Opinion of the Scientific Committee on Plants regarding the Evaluation of CARFENTRAZONE-ETHYL in the Context of Council Directive 91/414/EEC Concerning the Placing of Plant Protection Products on the Market (opinion adopted by the Scientific Committee on Plants, 26 January 2001)

1. TITLE

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2. TERMS OF REFERENCE

The Scientific Committee on Plants (SCP) is requested to respond to the following question in the context of the Commission's work on the implementation of Council Directive 91/414/EEC concerning the placing of plant protection products on the market:

"The Scientific Committee on Plants is requested to comment on the relevance for humans of the elevated levels of specific porphyrins detected in test animals."

In addition, the SCP noted that in Schnöder Lysimeter study [1] approximately 19-26 % of the radioactivity leached and that three unknown polar compounds were detected, each at average concentrations greater than 0.1 µg/l **(equivalents**) in the first year. The notifier was therefore requested to comment on the relevance of these three metabolites.

3. BACKGROUND

Carfentrazone-ethyl is a new active substance (a.s.) in the context of Council Directive 91/414/EEC [2]. The draft Commission Directive for the inclusion of carfentrazone-ethyl in Annex I to Directive 91/414/EEC concerning the placing of plant protection products on the market was submitted to the Committee for opinion. The Committee had been supplied with documentation comprising a draft evaluation report (monograph) prepared by the Rapporteur Member State (France) based on a dossier submitted by the notifier (FMC Europe NV), a review report prepared by the Commission and the Recommendations of the ECCO [3] Peer Review Programme.

Carfentrazone-ethyl is used as a post-emergence herbicide to control broad-leaved weeds in winter and spring cereals at the maximal dose of 20.6 g a.s./ha in autumn/winter and spring. Carfentrazone-ethyl belongs to the group of photo bleaching herbicides known to inhibit the protoporphyrinogen oxidase, an enzyme involved in heme synthesis.

4. OPINION

4.1 Question 1

"Can the Committee comment on the relevance for humans of the elevated levels of specific porphyrins detected in test animals."

Opinion of the Committee:

The Committee is of the opinion that the elevated levels of porphyrins detected in test animals are relevant for humans. The NOEL [4] established on the basis of pigment deposit in tissues and mild hepatotoxicity is considered appropriate. There is no evidence that humans are more sensitive than animals to inhibitors of heme synthesis or excess of porphyrins .

Scientific background on which the opinion is based: [5]

4.1.1 Short term toxicity studies

In 90-days studies in mice, rats and dogs, doses of 0, 1000, 4000, 8000, 14000 & 20000 ppm were used in the rodents and 0, 50, 150, 500 & 1000 mg/kg bw [6] /day in dogs. A common effect in the three species is porphyria with elevate urine porphyrins with slight differences in severity between species: the most sensitive is the rat and the least sensitive is the mouse (although dose spacing should be considered). It should be noted that the effects are observed even in the 28-day studies in rats and mice. The major effects can be summarised as follows:

- **In rats**: the effects observed include pink to brown abdominogenital staining, elevation of specific and total levels of porphyrins; at necropsy, hepatic pigment deposition and hepatocytomegaly. The NOEL of 1000 ppm (equivalent to 58 mg/kg bw/day for males and 73 mg/kg bw/day for females) is based on a decrease of food consumption, alterations in haematology parameters in males; elevated porphyrin levels in female; and liver cell necrosis in one male at 4000 ppm. The LOAEL [7] is 4000 ppm.
- **In mice**: the effects observed include pink to brown discoloration of the cage. The NOEL of 1000 ppm (equivalent to 160 mg/kg bw/day) is based on hepatotoxicity in females at 4000 ppm **.**
- **In dogs**: the effects observed include a dose-related increase in the urinary excretion of uroporphyrin I, 5-carboxylporphyrin and coproporphyrin I, decreased levels of MCV and MCH, no histopathological changes. The NOEL of 150 mg/kg bw/day is based on a decrease of body weight gain in females, alterations in haematology parameters and increased porphyrin levels in dogs at 500 mg/kg bw/day.

4.1.2 Long term toxicity studies

Two studies were submitted: a combined 104 weeks oral carcinogenicity and chronic toxicity study in rat and an 80 weeks oral carcinogenicity in mice. The doses were respectively 0, 50, 200, 800 and 4000 ppm and 0, 70, 700 and 7000 ppm. The principal effects observed are the following:

- **In rats:** in addition to the general toxicological effects, other effects linked indirectly or directly to porphyria include blood pigments and erythrocytes in the urine of animals given 4000 ppm, and clear treatment-related increase in the female total mean porphyrin concentrations. A red fluorescence at a wavelength consistent with

porphyrin deposits was observed in the liver at 200 ppm and above in females and in males from 800 ppm. At high dose, blood pigments and erythrocytes are detected in the urine in particular in females, the mean porphyrin concentration is increased time-proportionally in the female group of 4000 ppm. The NOEL in females is 50 ppm (3 mg/kg bw/day) and in males 200 ppm (9 mg/kg bw/day) based on the presence of the red fluorescence at a wavelength consistent with porphyrin deposits in the livers at the next higher dose level.

- **In mice:** a red fluorescence consistent with porphyrin deposits was observed in frozen liver sections from males at 700 ppm and in males and females at 7000 ppm. Signs of hepatotoxicity were evident in both sexes given 700 and 7000 ppm (centrilobular single cell necrosis and/or evidence of porphyrin deposition). The NOEL for female is 70 ppm (equivalent to 10-12 mg/kg bw/day). The Noel for males could not be determined because the reduction of body weight gain was observed at the lowest tested dose.

4.1.3 Conclusions of toxicological studies

The carfentrazone-ethyl induces an increase in urinary excretion and hepatic deposits of porphyrin in each tested species: rat, mouse and dog. The sensitivity is slightly different from one species to another with the rat being the most sensitive. The NOEL and the NOAEL [8, 9] are based on the absence of accumulation of porphyrin in tissues and not on the absence of effects secondary to the accumulation of porphyrin. In the 90-day feeding studies in rats and dogs and in the 2-year feeding study in rats, 6 different porphyrins and total porphyrins were measured in the urine: uroporphyrin I, 5-carboxylporphyrin, 6-carboxylporphyrin, 7-carboxylporphyrin, coproporphyrin I, mesoporphyrin IX. It appears that at the proposed NOEL, none of these parameters were significantly different from the control.

4.1.4 Relevance for humans

In humans, porphyria is a group of diseases in which genetic disorders of heme biosynthesis cause excessive accumulation and excretion of porphyrins and porphyrin precursors. In humans, disorders of porphyrin metabolism can be induced by exposure to some substances acting on the enzyme involved in heme synthesis (e.g. lead and HCB). The administration to mice during 9 days of photo bleaching herbicides results in experimental porphyria resembling the acute phase of human variegate porphyria. They caused a decrease of protoporphyrinogen oxidase (PPO) in liver and kidney.

There are no reasons to exclude the fact that the PPO inhibitors can interfere with the porphyrin biosynthetic pathway in man similar to that in laboratory animals. The difference in accumulation of porphyrins particularly protoporphyrin IX appears to be responsible for the difference of toxicity between species. The relative sensitivity of human compared to laboratory animals is unknown. There seems to be slight interspecies differences of sensitivity to carfentrazone-ethyl effects: rat > dog > mouse. The differences between the three species are low: + factor 3. The NOELs in the 90-day feeding study are respectively 58 mg/kg bw/day for male rats, 150 mg/kg bw/day for dogs and + 160 mg/kg bw/day for mice. In long term, the NOELs are 3 mg/kg bw/day for female rats and 10-12 mg/kg bw/day for male mice.

Carfentrazone-ethyl mainly induced protoporphyrin accumulation in liver and because of the lack of water solubility, it is poorly excreted in urine and is mainly excreted in faeces via bile. The cutaneous porphyria in man is a genetic disease, which produces a reaction to sunlight of

the porphyrins deposited in skin or circulating in the blood vessels. Since the porphyrins produced by carfentrazone exposure are not soluble in water, the changes are essentially an accumulation in liver and a low excretion in urine.

There is no evidence that humans present a much greater sensitivity to porphyrin inhibitors and to the adverse effects of porphyrin accumulation than animals. Because of the lack of water solubility, porphyrins might be poorly excreted in urine and mainly excreted in faeces via bile. Carfentrazone-ethyl acts mainly through the accumulation of protoporphyrin pigments in liver and induces hepatic effects. It is concluded that the interference with heme metabolism in experimental animals is relevant for human risk assessment of exposure to carfentrazone-ethyl. Based on the mechanistic approach, the NOEL established from pigment deposit in tissues and mild hepatotoxicity is considered appropriate.

4.2 Issue raised by the Committee

The SCP notes that in Schnöder Lysimeter [10] study approximately 19-26 % of the radio-activity leached and that three unknown polar compounds were detected, each at average concentrations greater than 0.1 µg/l (equivalents) in the first year. The Committee is of the opinion from the available data that these metabolites require further assessment. On request, the notifier provided additional information on these three metabolites .

During the course of the Committee's discussion, two of those metabolites were identified and the third was characterised by the notifier. The structure of this opinion and the following background reflects that information on those metabolites became available stepwise, each time requiring amendment of the opinion.

Opinion of the Committee:

On the basis of the data, in particular the lysimeter study and modelling data presented, neither carfentrazone-ethyl nor its initially identified metabolites are likely to contaminate groundwater in excess of 0.1 µg/l. However, in the leachates of the lysimeters in the first year three unidentified polar compounds were detected at average concentrations > 0.1 µg/l (equivalents). There are no specific toxicological and ecotoxicological data to determine the relevance of those compounds (which have been identified/characterised in the meantime), but the assessment indicates that those metabolites will not cause an unacceptable ecotoxicological or toxicological risk via the groundwater.

The lysimeter study presented by the notifier does not represent the full range of intended uses. In the lysimeter study carfentrazone-ethyl was only applied with one application in May at 13.1 g/ha (lysimeter 1) or 16 g/ha (lysimeter 2). Therefore, of the intended uses, only the spring application (one application of 15 g/ha) is supported by data. Other intended uses with two applications in spring and autumn and applications with rates up to 20.6 g/ha are not covered by the Committee evaluation.

Scientific background on which the opinion is based:

4.2.1 Route of degradation

Carfentrazone-ethyl (F8426) is rapidly degraded in soil under aerobic conditions. Mineralisation is not significant and bound residues are < 15 % after 100 days.

Under aerobic conditions, the following metabolites were identified above 10 % of applied active substance:

F8426-chloropropionic acid max. 49.3 - 86.6% (1.5 - 16 days)
F8426-propionic acid max. 21.7 % (180 days)
F8426-cinnamic acid max. 21.4 - 47.1 % (8 - 102 days)
F8426-benzoic acid max. 17.2 % (365 days)

The hydroxymethyl derivates of chloropropionic, cinnamic and benzoic acids are detected in amounts usually below 10 %.

Under anaerobic conditions F8426-chloropropionic acid was found in max. 95.9 % (7 days) and F8426-propionic acid in max. 27.3 % (180 days).

4.2.2 Rate of degradation

The rate of degradation in laboratory studies is strongly influenced by the temperature and other conditions (aerobic/anaerobic):

		Laboratory (aerobic conditions)		
		10 °C [11]	**20 °C** [12]	
F8426	**DT50** [13]	0.1 day	< 1.5 days	
	DT90 [14]	482 days	< 17 days (one case: 250 days)	
(Under **anaerobic** conditions F8426 is rapidly degraded with DT50 < 1 day)				
F8426-chloropropionic acid	**DT50**	92.4 days	11.3-24.8 days (one case: 85.6 days)	
	DT90			
(Under **anaerobic** conditions F8426-chloropropionic acid is rather stable)				

(Source: Volume 3 of the Monograph)

Under **field** conditions, F8426 is rapidly degraded in soil, with DT90 < 1 day for both winter and spring applications. Field studies on 9 sites with winter and spring applications are available: Germany (3 sites, bare soil);

UK (2 sites, bare soil);

Southern France (4 sites, wheat).

	Field conditions		
	DT50 (days)	**DT90 (days)**	**Remarks**

F8426-chloropropionic acid	3 - 14	11 - 47	DT50: 27 days, 1 UK site, spring) [15] DT90: 88 days, 1 UK site) [16]
F8426-cinnamic acid	5 - 29	17 - 97	
F8426-benzoic acid	11 - 31	37 - 104	
F8426-propionic acid	_	_	Not determined, no residue after 57 days

(Source: Volume 3 of the Monograph)

4.2.3 Adsorption and desorption

Because of the rapid degradation, adsorption of F8426 in soil cannot be measured. F8426-chloropropionic acid (Koc [17] = 6-48, average 23) and F8426-benzoic acid (Koc = 4-41, average 17) are poorly adsorbed and are likely to be mobile in soil.

F8426-propionic acid (Koc = 27-260, average 98) and F8426-cinnamic acid (Koc = 44-333, average 142) are more adsorbed and are likely to be less mobile.

4.2.4 Leaching into groundwater

By its rapid degradation in soil and its low use rates the potential of F8426 to move into groundwater is minimised. The PECs [18] for the parent compound and for the chloropropionic acid in groundwater are << 0.1 µg/l. F8426 propionic acid was never detected in significant amounts in soil under field conditions, therefore this compound is not expected to occur in groundwater.

Only F8426 benzoic acid and F8426 cinnamic acid were found in soil under field conditions below 10 µg/kg. The benzoic acid derivative was also found in the leachates of soil columns. Both metabolites have no herbicidal activity.

In 1999 a lysimeter study was made available. The lysimeter study was conducted using a monolith (1 m², 1.1 m depth) of sandy soil with application rates of 13.1 g a.s./ha (lysimeter 1) and 16 g a.s./ha (lysimeter 2) to winter wheat.

In the leachates, neither F8426 (LOQ [19] < 0.02 µ/l) nor the metabolites F8426 chloropropionic acid, F8426 propionic acid, F8426 cinnamic acid nor their 3-hydroxy derivatives could be detected.

F8426 benzoic acid was only detected in the first year with a mean concentration of 0.023 µg/l.

For these substances no contamination of the groundwater in concentrations above 0.1 µg/l is expected.

However, three unidentified polar compounds were detected (M_1, M_2, M_3) in the first year of the lysimeter study. The concentration ranges and the average of the non-identified radioactivity are presented in the table below.

	Non-identified radioactivity (NIR) µg/l (parent equivalent)			
	Range	average	range	average
Metabolite	Lysimeter 1	Lysimeter 1	Lysimeter 2	Lysimeter 2
M_1	0.02-0.28	0.15	0.02-0.35	0.15
M_2	0.03-0.53	0.25	0.07-0.58	0.28
M_3	0.11-0.67	0.32	0.09-0.54	0.22

In the second year the unidentified metabolites were detected only occasionally and always below 0.1 µg/l. There were no toxicological or ecotoxicological data to confirm the relevance of the NIRs and therefore the notifier provided additional information concerning the identification, characterisation and relevance of these metabolites.

Metabolite M_1 was investigated in detail by a specialist laboratory but a definitive identification was not possible. Based on the information available, it was concluded that the M_1 metabolite is a small, cleaved molecule, probably a carboxylic acid containing an amino-moiety. The molecular weight of this metabolite will be lower than that of the parent and therefore it is likely that leachate concentrations will be less than 0.1µg/l.

Metabolite M_2 was identified as a sulfodeschloropropionic acid derivative. The sponsor had previously identified this metabolite in a wheat metabolism study.

Metabolite M_3 was identified as a methyl triazole derivative (1-difluormethyl-5-methyl-1,3,4-triazol-2-on). If NIR's are corrected for the molecular weight of methyl triazole the year 1 average concentration of M_3 in the leachate of lysimeter 1 was 0.116µg/l and 0.080µg/l in lysimeter 2 (combined average 0.098µg/l).

In general it can be expected that sorption of all acid metabolites (chloropropionic, propionic, cinnamic, benzoic and sulfodeschloropropionic) decreases with increasing pH. The pH of the lysimeter soil was 5.6-5.9 which is not a realistic worst-case value. Furthermore, the lysimeter study does not cover the full range of intended uses e.g. application rates can be higher.

4.2.5 Ecotoxicological assessment of metabolites

The four main metabolites (in order of appearance in soil: F8426-chloropropionic acid, F8426-cinnamic acid, F8426-propionic acid, F8426-benzoic acid) have been tested each with the three aquatic standard species. For **Daphnia** and rainbow trout, toxicity of all 4 metabolites was much lower than for the parent substance (no effects at the highest test concentrations of 10 - 101 mg/l; with parent compound NOECs [20] in equivalent tests being in the range of 1.2 - 2.2 mg/l). For planktonic algae (**Selenastrum capricornutum** in all tests),

three of the 4 metabolites proved to be far less toxic (NOECs 0.1 - 5.14 mg/l) than the parent compound (NOEC 0.008 mg/l). However, the metabolite F8426-cinnamic acid (which occurs after F8426-chloropropionic acid but before F8426-benzoic acid) exhibited similar toxicity as the parent substance (NOEC 0.00846 mg/l and 0.008 mg/l, respectively). Although F8426-cinnamic acid does appear in water/sediment systems in considerable amounts (> 20%) after 2-3 weeks, the level during the first 1-4 days (which corresponds to the duration of the static algal test) is too low to explain the result of the algal test with the parent compound. Hence, the existing data show that the parent substance and F8426-cinnamic acid both exhibit toxicity at similar levels, while metabolites occurring before and after F8426-cinnamic acid were far less toxic. This is in line with general experience which shows that most metabolites have a lower or equal ecotoxicological activity than their parent compounds.

The three metabolites M_1, M_2 and M_3 have not been tested for ecotoxicity. The metabolite M_3 is smaller and of a different structure than the parent substance or the four metabolites discussed above, increasing the likelihood that it is less active than the parent compound. The structure of M_2 being similar to that of F8426-cinnamic acid, and in the light of the other considerations above, it is justified to assume similar toxicity for M_2, F8426-cinnamic acid and the parent compound. The characterisation of M_1 as possibly an amino acid does not raise concern from the ecotoxicological point of view, given the role of such substances in nature. Hence, the comparably extensive available data on the other (identified) metabolites as well as overall experience with metabolite ecotoxicity suggest that M_1, M_2 and M_3 are unlikely to be more toxic than the active substance, but that at least M_2 may exhibit toxicity at the same level as the parent substance.

For an assessment of ecotoxicological relevance, it is therefore considered justifiable to assume - as a reasonable worst case - that M_2 and M_3 are of less or equal toxicity as the parent.

The concentrations in the lysimeter leachate may be used as a worst-case exposure estimate for aquatic organisms for spring application (13.1 g a.s./ha and 16 g a.s./ha). For M_2 and M_3, the sum of their average concentrations is 0.57 and 0.5 µg/l respectively in the two lysimeters. This concentration is lower than 1/100 of most of the long term NOECs of the active substance (rainbow trout, 28 days: 0.11 mg/l; **Daphnia**, 21 days: 0.22 mg/l; sediment dwelling **Chironomus riparius**, 21 days: 7.4 mg/l), but only slightly lower than the NOECs for algae and aquatic plants (2 - 10 µg/l). Compared to the toxicity of the other metabolites, this concentration in groundwater is 5-6 orders of magnitude below the NOEC values for **Daphnia** and rainbow trout, 2-3 orders of magnitude lower for algae for three of the metabolites, and slightly lower (factor 4-20) than that for F8426-cinnamic acid. Hence, it can be concluded that sufficient margins of safety remain for the undiluted groundwater-PEC (ca. 0.6 µg/l) and subsequent surface water PECs (under most regional circumstances, in the case of entry of groundwater into surface water, dilution would increase the factor between concentrations of those metabolites and the above-mentioned NOEC values).

Conclusion of the ecotoxicity evaluation:

While there has been no direct proof of ecotoxicological non-relevance (i.e. ecotoxicity tests) for the metabolites M_1, M_2 and M_3, experience, available toxicity data and considerations of exposure suggest that the risk for aquatic organisms is low.

4.2.6 Toxicological assessment of metabolites

The average sums of M_1, M_2 and M_3 metabolites in the leachate of these two studies were 0.525µg/l [21] and 0.522µg/l [22] respectively. The metabolites M_2 and M_3 were respectively identified as a sulfodescloropropionic acid derivative of the a.s. and the triazol moiety of the parent or of the one of the main soil metabolites. M_1 has not been fully characterised being suggested to be a cleaved product of the parent compound formed by a carboxylic acid containing an amino-moiety, possibly an amino acid.

The high polarity of M_1, M_2 and M_3 would facilitate their excretion from mammals should they be ingested through drinking water.

The average exposure level from the consumption of 2 litres of water/day would be 1.047µg /day for the average sum of M_1, M_2 and M_3, a value below the threshold of toxicological concern of 1.5µg /person/day [23]. Individually, the exposure levels for the three metabolites would be lower. In the case of M_1 (the metabolite not fully characterised) the average amount ingested per day would be 0.300µg [24] i.e. almost five times lower than the threshold of concern.

The metabolic pathway for carfentrazone-ethyl in soil shows that the metabolite F8426-benzoic acid which appears in leachate was not found in the metabolism studies in rats. Therefore, this metabolite was not assessed in the toxicological studies performed with the parent compound in laboratory animals. However, acute oral and dermal studies carried out in rats with F8426-benzoic acid showed low toxicity for this compound. Furthermore mutagenicity tests supplied were negative. In the two-lysimeter studies F8426-benzoic acid was detected at concentrations well below 0.1µg/l.

Conclusion of the toxicology evaluation:

The SCP therefore considers that no significant health risk is likely to arise due to the presence of M_1, M_2 and M_3 and of F8426-benzoic acid in groundwater at the levels reported in the lysimeter studies. It should be noted that the lysimeter studies were not representative of all the intended uses and the possible contribution of previous applications has not been investigated.

5. REFERENCES

- 1. WHO/IPCS Hexachlorobenzene. EHC 195, Geneva, 1997.
- 2. WHO/IPCS Inorganic lead. EHC 165, Geneva, 1995.
- 3. International Agency for Research on Cancer (IARC) Hexachlorobenzene. Proceedings of an international symposium. (Morris and Cabral eds), Lyon, 1986.
- 4. 14C-carfentrazone-ethyl: Lysimeter study according to BBA guideline IV, 4-3 (1990) - Report 1354-073-106 - F. Schnöder (1999).
- 5. Opinion of the Scientific Committee on Plants on the draft Guidance Document on Aquatic Ecotoxicology (DG VI - 8075/VI/97-Rev.4 of 18.12.1998) (Opinion expressed by the SCP on 24 September 1999) click here
- 6. L'homogénéité dans la manière d'évaluer la toxicité de produits par un même mécanisme et plus spécifiquement le mécanisme utilisé par les herbicides agissant comme inhibiteurs de la photosynthèse. Dr. M-P. Delcour-Firquet, February 2000 - (Doc. SCP/CARFEN/004-FR).

- 7. Products acting by the same mechanism and more specifically the mechanism used by weedkillers acting as inhibitors of photosynthesis. (English translation of Reference 6 - Doc. SCP/CARFEN/004-EN).
- 8. Opinion of the Scientific Committee on Plants regarding the draft guidance document on relevant metabolites. (http://ec.europa.eu/food/sites/food/files/safety/docs/sci-com_scp_out82_ppp_en.pdf)

6. DOCUMENTS MADE AVAILABLE TO THE COMMITTEE

- 1. Evaluation of carfentrazone-ethyl in the context of Council Directive 91/414/EEC concerning the placing of plant protection products on the market. (Doc SCP/CARFEN/001) submitted 26 November 1999.
- 2. Carfentrazone-ethyl: evaluation table Doc. SANCO 7472/98rev 5 (Doc. SCP/CARFEN/003-rev1) submitted 29 May 2000.
- 3. Carfentrazone-ethyl: Addendum to the monograph section B.7 Lysimeter study. (Doc. SCP/CARFEN/005) submitted 18 February 2000.
- 4. Draft review report for the active substance Carfentrazone-ethyl. (Doc. SCP/CARFEN/006) submitted 24 February 2000.
- 5. Carfentrazone-ethyl: Appendix I: identity, physical and chemical properties, Appendix II: end points and related information, Appendix III: list of studies which were submitted during the evaluation process and were not cited in the draft assessment report (Doc. SCP/CARFEN/007) submitted 24 February 2000.
- 6. Questions raised by the SCP (Doc. SCP/CARFEN/008) submitted by the SCP, 4 May 2000.
- 7. Carfentrazone-ethyl: comments from Denmark relating to lysimeter study. (Doc. SCP/CARFEN/010) submitted 24 July 2000.
- 8. Carfentrazone-ethyl: lysimeter study, response from notifier to question raised by the SCP (SCP/CARFEN/008). (Doc. SCP/CARFEN/011) submitted 20 July 2000.
- 9. Carfentrazone-ethyl: Identification, characterisation and relevance of carfentrazone-ethyl polar metabolites found in lysimeter study (Doc. SCP/CARFEN/011B), submitted by FMC, 27 October 2000.
- 10. Carfentrazone-ethyl: Report Addendum II C-F8426: Lysimeter Study According to BBA Guideline IV, 4-3, 1990 Subtitle: Characterization of Metabolite (M-1) from Leachate (Doc. SCP/CARFEN/012) submitted by FMC, 27 October 2000.
- 11. Carfentrazone-ethyl: Study Title 14 C-F8426: Lysimeter Study According to BBA Guideline IV, 4-3 (1990) Subtitle: Characterization and Identification of Metabolite (M-2) from Leachate Samples (Doc. SCP/CARFEN/013) submitted by FMC, 27 October 2000.
- 12. Carfentrazone-ethyl: Overview F8426 - Sulfodeschloropropionic acid (Doc. SCP/CARFEN/014), submitted by FMC, 27 October 2000.
- 13. Carfentrazone-ethyl: Toxicity assessment of metabolite II of carfentrazone-ethyl (Doc. SCP/CARFEN/015), submitted by FMC, 27 October 2000.
- 14. Carfentrazone-ethyl: Revised final report II 14C-F8426: Lysimiter study according to BBA Guideline IV, 4-3 (1990) (Doc. SCP/CARFEN/016), submitted by FMC, 27 October 2000.
- 15. Carfentrazone-ethyl: F8426-Methyl-triazole and F8426- -Sulfodeschloropropionic-Acid Metabolites: Polarity Characteristics and Impact on their ADME Behavior (Doc. SCP/CARFEN/017), submitted by FMC, 27 October 2000.

7. ACKNOWLEDGEMENTS

The Committee wishes to acknowledge the contributions of the following working groups that prepared the initial draft opinion.

Toxicology: Prof. Maroni (Chairman) and Committee Members: Dr. Delcour-Firquet, Prof. Leszkowicz, Dr. Meyer, Dr Moretto, Prof. Petzinger, Prof. Savolainen, Prof. Silva Fernandes, Dr. Speijers, and invited expert Dr. Fait, Dr. McGregor.

Environmental assessment WG: Prof. Hardy (Chairman) and Committee members: Mr. Koepp, Prof. Papadoupoulou Mourkidou, Dr. Sherratt, Prof. Silva Fernandes, invited experts: Dr. Boesten, Dr. Carter, Dr. Forbes and Dr. Luttik.

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[1] Report 1354-073-106 - F. Schnöder (1999).
[2] OJ N° L 230, 19. 8.1991, p. 1.
[3] European Commission Co-ordination.
[4] No Observed Effect Level.
[5] The SCP has made an extensive appointment on porphyrias available on request. See Section 5 Ref. 6 & 7.
[6] Body weight.
[7] Lowest adverse effect level.
[8] No observed adverse effect levels.
[9] It is noted that the NOEL and the NOAEL have the same values.
[10] Report 1354-073-106 - F. Schnöder (1999).
[11] Study carried out with one type of soil (German soil).
[12] Study carried out with four types of soil (2 UK soils, 1 German and 1 US).
[13] Period required for 50% dissipation.
[14] Period required for 90% dissipation.
[15] Unfavourable conditions.
[16] Unfavourable conditions.
[17] Organic carbon adsorption coefficient.
[18] Predicted environmental concentrations.
[19] Limit of quantification.
[20] No observed effect concentration.
[21] M1 expressed in parent equivalent; M2 and M3 based on their molecular weight.
[22] M1 expressed in parent equivalent; M2 and M3 based on their molecular weight.
[23] See ref. 8 in Section 5.
[24] Source doc SCP/CARFEN/016.