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SCIENTIFIC COMMITTEE ON PLANTS **SCP/FLUFEN/002-Final**
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OPINION OF THE SCIENTIFIC COMMITTEE ON PLANTS ON SPECIFIC QUESTIONS FROM THE COMMISSION CONCERNING THE EVALUATION OF FLUFENACET [FOE 5043] IN THE CONTEXT OF COUNCIL DIRECTIVE 91/414/EEC

(Opinion adopted by the Scientific Committee on Plants, 27 September 2001)

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A. TITLE

OPINION OF THE SCIENTIFIC COMMITTEE ON PLANTS ON SPECIFIC QUESTIONS FROM THE COMMISSION CONCERNING THE EVALUATION OF FLUFENACET [FOE 5043] IN THE CONTEXT OF COUNCIL DIRECTIVE 91/414/EEC

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B. TERMS OF REFERENCE

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

1. Is the Committee satisfied that the relevance of metabolites M2 and M4 has been sufficiently addressed?

2. Can the Committee confirm that the operator exposure has been sufficiently addressed?

C. OPINION OF THE COMMITTEE

Question 1

Is the Committee satisfied that the relevance of metabolites M2 and M4 has been sufficiently addressed?

Opinion of the Committee:

Insufficient information is available to confirm that the relevance of the M2 metabolite has been fully addressed with regard to non-target terrestrial organisms. Insufficient information is available on environmental concentrations or the aquatic or terrestrial ecotoxicology of the metabolite M4. The SCP's own assessments indicate that the risk to non-target aquatic organisms is likely to be acceptable for M2 and M4 metabolites.

The SCP notes that the ecotoxicology data for the M9 metabolite indicates that there may be a chronic risk to aquatic organisms which has not been fully addressed by data but which appears acceptable if assumptions on the extrapolation of chronic toxicity from acute data are valid in this case. The Committee also notes that there are six other environmental metabolites, for which the risk to non-target organisms has not been adequately assessed by the notifier.

The Committee concludes that no unacceptable risks are expected from exposure via drinking water to M2 and M4.

Question 2:

Can the Committee confirm that the operator exposure has been sufficiently addressed?

Opinion of the Committee:

The Committee is of the opinion that operator risk assessment of flufenacet has been adequately addressed. Although the estimated exposure according to the UK POEM exceeds the AOEL, safe uses are identified by using the German model.

The Committee notes that the sensitising potential of the formulation deserves proper attention.

A. TITLE

REPORT OF THE SCIENTIFIC COMMITTEE ON PLANTS ON SPECIFIC QUESTIONS FROM THE COMMISSION CONCERNING THE EVALUATION OF FLUFENACET [FOE 5043] IN THE CONTEXT OF COUNCIL DIRECTIVE 91/414/EEC

B. TABLE OF CONTENTS

C. BACKGROUND

Flufenacet (FOE 5043 formerly fluthiamide) is a new active substance (a.s.) in the context of Council Directive 91/414/EEC[1]. A draft assessment report (monograph) has been prepared by the Rapporteur Member State (RMS, France) on the basis of a dossier presented by the notifier (Bayer AG). In order to prepare its opinion the Scientific Committee on Plants had access to this draft evaluation report, the evaluation table and other documents as listed below.

Flufenacet is an oxyacetamide herbicide for annual grass weeds, to be used as a single application, pre-emergence, to maize, winter cereals, soy bean and sunflowers or early (autumn) post emergence to winter cereals. It is applied at rates between 0.12-0.60 kg a.s./ha.

Source documents made available to the Committee:

1. Flufenacet: Evaluation in the context of Council Directive 91/414/EEC concerning the placing on the market of plant protection products: Terms of reference, submitted by DG Health and Consumer Protection, 7 August 2000 (SCP/FLUFEN/001).

[1] OJ N° L 230, 19. 8.1991, p. 1.

2. Flufenacet: Evaluation table Doc. 7468/VI/98 rev. 7 (12.07.00), submitted by DG Health and Consumer Protection, 7 August 2000 (SCP/FLUFEN/003).

3. Flufenacet: Addendum to the monograph, 09 addendum_2 - 29.03.99, submitted by DG Health and Consumer Protection, 7 August 2000 (SCP/FLUFEN/004).

4. Flufenacet: FOE 5053 residues in succeeding crops, submitted by DG Health and Consumer Protection, 7 August 2000 (SCP/FLUFEN/005).

5. Flufenacet: Assessment of the toxicological significance of metabolite M4 (thioglycolate sulfoxide), submitted by Bayer, 3 February 2000 (SCP/FLUFEN/006).

6. Flufenacet: Addendum to the Monograph of the active substance flufenacet, submitted by DG Health and Consumer Protection, 7 August 2000 (SCP/FLUFEN/007).

7. Flufenacet: Addendum to the monograph of Flufenacet (FOE 5043), Environmental fate, submitted by DG Health and Consumer Protection, 7 August 2000 (SCP/FLUFEN/008).

8. Flufenacet: Addendum to the monograph submitted by France (RMS), section Toxicology and metabolism, January 2001, submitted by DG Health and Consumer Protection, 25 January 2001 (SCP/FLUFEN/009).

9. Flufenacet: Danish comments 7 July 1999 (SCP/FLUFEN/010).

10. Flufenacet: RMS response to Danish comments (SCP/FLUFEN/011).

11. J.J.M. van de Sandt, *In vitro* percutaneous absorption of [phenyl-UL-14C]FOE 5043 60 WG though rat and human epidermal membranes, TNO report V99.860, 54 pages, 9 November 1999 (Property of Bayer AG).

12. W. Maasfeld, Assessment of operator exposure when applying flufenacet containing products, 24 Feb. 2000, 10 pages (Property of Bayer AG).

13. Flufenacet: Draft Assessment Report prepared by France in the context of the inclusion in Annex I to Council Directive 91/414/EEC, Volumes 1 to 3, August 1997.

D. SCIENTIFIC BACKGROUND ON WHICH THE OPINIONS ARE BASED

I. Question 1

"Is the Committee satisfied that the relevance of metabolites M2 and M4 has been sufficiently addressed?"

Opinion of the Committee:

Insufficient information is available to confirm that the relevance of the M2 metabolite has been fully addressed with regard to non-target terrestrial organisms. Insufficient information is available on environmental concentrations or the aquatic or terrestrial ecotoxicology of the metabolite M4. The SCP's own assessments indicate that the risk to non-target aquatic organisms is likely to be acceptable for M2 and M4 metabolites.

The SCP notes that the ecotoxicology data for the M9 metabolite indicates that there may be a chronic risk to aquatic organisms which has not been fully addressed by data but which appears acceptable if assumptions on the extrapolation of chronic toxicity from acute data are valid in this case. The Committee also notes that there are six other environmental metabolites, for which the risk to non-target organisms has not been adequately assessed by the notifier.

The Committee concludes that no unacceptable risks are expected from exposure via drinking water to M2 and M4.

Scientific background on which the opinion is based:

The Committee understands that the question regarding the relevance of the metabolites M2 (FOE sulfonic acid) and M4 (FOE thioglycolate sulfoxide) refers to potential residues in soil and water including groundwater since these were the two metabolites positively identified in all lysimeters leachates. Mammalian toxicology and aquatic and terrestrial ecotoxicology for these metabolites have therefore been considered by the Committee.

I.1 Formation of the metabolites

Flufenacet is photolytically stable but degrades when incorporated into soil. Laboratory DT_{50}s[2] range from 10-64 days, to higher application rates (up to 3 times the maximum field rate) being responsible for the longer half-lives. Rates of degradation at typical field application rates were 10-34 days. A total of nine metabolites were identified by the notifier in the laboratory soil or in the water sediment metabolism studies. An additional sediment water study evaluated by the RMS demonstrated that the metabolite M9 (thiadone) was present (up to 82% in water and <10% in sediment) and it was very persistent (80% remained after 55 days). M9 has therefore also been included in the Committee's assessment.

Since studies on the route of degradation indicated that the maximum % of radioactivity was <10% of the applied radioactivity, the risk to non-target organisms for the other metabolites was not considered by the RMS. Metabolites M2 and M4 were considered by the RMS as these were the main metabolites which were positively identified in all lysimeter leachates. However, in its opinion on the relevance of metabolites the SCP argued that the mammalian and ecotoxicological relevance of all metabolites should be considered (SCP, 2000).

In laboratory soil degradation studies the M2 sulfonic acid metabolite reached a maximum of 26.3% of applied dose at 100 days. Its Koc[3] indicates it is very mobile (6-19) and half-lives ranged from 189-270 days. The RMS reports that in field degradation studies only a few values of the M1 and M2 metabolites were detected above 0.01 mg/kg (the limit of determination) in the 0-10 cm layer, with a maximum value detected of 0.0208mg/kg, though it is not specified which metabolite peaked at this value. Residues remained in 0-10 cm soil layer throughout the duration of the tests but no residues were detected in deeper layers. The M4 thioglycolate sulfoxide metabolite peaked at 5.5% of the applied radioactivity at 28 days but no data have been provided concerning its sorption or persistence.

Predictive modelling, by the notifier, using PELMO (version 2.01), was carried out for the active substance and the M1 and M2 metabolites only. Concentrations of M2 ranged from 10-30 µg/L depending on the cropping scenario. These levels could be attained after one year and

[2] Period required for 50% dissipation.
[3] Organic carbon adsorption coefficient.

M2 predictions can be compared to the concentrations detected in the lysimeter studies (Table 1). The lysimeter studies were carried out in accordance with the BBA Guideline Part IV, 4-3 however rainfall and irrigation were in excess of the annual average and heavy rainfall was experienced during the main autumn/winter leaching period of the environmental studies. Predictive modelling was not carried out, by the notifier, to estimate the concentration of the M4 metabolite in leachate. The Committee could not either makes its own prediction because of the absence of the appropriate physical and chemical data necessary to run models.

Table 1 Concentrations (µg/L) of M2 and M4 metabolites in leachate from 2 replicate lysimeters –
a) Corn/corn-rotation (2x480g a.s. /ha)

	M2		**M4**	
Year 1	**Lysimeter 15**	**Lysimeter 16**	**Lysimeter 15**	**Lysimeter 16**
maximum	1.295	1.094	0.079	0.036
mean	0.573	0.474	0.016	0.014
Year 2				
maximum	n/r	n/r	n/r	n/r
mean	0.237	0.149	0.020	0.015

b) Corn/winter wheat rotation (480+180g a.s./ha)

	M2		**M4**	
Year 1	**Lysimeter 17**	**Lysimeter 19**	**Lysimeters 17&18**	
maximum	3.4	3.7	0.028*	
mean	1.42	1.69	0.029*	
Year 2				
maximum	n/r	n/r	n/r	
mean	0.015*		0.020*	

* Reported value for both lysimeters for the year – results not fully described in the RMS monograph - n/r, not reported.

M2 and M4 metabolites were positively identified in the leachate samples for both studies and their concentrations reported. However the RMS noted that M3, the FOE alcohol, was also positively identified in one corn/wheat rotation lysimeter at a maximum concentration of 0.16 µg/L but no further assessments of its fate or relevance were made. The M2 metabolite leached to a depth of 1.2 m with a maximum concentration 3.7 µg/L. The M4 metabolite was identified at a maximum concentration of 0.079 µg/L.

I.1.1 *Relevance of lysimeter study*

The lysimeter study was carried out in accordance with the BBA guidelines using a sandy loam soil which is likely to have a pH of approximately 6.5 or less. The sulfonic acid metabolite (M2) is expected to be more mobile in neutral or alkaline soils. It is the Committee's opinion that the maximum concentrations identified in the lysimeter studies may not represent a worst case scenario. The PELMO modelling predictions consider a range of application rates and crop uses but use only one soil type (Borstel, sandy loam). However,the specific choice of input parameters or soil properties are not reported by the RMS. Predicted results for the M2 metabolite are an order of magnitude greater that those monitored in the lysimeter study. Since there are no lysimeter data to represent the worst case scenario (soil pH>7.0), the Committee believes that a conservative approach which uses the maximum PELMO predicted M2 concentration of 30 µg/L should be adopted for use in toxicological assessments. The maximum concentration of 3.7 µg/L detected in the lysimeter study can only be used to represent a sandy loam/pH<7.0 scenario.

The sulfoxide metabolite (M4) is also expected to be more mobile in neutral or alkaline soils and it is the Committee's opinion that the maximum concentrations identified in the lysimeter studies may not represent a worst case scenario. No predictive modelling was carried out for the M4 metabolite and the same conservative approach of using the PELMO data used for M2 cannot be applied. The Committee is aware that the M2 and M4 metabolites have similar structures and consider that it would be acceptable to assume that the order of magnitude difference observed for M2, between lysimeter and predictive modelling data, can also be applied to the M4 metabolite. A concentration of 0.64 µg/L would therefore represent a conservative value for the M4 metabolite and the Committee recommends it should be used in toxicity assessment.

I.1.2 *Water sediment study*

The metabolism of the active substance in water sediment studies was found to involve the same steps as in soil and the RMS concluded that there were no relevant metabolites (i.e. >10%). The SCP has identified that the formation of 5 of the metabolites may not have peaked during the duration of the study since their maximum values were recorded at the last sampling date of 157 days.

A new sediment/water study (from the evaluation table, SCP/FLUFEN/003) identified that thiadone (M9) was the only metabolite found >10%, up to 82% in water after 55 days but < 10% in sediment. The M9 metabolite persisted in water, 52-65% remained after 156 days. M2 and M4 together also reached maximum levels in the water phase, of 4.4% after 156 days (3% and 1.4%, respectively).

I.1.3 *Summary of the environmental concentrations of M2 and M4 metabolites*

Estimated concentrations of the M2 and M4 metabolites in the different environmental compartments are required in order to determine their mammalian and ecotoxicological relevance. Table 2 summarises the concentrations used by the SCP to form its opinion.

Table 2 Concentrations used for toxicological assessments in this opinion.

	M2	**M4**	**M9**
Soil	0.0208 mg/kg	0.0208 mg/kg	-
Groundwater PELMO sandy loam pH<7.0	 30 µg/L 3.7 µg/L	 0.64 µg/L 0.079 µg/L	
Surface water Drift from PELMOgw	 0.24 µg/L 30 µg/L	 0.16 µg/L 0.64 µg/L	 6.4 µg/L -

In the data of the field dissipation studies, no details are provided concerning the concentrations of the M2 or M4 metabolites in topsoil. The maximum value reported for M1/M2 (not specified by the RMS) is therefore used by the SCP *i.e.* 0.0208mg/kg.

The maximum concentration estimated in leachate in the PELMO simulations was 30 µg/L for the M2 metabolite. This value was used for drinking water and aquatic toxicology assessments. A concentration of 0.64 µg/L is proposed for the M4 metabolite based on assumptions of its similar structure, properties, the ratio of lysimeter and predictive modelling concentration data to metabolite M2.

No predictions for metabolite concentrations in surface water arising from spray drift or other routes of entry were made by the notifier. The concentrations identified in the preceding paragraph for M2 and M4 are used, assuming that the route of entry is via drainage. In structured, artificially drained soils where by-pass flow occurs, the predicted concentrations of M2 and M4 are likely to be higher. For spray drift, the SCP calculated the PEC's[4] in Table 2 using the following standard assumptions: an application rate of 0.6 kg/ha; a drift rate at 1 m distance = 4%; water depth 30 cm; M9 ~ 80% of a.s.; M2 ~ 3% of a.s.; M4 ~ 2% of a.s..

I.2 Ecotoxicological relevance of the metabolites

I.2.1 *Aquatic organisms*

The lysimeter studies indicate that the M2 metabolite is mobile and it therefore could be present in surface waters (from surface runoff or drainflow). Acute toxicological data using the base set of organisms and *Lemna gibba* show that the NOEC[5] is >87 mg/L, indicating that M2 is far less toxic than the parent compound and therefore there are no concerns for aquatic organisms at the concentrations predicted to enter surface waters (maximum 30 µg/L from PELMO for M2). TER[6] values >23000 are indicated.

No physico-chemical data are available concerning the properties of the M4 metabolite but the SCP believes that data can be expected to be similar to that of M2, because both occur in leachate and the molecule structures are quite similar. Based on similar molecule structure and fate properties (i.e., sorption, water solubility), similar uptake and ecotoxicological properties could be assumed. However, no assessment of its ecotoxicological relevance has been submitted by the notifier.

Acute aquatic toxicology data are provided for the base set of organisms for thiadone (the M9 metabolite):
- *Oncorhynchus mykiss* LC_{50}[7] (96 h) = 9.1 mg thiadone/L;
- *Daphnia magna* EC_{50}[8] (48 h) = 31.7 mg thiadone/L;
- *Selenastrum capricornutum* EbC_{50}[9] (72 h) = 4.1 mg thiadone/L.

With appropriate mitigation (1 m buffer zone), the SCP considers that the short-term risk for M9 is acceptable, given the TER's of 640 (*Selenastrum*) to 5000 (*Daphnia*). However, the new sediment study (SCP/FLUFEN/003, 2.2) indicates that this metabolite is very persistent in the water phase (max. 82 % after 55 days and 52-65 % after 156 days) but no data have been presented for its chronic impact on aquatic organisms. Assuming an acute/chronic ratio of 10 (as is the case for the parent molecule), TERlt's[10] of approximately 50-500 are calculated which appear acceptable. The Committee thus confirms the assessment of the RMS (SCP/FLUFEN/003 p.38) if the assumption on the extrapolation of chronic toxicity from acute data valid.

The Committee has made no assessment for the remaining metabolites the relevance of which could be addressed in accordance with the principles laid down in the Opinion of the

[4] Predicted Environmental Concentration.
[5] No Observed Effect Concentration.
[6] Toxicity Exposure Ratio.
[7] Lethal concentration, median.
[8] Median effective concentration.
[9] Median effective concentration (based on biomass).
[10] Long term Toxicity Exposure Ratio.

Scientific Committee on Plants on the draft guidance document on relevance of metabolites (SCP, 2000). The Scientific Committee on Plants has also published a detailed opinion on imazosulfuron and the relevance of its metabolites (SCP, 2001) which could also be referred to as a model for interpretation.

I.2.2 *Terrestrial organisms*

M2 is very persistent (half-life 189-270 days) in laboratory studies, and therefore both acute and earthworm reproduction studies should have been triggered but no case was presented for only submitting an acute study. The SCP notes that field dissipation and lysimeter studies indicated that a more rapid dissipation was taking place than in the laboratory studies and that under field soil conditions, concentrations of concern were not being detected even with the highest use scenario (2x 480 g a.s./ha application). The maximum concentration identified in field studies was 0.0208 mg/kg. Exposure to non-target organisms is therefore considered to be low and acute toxicity to earthworms is also very low (LC_{50} >1000 mg/kg); thus a reproduction study was not subsequently triggered. However, the acute and long-term impact of the M2 metabolite on other indicative non-target soil invertebrates was not considered and a reasoned case should be made to assess this risk. No data are available for M4 concentrations in soil, and a reasoned case should be submitted concerning the risks to non-target soil organisms. The thiadone M9 metabolite was not identified in soil dissipation studies (detection limit 0.01mg/kg) and therefore exposure to non-target organisms is unlikely.

The Committee has made no other assessments for the remaining metabolites the relevance of which could be addressed in accordance with the principles laid down in the Opinion of the Scientific Committee on Plants on the draft guidance document on relevance metabolites (SCP, 2000). The Scientific Committee on Plants has also published a detailed opinion on imazosulfuron and the relevance of its metabolites (SCP, 2001) which could also be referred to as a model for interpretation.

I.3 Toxicological relevance of the metabolites

M2 is found in soil and in the lysimeter leachate and thus has the potential to reach groundwater. On the basis of the lysimeter test the level of M2 in groundwater is equal to or lower than 3.7 µg/L (see Table 1). Assuming an average intake of 2 litres of drinking water/day, this corresponds to a daily exposure of 7.4 µg/person. The Committee considers that this estimate may not be representative of a worst case scenario and therefore the maximum concentration predicted by the PELMO model, 30 µg/L should also be considered to represent scenarios which may give rise to higher concentrations of M2 in the leachate (Table 2). Assuming an average intake of 2 litres of drinking water/day, this corresponds to a daily exposure of 60 µg/person.

M2 is not a major metabolite in mammals, it is present at 0.5 – 1.0% of the total of administered parent compound. However, as M2 is the sulfonic acid metabolite of the parent compound which makes the compound more water soluble, it is unlikely that this metabolite is more toxic than the parent compound.

Taking the ADI[11] of flufenacet (0.01 mg/kg bw/day) as representative for M2 and assuming that the intake from drinking water does not exceed 10% of the ADI, the maximum acceptable

[11] Acceptable Daily Intake.

daily intake via drinking water is therefore 1 µg/kg bw or 60 µg/day equal to the conservative estimate of daily exposure based on PELMO calculations (60 µg/day).

M4 is detected at levels up to 0.079 µg/L in the lysimeter tests which represents a potential daily intake of 0.158 µg/L/person. The Committee considers that this estimate may not be representative of a worst case scenario and therefore a maximum concentration of 0.64 µg/L should be used (see section I.1.1). Assuming an average consumption of 2 litres drinking water/person/day, the exposure is 1.3 µg/person/day which is below the threshold of toxicological concern[12] (1.5 µg/person/day, SCP (2000)).

The Committee concludes that no unacceptable risks are expected from exposure via drinking water to M2 and M4.

I.4 Conclusion

Information concerning the relevance of the M2 and M4 metabolites is incomplete. In this opinion, the Committee has considered the information available.

Insufficient information is available to confirm that the relevance of the M2 and M4 metabolites has been fully addressed with regard to non-target terrestrial species. Insufficient information is available concerning the aquatic ecotoxicology of the metabolite M4. The SCP's own assessments indicate that the risk to non-target aquatic organisms is acceptable for M2 and M4 metabolites. The SCP considers that the short-term risk for M9 is acceptable but the SCP notes that ecotoxicology data for the M9 metabolite indicates that there may be a chronic risk to aquatic organisms but this has not been assessed. The Committee also notes that there are a total of six other environmental metabolites, for which the risk to non-target organisms has not been adequately assessed by the notifier.

With respect to human exposure via drinking water, the Committee concludes that no unacceptable risk are expected from exposure via drinking water to M2 and M4.

II. Question 2

Can the Committee confirm that the operator exposure has been sufficiently addressed?

<u>Opinion of the Committee:</u>

The Committee is of the opinion that operator risk assessment of flufenacet has been adequately addressed. Although the estimated exposure according to the UK POEM exceeds the AOEL, safe uses are identified by using the German model.

The Committee notes that the sensitising potential of the formulation deserves proper attention.

[12] Dose of a chemical in the diet that is consumed at levels below which this threshold (value) poses no appreciable risk. - ILSI Europe Report Series. August 2000. Threshold of Toxicological Concern for Chemical Substances Present in the Diet. Report of a workshop held on 5-6 October 1999 in Paris, France. Organised by ILSI Europe Threshold of Toxicological Concern Task Force.

Scientific Background on which the opinion is based:

The SCP understands that the question should address the health risk associated with operator exposure, and not merely the exposure assessment.

II.1 Toxicity profile

Flufenacet has a low to moderate acute oral toxicity to mice and rats, and a low acute dermal and inhalation toxicity. It is not irritant, and the skin sensitisation tests showed equivocal evidence of allergenic potential (the M&K test was positive, the Buehler test negative). The overall toxicological evaluation shows no evidence of reproductive toxicity, teratogenicity, embryotoxicity, mutagenicity, carcinogenicity. Chronic feeding studies in dog and rat showed structural or functional alterations in liver, kidney, haematology, spleen, and thyroid. Flufenacet induces neuropathogical changes in the brain and spinal cord (axonal swelling) in rat and dog. The overall evaluation of the observed changes demonstrates that these effects occur only after repeated and prolonged exposure to high dose levels of flufenacet, which saturate metabolic pathways, and exceed the animal capacity to rapidly metabolise and excrete it. The liver was considered the primary target organ, with increases in organ weight, cell size and number, and/or associated changes in liver function tests.

The WG 60 formulation is not irritant to the skin, slightly irritant to the eyes and has a skin-sensitising potential (Buehler test).

II.2. Acceptable Operator Exposure Level

During the ECCO[13] peer review, a systemic AOEL[14] of 0.017 mg/kg bw was set, based on the NOAEL[15] of 1.67 mg/kg bw in the 90-day study in dog, and a safety factor of 100. The effects observed at the LOAEL[16] of 6.9 mg/kg bw were clinical chemistry changes in liver function parameters, decrease in serum thyroxine secondary to increased hepatic clearance, increased relative kidney weight, and spleen pigment. The toxicity profile of flufenacet was addressed in a proper way, and the Committee agrees with the NOAEL selected for AOEL setting.

II.3 Operator Exposure

Flufenacet is applied by spray application with standard field sprayers at a rate of 0.12-0.6 kg a.s./ha. Operator exposure was estimated on the basis of the UK POEM[17] and the German model for tractor-mounted applications in field crops, assuming a maximum application rate of 600 g a.s./ha (corn, soybean, sunflower), and a work-rate of 20 ha/day (German model) or 50 ha/day (UK POEM). The AOEL was exceeded only with the UK POEM, under the assumption of a 10% dermal absorption default value.

A comparative human/rat *in vitro* percutaneous absorption study was subsequently performed to refine exposure estimates using a radiolabelled formulation identical to the commercially available product, at different concentrations. The results showed that human epidermal membranes were at least three times less permeable than rat epidermal membranes. Skin absorption in humans was estimated at 3% and 20% of the applied dose for the undiluted and

[13] European Commission Co-ordination.
[14] Acceptable Operator Exposure Level.
[15] No Observed Adverse Effect Level.
[16] Lowest Observed Adverse Effect Level.
[17] Predicted Operator Exposure Model.

diluted product, respectively. The new evaluation reported in the Addendum to the Monograph (SCP/FLUFEN/009) shows that the estimated exposure was acceptable according to the German Model, under the assumption that PPE[18] is worn. With the UK POEM, the calculated exposure was about 417% of the AOEL, even if using PPE, for a maximum application rate of 0.6 kg a.s./ha (corn, soybean, sunflowers), and about 166% of the AOEL for a maximum application rate of 0.24 kg a.s./ha (winter cereals).

Given that a single standardised European model for operator exposure assessment is not yet available, and also considering the large experience in the use of the German and UK models, each of these models can be used to assess operator exposure in Europe. On the other hand, it should be noted that modelling implies data, probabilistic evaluations, and assumptions, and that these models are based on schematic scenarios, which do not always represent all possible European scenarios of exposure. The evidence of different exposure estimates provided by the German and UK models is not unusual, and is due to differences in the database, in the probabilistic approach, and in the underlying assumptions.

II.4 Conclusion

The Committee is of the opinion that operator risk assessment of flufenacet has been adequately addressed. Although the estimated exposure of flufenacet exceeds the AOEL according to the UK POEM, safe uses are identified by using the German model.

The Committee notes that the sensitising potential of the formulate should receive proper attention.

E. REFERENCES

SCP, 2000: Opinion of the Scientific Committee on Plants regarding the Draft guidance document on relevant metabolites (SANCO/221/2000-Rev.2, October 1999) (Opinion adopted by the SCP on 30 November 2000), http://europa.eu.int/comm/food/fs/sc/scp/out82_ppp_en.html

SCP, 2001: Opinion of the Scientific Committee on Plants regarding the evaluation of Imazosulfuron (TH-913) in the context of Council Directive 91/414/EEC concerning the placing of plant protection products on the market (Opinion adopted by the SCP on 25 April 2001) http://europa.eu.int/comm/food/fs/sc/scp/out103_ppp_en.pdf

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Toxicology assessment WG: 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 experts Dr. Fait, Dr. McGregor.

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

[18] Personal Protection Equipment.