJ2640B	
Author(s):	Marriott, S.H, Duley, J., Hand, L.	
Date of report:	1998	
Published:	No	
Testing facility:	Jealott's Hill Research Station, Bracknell, Berkshire, UK	
Test substance:	^{14}C-cyclopropane and ^{14}C-phenoxy *lambda*-Cyhalothrin, radiochemical purity [redacted] respectively.	X1
Study dates	February 1998 to June 1998	
GLP:	Yes	
Reliability indicator	1	

	Official use only
Materials and methods: ^{14}C-cyclopropyl labelled *lambda*-Cyhalothrin was applied at a rate equivalent to 8 g ai/ha (evenly distributed throughout a water column of 30 cm depth) to two water-sediment systems (Old Basing and Virginia Water). In addition, both ^{14}C-cyclopropyl and ^{14}C-phenoxy labelled *lambda*-Cyhalothrin were applied at rates equivalent to 80 g ai/ha to similar systems.	X2
The water and sediments were mixed in ratios of 7:1 for Old Basing and 4:1 for Virginia Water systems. The systems were equilibrated for 40 - 41 days prior to treatment with *lambda*-Cyhalothrin. The systems were incubated at 20°C ± 2°C in the dark and $^{14}CO_2$ and any other volatile products were trapped. Samples were taken for analysis at 3 and 6 hours and 1, 2, 4, 7, 14, 30, 58 and 98 days after treatment.	X3 X4
The sediments used in this study are detailed below. Both sediments were shown to be microbially active throughout the study. Old Basing: pH 7.8, % organic carbon 7.5, sandy loam soil type Virginia Water: pH 7.1, % organic carbon 0.5, sand soil type	X5 X6
Findings: *Lambda*-Cyhalothrin dissipated rapidly from the water column and was subsequently degraded by cleavage of the ester linkage to yield the cyclopropane acid metabolite (Compound Ia) and the corresponding 3-phenoxybenzyl alcohol metabolite (Compound VI) and, subsequently, the 3-phenoxybenzoic acid metabolite (Compound V). Neither of these metabolites was present at levels exceeding 5% of the applied chemical. Compound Ia was the major metabolite formed, reaching a maximum level of 29% in the surface water and 11% in the sediment. Further degradation then followed leading, ultimately, to significant mineralisation to CO_2 (up to a maximum of 48% after 98 days incubation). Hydroxylated	X7 X8 X9

lambda-Cyhalothrin (Compound XV) was also observed at maximum levels of 1.3% in the surface water and 9.6% in the sediment. The DT_{50} and DT_{90} values for dissipation of *lambda*-Cyhalothrin from the water column and in the total system were estimated, using a first order multi-compartment model, for each water-sediment system after treatment at 8 g ai/ha. These DT_{50} and DT_{90} values are summarised below.	X10

System	Disappearance Time	
	DT_{50}	DT_{90}
Old Basing - Surface Water	5 Hours	3.3 Days
Old Basing - Total System	15 Days	151 Days
Virginia Water - Surface Water	11 Hours	4.6 Days
Virginia Water - Total System	7 Days	45 Days

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	Not relevant
Materials and Methods	[redacted]

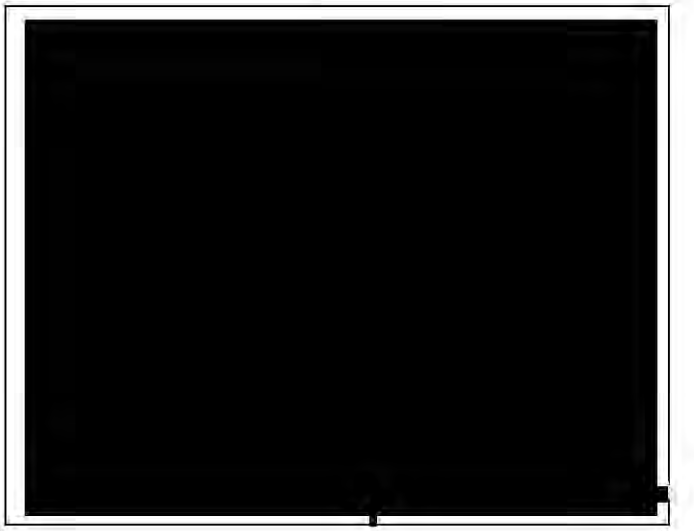
	[redacted]
Results and discussion	[redacted]

[redacted]

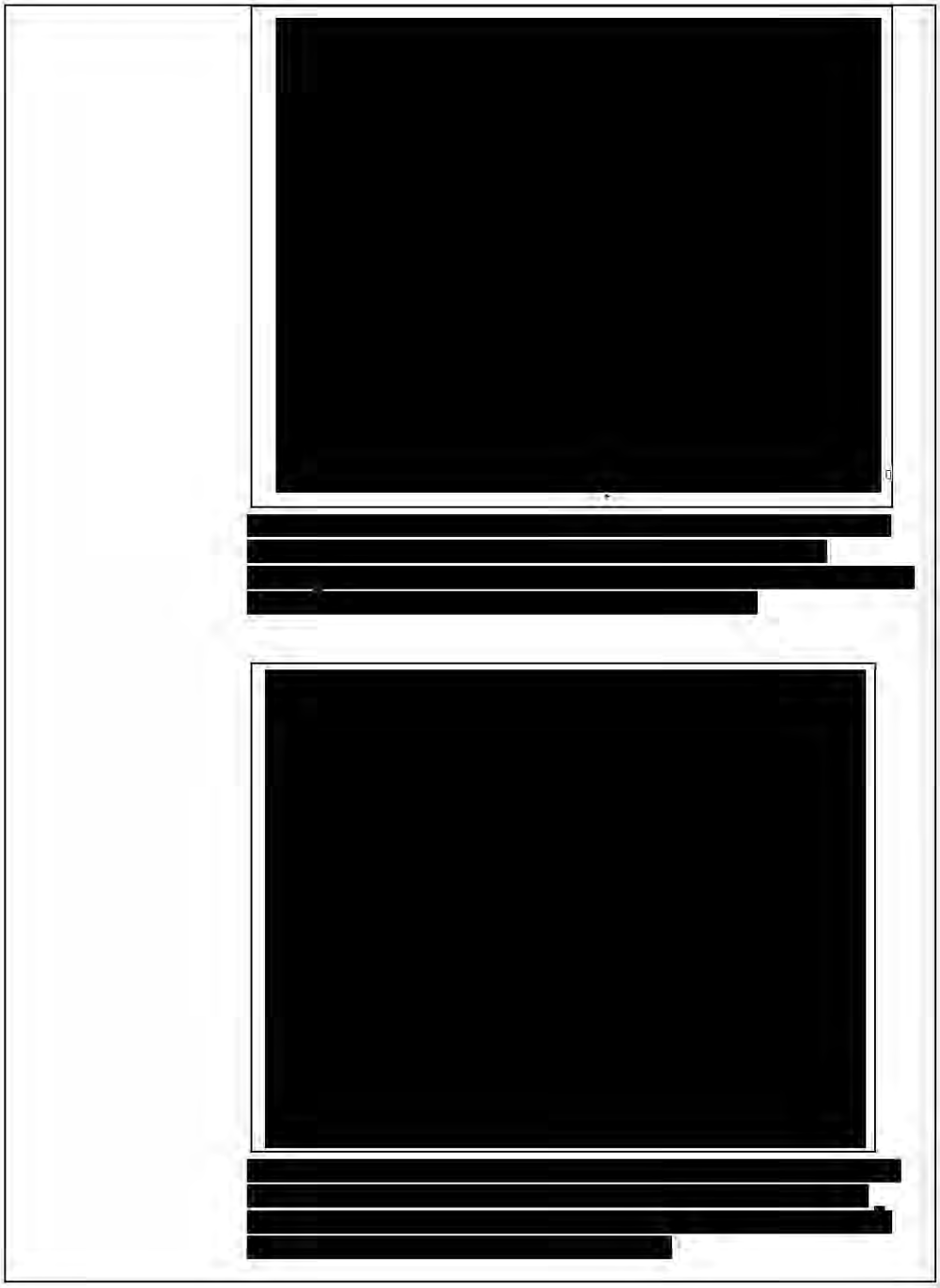
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

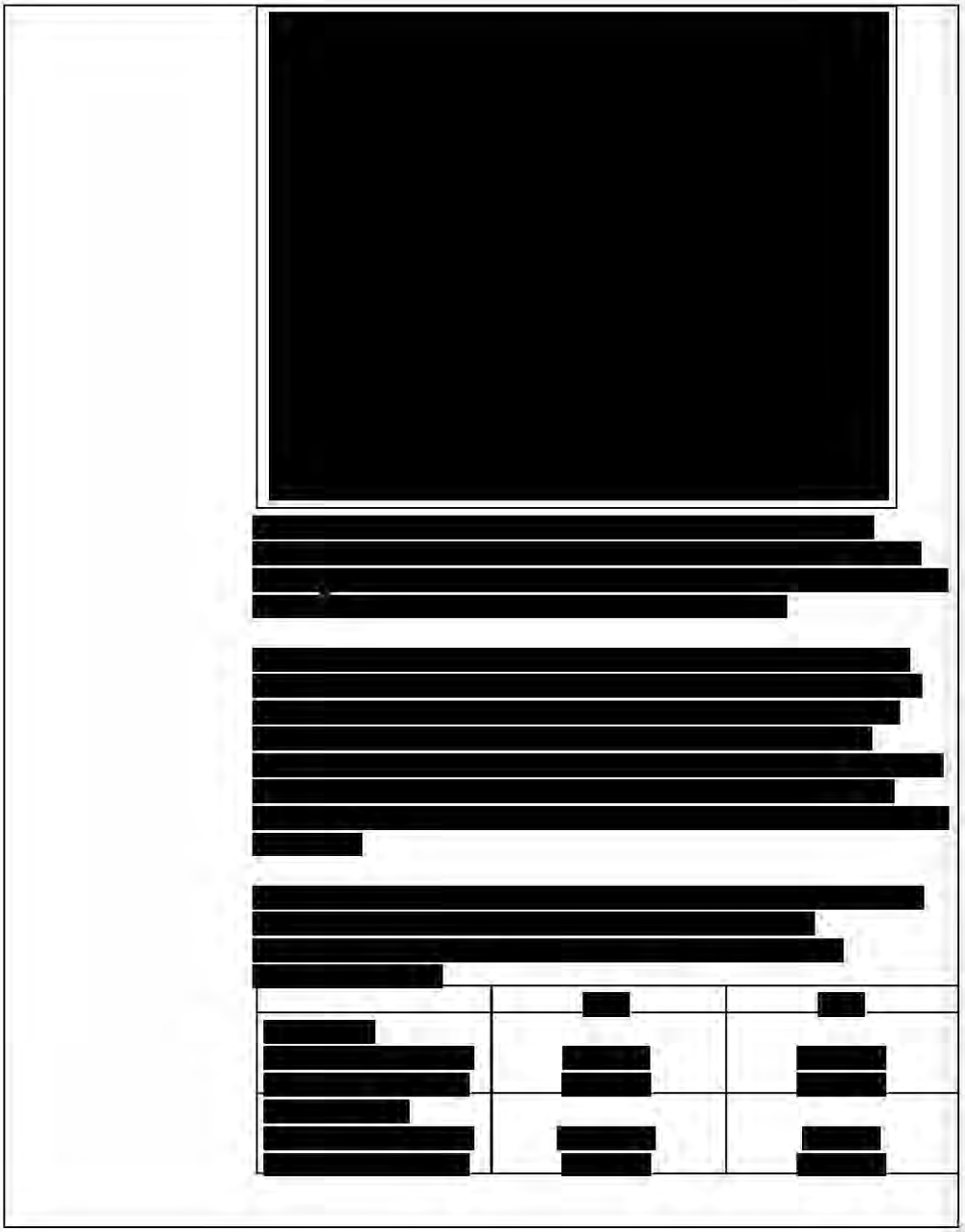
[redacted]

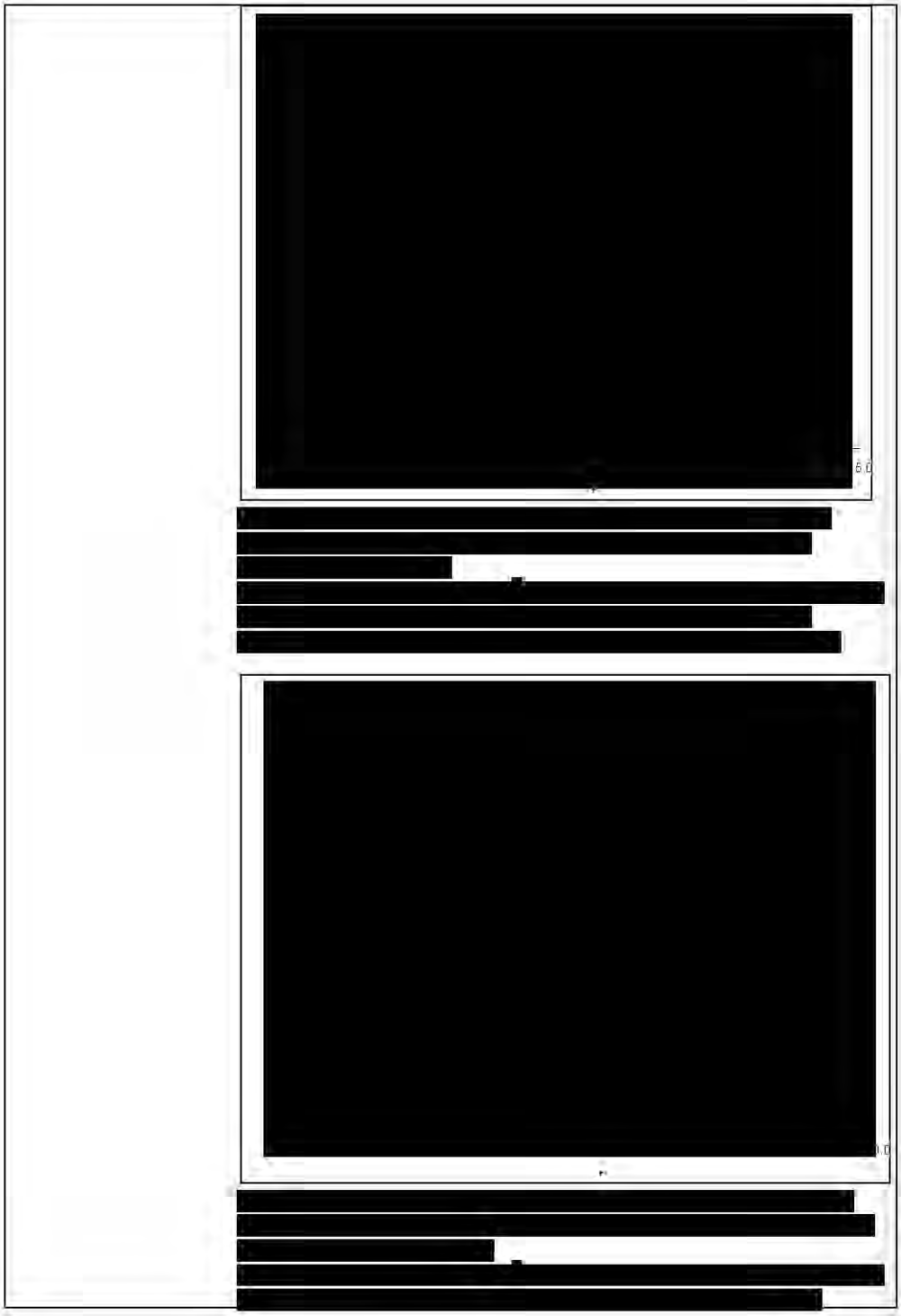
[redacted]

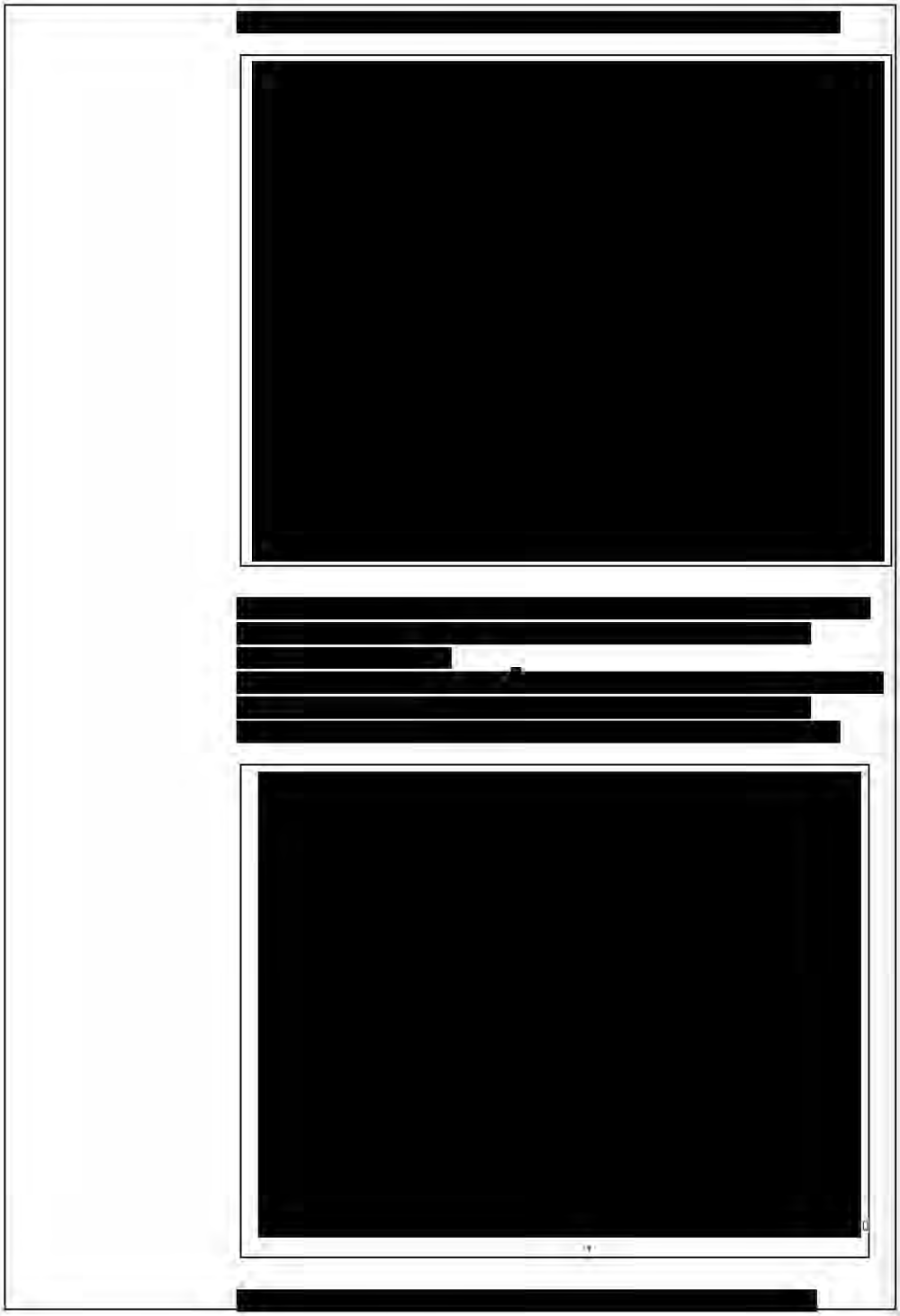


[redacted]









	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	[redacted]

		Official use only
Reference point in dossier	**7.1.2.2.2/03**	
Title:	Fate of the insecticide *lambda*-Cyhalothrin in ditch enclosures differing in vegetation and nutrient level.	
Project/Report number:	Not applicable, published research.	
Author(s):	Leistra M *et al*	
Date of report:	2003	
Published:	Yes (Alterra/Syngenta).	X1
Testing facility:	Alterra Green World Research.	
Test substance:	*lambda*-Cyhalothrin (100g/L, Karate)	
Study dates	Not stated.	
GLP:	Not applicable, published research.	
Reliability indicator	1	

	Official use only
Material and methods: The aquatic fate of *lambda*-Cyhalothrin was investigated in experimental ditches at the Sinderhoeve Experimental Station near Renkum, the Netherlands. The ditches were constructed in the mid-1980s and contained silty clay loam sediment from a clean fresh-water lake to a depth of 0.25m and water to depth of 0.5m. The ditches had been subjected to different regimes of macrophyte growth and nutrient supply (eutrophication) over several years to produce distinctive, stable ecosystems. Three experimental ditches were used: Ditch 2: Non-eutrophicated, macrophyte dominated. Ditch 19: Eutrophicated, plankton dominated Ditch 8: Non-eutrophicated, macrophyte dominated (submerged macrophytes pruned to provide a range of macrophyte densities within the ditch). In spring 2000, twelve enclosures were placed in each of the Ditches 2 and 19 (three weeks before treatment). Two of these replicate enclosures in each ditch were used for the fate determinations summarised here. Later in the summer 2000, eighteen enclosures were placed in Ditch 8 (three weeks before treatment) and six of these enclosures with varying macrophyte densities were used for fate determinations. The enclosures consisted of polycarbonate cylinders with an inner diameter of 1.05 m (surface area 0.865 m^2) and a height of 0.9 m. The bottom rim of each cylinder was inserted into the ditch sediment to a depth of about 0.15 m. At the end of the experimental period, the biomass of aquatic macrophytes in Ditches 2 and 8 was determined by harvesting all the macrophyte material in each enclosure. The macrophytes were cut close to the sediment, any roots were removed and the material dried at 35°C before weighing. Each enclosure was treated with formulated *lambda*-Cyhalothrin („Karate" Zeon; 100 g *lambda*-Cyhalothrin per L as a capsule suspension) to provide a nominal concentration in the water of 0.250 µg/L, assuming even distribution through the water column of 0.5 m. This	X2

concentration corresponds to the predicted environmental concentration in water body of 0.3 m deep (the standard water depth in EU shallow surface water models), following 1.5% drift from a field application of „Karate"Zeon of 5.0 g ai/ha. The *lambda*-Cyhalothrin applications were made to the enclosures in Ditches 2 and 19 on 16th May 2000 and to the enclosures in Ditch 8 on 15th August 2000. Each enclosure was dosed with 4 L of an aqueous *lambda*-Cyhalothrin application solution (27.0 µg *lambda*-Cyhalothrin/L tap water) which was poured into the water column and stirred gently with a rod to aid mixing, taking care not to disturb the sediment layer or to damage the macrophytes. The concentration of *lambda*-Cyhalothrin in the application solutions was analysed by GLC after extraction with hexane (1+1, by volume).	
Water samples were taken at 24 h before the application (blank check) and at 1, 3, 6, 9, 24, 72 and 168 h after application. Samples of macrophytes, sediment and suspended solids were taken at 24 h before the application (blank check) and at 6, 24, 48, 72 and 168 h after application. All samples were then extracted into hexane and analysed by gas chromatography to determine the concentrations of *lambda*-Cyhalothrin remaining.	X3
The DT_{50} values (disappearance time for 50% of the applied chemical) for dissipation from the water column were estimated using a First Order Multi-Compartment (FOMC) Model (ModelManager version 1.1, Cherwell Scientific, UK). This model generally gave the best statistical fit to the experimental data.	X4
	X5
Findings: The characteristics of the water and sediment from the ditches (at the end of the experimental periods) and the masses of aquatic macrophytes recovered from the enclosures in the two non-eutrophicated macrophyte dominated ditches (2 and 8) at the end of the residue sampling period are shown in the following tables.	X6
The dominant macrophyte species was *Myriophyllum spicatum* with some *Elodea nuttallii* also present.	
The measured concentrations of *lambda*-Cyhalothrin in the application solutions used in May (Ditches 2 and 19) and in August (Ditch 8) were between 96 and 110% of nominal for Ditches 2 and 19 in May and between 107 and 118% of nominal for Ditch 8 in August. The distribution of *lambda*-Cyhalothrin, between the ditch compartments with time, after the May and August applications are given in the following tables.	X7
In both the macrophyte dominated and the phytoplankton dominated ditches, *lambda*-Cyhalothrin concentrations in the water column in the enclosures declined rapidly after application. For all ditches, water concentrations were less than half the nominal values within a day.	
Concentrations of *lambda*-Cyhalothrin in the sediment in both ditch types treated in May were below the limit of detection (equivalent to 8% of the applied dose) at all occasions over the 7-day sampling period following application. In enclosures in the macrophyte-dominated ditch (Number 8), treated in August, sediment residues were again low and increased over day 1 to 3 after treatment to a maximum of 17% of the applied dose. The percentage of *lambda*-Cyhalothrin in the sediment in Ditch 8 tended to be lowest in enclosures with the highest macrophyte density.	
The highest concentration of *lambda*-Cyhalothrin in macrophytes taken in May from the enclosures in Ditch 2, with 90 g macrophyte dry mass per enclosure, was determined in samples taken 1 day after treatment and amounted to 3 to 5% of the applied dose. The maximum residues in the macrophytes taken from Ditch 8 in August were also found in samples taken 1 and 2 days after treatment. These macrophyte residues amounted to	

approximately 10% of the dose applied to enclosure 6 with approximately 43 g macrophyte dry mass and 50% of the dose applied to enclosure 6 with approximately 145 g macrophyte dry mass. In all cases, the residues of *lambda*-Cyhalothrin in the macrophyte compartment tended to decline significantly from day 1 to 2 following application. It is possible that macrophyte residues did in fact peak at higher levels, particularly in Ditch 2, but that the sampling interval of 24 hours was too wide to catch these maxima, given the relatively rapid rate of degradation in the macrophyte compartment.	X8 X9 X10
The DT_{50} values for dissipation from the water column are given in the following tables.	X11
Conclusion: *Lambda*-Cyhalothrin dissipated rapidly from the water column in experimental field ditches. DT_{50} times in the water column ranged from 7 to 17 hours and were similar in the two distinctly different aquatic environments (non-eutrophicated/macrophyte dominated and eutrophicated/phytoplankton dominated) and in both early and late summer. The most rapid dissipation was observed in the enclosure with the highest macrophyte density (i.e. the naturally occurring density in the non-eutrophicated ditch), whilst the slowest dissipation was observed in the phytoplankton dominated enclosures. This dissipation rate, although the slowest of the range, is nonetheless rapid. The portion of *lambda*-Cyhalothrin entering the water column that associated with the macrophyte compartment tended to increase with higher macrophyte density. Macrophyte residues in the ditch enclosures peaked within 1 to 2 days and then declined rapidly. Only small amounts of *lambda*-Cyhalothrin reached the ditch sediment (<8% to 17% of the applied dose), even when there were virtually no macrophytes present, suggesting that extensive degradation of *lambda*-Cyhalothrin occurred both in the macrophyte and in the water column compartments under all conditions studied.	X12

Characteristics of the Water in the Experimental Ditches

Characteristic	Ditch 2 Sampled 23/05/00	Ditch 19 Sampled 23/05/00	Ditch 8 Sampled 22/08/00
pH	8.2	7.6	7.15
Conductivity µS/cm	137	90.5	139
Alkalinity mg HCO_3/l	71.7	34.4	65
Total carbon mg C/l	37.2	49.4	48.7
Total inorganic carbon mg C/l	14.1	6.8	12.7
Total organic carbon mg C/l	23.1	42.6	36.0
Total suspended solids mg/l (TSS)	4.9	14	16
Organic matter of TSS % w/w	96.1	97.1	71.4
Chemical oxygen demand mg/l	4	90	<2
Biochemical oxygen demand mg/l	2	10	<2
Nitrite mg N/l	<0.10	<0.10	<0.10
Nitrate mg N/l	<0.10	<0.01	<0.10
Ammonia mg/N/l	<0.23	<0.10	0.2
Total phosphate mg/l	<0.50	<0.50	3.8
Orthophosphate mg/l	<0.50	<0.50	<0.50
Total hardness mg $CaCO_3$/l	66.3	39.1	62.6
Total iron mg/l	0.58	0.72	0.07
Total zinc mg/l	<0.001	<0.005	<0.001
Total lead mg/l	<0.01	<0.01	<0.01
Total copper mg/l	<0.001	0.106	<0.001
Total calcium mg/l	23.3	12.9	22.7
Total magnesium mg/l	1.7	1.3	1.4
Total potassium mg/l	0.8	1.2	0.4
Sulphate mg/l	3.1	3.4	5.5

Chloride mg/l	5.8	5.6	5.3
Fluoride mg/l	0.7	0.8	<0.1

Characteristics of the Sediment in the Experimental Ditches

Characteristic	Ditch 2 Sampled 29/05/00	Ditch 19 Sampled 29/05/00	Ditch 8 Sampled 22/08/00
pH	6.9	6.1	7.3
Cation exchange capacity meq/100 g	41.3	40.4	41.2
Organic carbon % w/w	15.3	13.8	13.3
Total nitrogen % w/w	1.87	2.13	1.39
Sand Fraction 2.00-0.050 mm	11	41	52
Silt Fraction 0.050-.002 mm	32	14	31
Clay Fraction <0.002 mm	57	45	17
Textural class	Clay	Clay	Silty Clay Loam

Densities of aquatic macrophytes in Ditches

Ditch No. (Application Date)	Enclosure No.	Description	Macrophyte dry mass (g)
2 (16 May 2000)	2	Dominated by submerged macrophytes; not eutrophic.	90.0
	9		90.0
19 (16 May 2000)	4	Dominated by phytoplankton (algae etc.); eutrophic.	NA
	13		NA
8 (15 August 2000)	6	Dominated by submerged macrophytes; not eutrophic.	42.8
	8		145
	15	About half of the macrophytes removed; not eutrophic.	27.6
	18		44.8
	16	Nearly all macrophytes removed, not eutrophic.	1.3
	17		1.1

NA : Not applicable

Distribution of *Lambda*-Cyhalothrin over the Compartments in the Enclosures in Ditches 2 and 19 (May Experiment).

Ditch No.	Enclosure No.	Time (days)	Percentage of the dose in/on		
			Water	Macrophytes	Sediment[2]
Ditch 2: (Macrophyte dominated with 90 g dry mass per enclosure)	2	0.13	100[1]	1.9	--
		0.25	--	3.3	< 8
		1.0	25.3	4.7	< 8
		3.0	7.2	3.9	--
		7.0	1.8	1.5	--
	9	0.13	100[1]	2.1	--
		0.25	--	1.9	< 8
		1.0	23.4	3.2	< 8
		3.0	5.5	3.0	--
		7.0	2.1	2.7	--
Ditch 19: (Phytoplankton dominated).	4	0.25	100[1]	--	< 8
		1.0	37.4	--	< 8
		3.0	3.3	--	--
		7.0	1.0	--	--
	13	0.25	100[1]	--	< 8
		1.0	30.7	--	< 8
		3.0	3.6	--	--
		7.0	1.3	--	--

[1]: Nominal value. Determination of the concentration of the dose solution had demonstrated that the dose solution had been correctly prepared.
[2]: All *lambda*-Cyhalothrin residues in the sediment were <LOD (0.001 mg/kg, ≡ 8% of applied chemical).
-- : No sample taken for analysis.

Percentages of *Lambda*-Cyhalothrin in the Compartments of the Enclosures in Ditch 8 (August Experiment).

Enclosure No. (Macrophyte dry mass per enclosure)	Time (days)	Percentage of the dose in/on		
		Water	Macrophytes	Sediment
6: (43 g)	0.04	86.5	--	--
	0.13	84.7	--	--
	0.25	68.8	5.8	< 8(1)
	0.38	43.7	--	--
	1.0	38.1	7.5	< 8
	2.0	--	10.4	< 8
	3.0	1.9	1.2	11.4
	7.0	1.9	0.2	11.4
8: (145 g)	0.04	87.4	--	--
	0.13	78.1	--	--
	0.25	53.0	17.3	< 8
	0.38	30.7	--	--
	1.0	23.3	49.7	< 8
	2.0	--	26.6	< 8
	3.0	1.9	16.1	11.4
	7.0	0.9	8.7	< 8
15: (28 g)	0.04	90	--	--
	0.13	78	--	--
	0.25	68	--	8
	0.38	45	--	--
	1.0	37	--	12
	2.0	-	--	12
	3.0	4.0	--	12
	7.0	0.7	--	12
18: (45 g)	0.04	91	--	--
	0.13	77	--	--
	0.25	70	--	< 8
	0.38	41	--	--
	1.0	31	--	< 8
	2.0	--	--	12
	3.0	2.3	--	12
	7.0	0.4	--	12
16: (1.3 g)	0.04	98	--	--
	0.13	80	--	--
	0.25	64	--	8
	0.38	41	--	-
	1.0	40	--	12
	2.0	--	--	12
	3.0	4.2	--	12
	7.0	0.7	--	12
17: (1.1 g)	0.04	98	--	--
	0.13	87	--	--
	0.25	68	--	8
	0.38	50	--	--
	1.0	39	--	12
	2.0	--	--	12
	3.0	3.3	--	17
	7.0	0.6	--	12

(1) : Residue <LOD (0.001 mg/kg, ≡ 8% of applied chemical).
-- : No sample taken for analysis

DT_{50} Values for Dissipation of *Lambda*-Cyhalothrin from the Water Column in the Experimental Ditches.

Application	Ditch No.	Description	Enclosure No.	Macrophyte Dry Mass (g)	DT_{50} (Hours)
May 2000	2	Non-eutrophicated, macrophyte dominated.	2	90	9.7
			9	90	9.2
	19	Eutrophicated, plankton dominated.	4	NA	16.6
			13	NA	13.8
August 2000	8	Non-eutrophicated, macrophyte dominated (submerged macrophytes pruned to provide a range of macrophyte densities within the ditch).	6	43	10.8
			8	145	6.6
			15	28	10.3
			16	1.3	10.1
			17	1.1	12.4
			18	45	9.5

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	Not relevant
Materials and Methods	[redacted]

	[redacted]
Results and discussion	[redacted]

	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	[redacted]