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OPINION ON 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 Scientific Committee on Plants on 25 April 2001)

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1. TITLE

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 expressed by the Scientific Committee on Plants, 25 June 2001)

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:

"Can the Committee comment on the relevance of the metabolite IPSN due to its presence in soil and water?"

3. BACKGROUND

Imazosulfuron (TH-913) is a new active substance (a.s) in the context of Council Directive 91/414/EEC[1]. The draft Commission Directive for the inclusion of imazosulfuron 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 (Germany) based on a dossier submitted by the notifier (Takeda Chemical Ltd representated by Urania Agrochem Gmbh), a review report prepared by the Commission and the Recommendations of the ECCO[2] Peer Review Programme.

Imazosulfuron is a herbicide of the sulfonylurea class. It is intended for use in cereal crops (wheat, barley, rye and triticale) for the control of broad leaved weeds in autumn or spring. The rate of use ranges from 25 g a.s/ha to 50 g a.s/ha.

4. OPINION

Question

"Can the Committee comment on the relevance of the metabolite IPSN due to its presence in soil and water?'

Opinion of the Committee:

The metabolite IPSN was not identified in the leachates of the lysimeter study. The Committee considers therefore that no significant health risk is likely to arise from this metabolite in ground water.

[1] OJ N° L 230, 19. 8.1991, p. 1.
[2] European Commission Co-ordination.

The Committee considered that existing studies provide an adequate margin of safety regarding the risks from IPSN to soil micro-organisms, aquatic invertebrates and fish, and the acute risks to earthworms.

The Committee considered that further information was required to assess other risks from IPSN, to ground-dwelling predatory arthropods, soil macro-organisms, higher aquatic plants and sediment-dwelling organisms, and also the chronic risks to earthworms. These conclusions are based on worst-case exposure estimates (including overspray of surface water) and may need to be adjusted if risk mitigation measures are applied.

The Committee considered that there is a concern about risks to non-target plants from the parent molecule and/or its metabolites including IPSN. Therefore, an appropriate assessment of these risks should be conducted using existing data. The Committee also considered that the risks to mammals and birds from metabolites present in or on potential feed items should be fully assessed.

The Committee notes that other metabolites were formed in some studies, sometimes at levels comparable to IPSN. Risks from these metabolites should be addressed.

SCIENTIFIC BACKGROUND ON WHICH OPINION IS BASED:

4.1 Approach taken in assessing metabolites

In forming its opinion the Committee applied the principles and approaches published in its earlier opinion on the Guidance document on relevant metabolites (SCP, 2000b).

Specifically, the Committee first considered the potential for exposure of non-target organisms to IPSN in soil and water, by all possible routes. It then used a risk-based approach to assess the potential significance of those exposures, applying the same procedures as would be used for the active substance (including consideration of both acute and long-term risks for a range of organisms). Where possible, the Committee considered whether risks from metabolites could be addressed using existing information such as the likely level of exposure, the molecular structure of the metabolites, the ecotoxicological profile of the active substance, the occurrence of the metabolites in existing tests with the active substance, and general knowledge on the relationship between the toxicity of metabolites and their parent substances (SCP, 2000b).

The Committee intends this opinion should be used as an example for future reference.

4.2 Fate and Behaviour assessment

4.2.1 Soil metabolism and degradation rates in laboratory studies

Half-lives of imazosulfuron of about 25 and 50 days were found in laboratory studies with two aerobic soils (one at 20^{o}C and one at 30^{o}C). In these studies the following metabolites were formed:

– IPSN (2-chloroimidazo(1,2-a)pyridin-3-yl-sulfonamide);

– HMS 1-[2-chloroimidazo(1,2-a)pyridin-3-yl-sulfonyl]-3-(4-hydroxy-6-methoxy-pyrimidine-2-yl)urea;

– ADPM (2-amino-4,6-dimethoxypyrimidine).

For the metabolite IPSN maximum percentages of 26-47% were found and for HMS and ADPM these values were 4-6% and 5-8%. Maximum percentages of soil bound residues were 30-50% for a radioactive label in the imidazole ring and 39-67% for a label in the pyrimidine ring.

The Committee estimated that the half-life of IPSN exceeded 100 days in these two soils (almost no measurable decline in IPSN was found).

The formation of considerable percentages of IPSN was confirmed in an aged-residue leaching study with four relevant soils: at the end of the study (after 30 days of incubation and 1 day of leaching), the total amount of IPSN was 25-43% of the applied radioactivity.

4.2.2 Sorption and mobility

Sorption studies with imazosulfuron resulted in K_{OC}[3] values of 174-215 L/kg. No sorption data are available for IPSN. The Committee estimated from aged residue leaching studies with four relevant soils that the K_{OC} of IPSN is higher than 300 L/kg for soils with pH values not exceeding 6.

4.2.3 Field persistence studies

Nine field persistence studies were carried out in Germany after spraying imazosulfuron (as a wettable powder) in autumn or winter to bare soil (plot size was 20 m^2). Soil was sampled at a number of times up to 276 days after application. The number and size of soil samples, and the pH of the soils were not reported. In five studies only the parent compound was followed and in the remaining four also the metabolites IPSN, HMS and ADPM at one or two sampling dates. In the first five studies the dose was 50 g/ha and in the remaining four the dose was 100 g/ha.

Several problems of interpretation arise from these studies:

1. In the first study, the total amount of imazosulfuron recovered from the 10-30 cm layer was higher than the total amount recovered from the 0-10 cm layer in the soil samples taken immediately after spraying. This indicates a serious flaw in either sampling or analytical procedures. The Committee estimated the total amount recovered from soil immediately after spraying assuming a dry bulk density in the top 5 cm of 1.3 kg/L and using the reported recovery percentage of 81%. This amount was found to be 260%.

2. The Committee estimated also the total amounts of imazosulfuron recovered immediately after spraying for the other eight studies and found a range from 40 to 150% and an average of 70%.

3. DT_{50}[4] values of imazosulfuron from these field studies were reported to range from 8 to 91 days. These DT_{50} values were based on only part of the sampled layers (e.g. 0-5 cm layer) whereas the results indicated leaching to deeper sampled layers. Therefore these DT_{50} values include losses resulting from imazosulfuron leaching.

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

In the last four studies soil samples were analysed for ADPM, IPSN and HMS at one or two sampling dates. All measurements were below the detection limits of these compounds (0.003 mg/kg for IPSN). A detection limit of 0.003 mg/kg of IPSN is equivalent to a total amount of imazosulfuron of 8 g/ha in a 10-cm thick soil layer (considering the difference in molar mass, an extraction efficiency of 87% and assuming a dry bulk density of 1.3 kg/l). The average recovered dose of imazosulfuron immediately after application was about 70 g/ha. So if IPSN had been formed in significant amounts in these field persistence studies and if it were persistent, it should have been detected given the estimated K_{OC} values. This is in conflict with the results of laboratory studies with six soils in which maximum levels of IPSN of 25-47% of the dose were detected as described in Section 4.2.1. However, at the same time such a large discrepancy between soil metabolism in laboratory and field studies is unlikely.

Because of these difficulties, the Committee considered the results of the field studies to be unreliable. It therefore decided to use the results of the laboratory studies when estimating predicted concentrations (see below).

4.2.4 Leaching to groundwater

A lysimeter study was conducted in which 50-100 g/ha imazosulfuron was applied in November (triplicate lysimeters). The organic carbon content of the soil was 1.3% in the top 30 cm and 0.1-0.2% below. The soil pH was 5.6-5.8. The cumulative percolated amount of water was on average 410 mm in the first year, 360 mm in the second year and 220 mm in the third year. Lysimeter 1 received imazosulfuron at a rate of 100 g/ha with radiolabel in the imidazole ring. Lysimeter 2 received imazosulfuron at a rate of 50 g/ha with radiolabel in the pyrimidine ring. Lysimeter 3 received imazosulfuron at a rate of 50 g/ha with a 1:1 mixture of the two radiolabels. The metabolites IPSN, IPSA and HMS contain the imidazole ring and the metabolites ADPM and HMS contain the pyrimidine ring. The following table shows the average radioactivity concentrations in the leachate expressed in µg/L as imazosulfuron equivalents:

	Lysimeter 1	Lysimeter 2	Lysimeter 3
Year 1	0.08	<0.01	0.03
Year 2	0.05	<0.01	<0.01
Year 3	0.17	<0.01	<0.01

In the first two years imazosulfuron was detected in the leachate but concentrations were below 0.02 µg/L. In the last year the average imazosulfuron concentration in the leachate of lysimeter 1 was 0.06 µg/L. The metabolite IPSN was never detected in the leachate (detection limit not reported). The metabolite ADMP could not be detected because equivalent concentrations of the pyrimidine label never exceeded 0.01 µg/L. The metabolite IPSA was not detected in the first two years but it was detected in the third year at an average concentration in the leachate of lysimeter 1 of 0.01 µg/L. The metabolite HMS was detected in the third year at an average concentration in the leachate of lysimeter 1 of 0.02 µg/L. Three unknown metabolites (no properties available) were detected in the third year at average concentrations in the leachate of lysimeter 1 of 0.04, 0.02 and 0.01 µg/L.

IPSN was detected in the soil profile at the end of the lysimeter study three years after application. The report implies that the average content of IPSN in the top 40 cm was 1.2 µg/kg for a imazosulfuron dose of 100 g/ha. Assuming a dry bulk density of 1.4 kg/L, this corresponds with 6.7 g of IPSN per ha. Accounting for the difference in molar mass between imazosulfuron and IPSN, this would correspond with about 13% of the radioactivity dose. However, the report states also that total extractable radioactivity was 15% for the 0-40 cm layer whereas less than 50% of these 15% appeared to be IPSN. Irrespective of this uncertainty, the lysimeter study demonstrated that in the order of 10% of the dose was still present as IPSN three years after application which supports the high percentages of IPSN formed in the laboratory studies.

4.2.5 Estimated contents of IPSN in soil based on worst-case assumptions for persistence in soil

The Committee estimated contents of IPSN in the plough layer based on worst-case assumptions:

1. imazosulfuron is applied each year to bare soil at a dose of 50 g/ha over a period of 10 years;

2. IPSN does not disappear from the 0-25 cm plough layer (so no degradation, leaching, uptake etc.);

3. 50% of the imazosulfuron molecules are transformed into IPSN;

4. the plough layer is 25 cm thick and has a dry bulk density of 1.3 kg/L.

These assumptions result in an average content in soil of 0.04 mg/kg IPSN at the end of this 10-year period.

The Committee acknowledges that IPSN was not detected in soil in the field persistence studies but considers this result unreliable because (a) 25-47% of IPSN was formed in laboratory studies with six soils and (b) about 10% of the dose was still present as IPSN at the end of a three-year lysimeter study.

4.2.6 Fate in surface water

Hydrolysis studies in buffers showed that IPSN and ADPM are formed quantitatively out of imazosulfuron: 1 molecule of imazosulfuron results in 1 molecule of IPSN and 1 molecule of ADPM. Half-lives for hydrolysis of 27 days at pH=5 and of about 400 days at pH=7 were found at 25^{o}C.

A photolysis study in a buffer and in natural river water of pH=7.6 showed rapid photolysis (half-lives of about 3 h). Five transformation products were detected but no IPSN.

The metabolism of imazosulfuron was studied in a water-sediment system in the dark at 20^{o}C. The sediment was a sandy loam with a pH-H_2O of 7.6. The dose of imazosulfuron and the solid-liquid ratio of the water-sediment system were not reported. A half-life of imazosulfuron for the whole system of about 25 days was found. The maximum percentages of IPSN in water and sediment were 0.8% and 1.7%, respectively (found after 59-120 days). The main transformation product was soil-bound residue (79% for radioactive label in imidazole ring and 85% for radioactive label in pyrimidine ring). The

metabolism of imazosulfuron was also studied in a water-sediment system in the dark at 20°C but now using a sandy sediment with a pH of 7.5 and only 0.1% organic carbon and 0.5% clay. In this system, the transformation rate of imazosulfuron was slow (at the end after 120 days 83% of imazosulfuron was still remaining). The maximum percentages of IPSN in water and sediment were 5% and 1.0%, respectively (found after 120 days).

4.2.7 Estimated concentrations of IPSN in surface water and sediment based on worst-case assumptions

In principle, IPSN may reach surface water via drainage, runoff, spray drift or overspray (e.g. in the case of aerial application). IPSN is very persistent in soil and there is only information about its mobility for soils with pH below 6 (via the aged-residue leaching studies and the lysimeter study). So drainage cannot be excluded; but it is difficult to quantify in view of the lack of information about the mobility of IPSN. Given the persistence in soil, runoff can also not be excluded but is similarly difficult to quantify (e.g. because of the limited experience with estimating runoff of soil metabolites). The Committee assumed tentatively that 1% of the amount of IPSN present in soil will reach surface water resulting from a worst-case runoff or drainage event (e.g. via preferential flow of pesticide through macropores) and that this happens in a water layer of 5 mm. Assuming 25% formation of IPSN from a dose of 50 g/ha, gives 7 g/ha of IPSN. This results in a concentration of 1.4 µg/L in these 5 mm of water which will of course be diluted when reaching surface water.

In view of the rapid photolysis it is unlikely that hydrolysis is an important process in surface water. As described above, the metabolic pathway derived from the photolysis study implies that IPSN is not formed as a result of this process. Therefore it is most likely that levels of IPSN formed in surface water or sediment as a result of spray drift or overspray will be below the limit of detection. However, there is uncertainty when extrapolating transformation rates in photolysis studies with water from laboratory to field conditions. For instance, imazosulfuron is moderately sorbed so within a few hours at least a few percent will sorb to plant or sediment surfaces which may stop the photodegradation. In the absence of a higher tier study to confirm the possible absence of IPSN in water and sediment in natural conditions, the Committee used the result of the available water sediment studies.

Therefore the Committee estimated IPSN concentrations in surface water and sediment resulting from overspray (given the absence of information on the method of application, e.g terrestrial or aerial, overspray is considered as a worst case scenario) using the following worst-case assumptions derived from direct spray:

1. The full application rate of 50 g/ha reaches the surface water (i.e. overspray).

2. The maximum percentages of IPSN formed in the water-sediment studies are used. It is assumed that the maximum formed in the water (5%) is present in a 30-cm thick surface water layer and that the maximum formed in the sediment (1.7%) is present in a 0-5 cm thick sediment layer with a dry bulk density of 0.5 kg/L.

These worst-case assumptions result in a concentration in surface water of about 0.4 µg/L and in a sediment content of 2 µg /kg.

The Committee concluded that worst-case concentrations in surface water estimated for drainage, runoff and overspray are within a factor of ten of one another (0.4 µg/L for

overspray and 1.4 µg/L for runoff and drainage). Because the assumptions made for runoff and drainage were more tentative than those for overspray, the Committee decided to use the estimates derived from overspray in assessing risks to aquatic and sediment-dwelling organisms.

4.3 Ecotoxicological risk assessment

4.3.1 Risks to non-target organisms due to the presence of IPSN in soil

The extent to which IPSN is formed and its persistence indicate that exposure of soil organisms will occur, with a worst-case PEC_s[5] of 0.04 mg/kg IPSN after 10 years. The consequent risks should therefore be assessed (SCP, 2000b).

The toxicity of IPSN to soil organisms has not been tested. The Committee therefore considered whether other information on structure of the metabolite or on ecotoxicity of the parent substance could be used to address the risk of IPSN.

No conclusion could be reached based on the structure of the metabolite. IPSN is formed by splitting the parent molecule into two parts and contains the imidazole ring from the parent molecule. There is insufficient information concerning the parent molecule's mode of action for non-target organisms to draw any conclusions regarding the ecotoxicity of IPSN.

Other lines of evidence regarding the ecotoxicity of IPSN were considered for each of the groups of organisms which are likely to be exposed to the metabolite in soil, i.e. earthworms, soil-dwelling predatory arthropods, soil macro-organisms, soil micro-organisms and non-target terrestrial plants.

Earthworms

The Committee considered the occurrence of IPSN in existing studies with the active substance. Acute toxicity studies for the parent molecule with earthworms lasted 14d at a range of concentrations up to 1000 mg a.s./kg, and no adverse effects were seen. The actual concentrations of IPSN in these studies were not measured. To provide a margin of safety of 10x, 50% mortality should not occur at concentrations up to 0.4 mg IPSN/kg (i.e. 10x the worst case PEC for IPSN in soil). At the highest concentration tested, this would require 0.04% of the parent molecule to be metabolised to IPSN. The Committee briefly assessed how quickly such a concentration would have been formed in the toxicity studies[6]. The Committee concluded that the required concentration would be formed within 1.1 days, i.e. with 13 days of the test remaining. Given that no mortality was seen at the highest concentration and only incidental mortality at lower concentrations, the

[5] Predicted Environmental Concentration in soil.

[6] There is one study with a Japanese soil that shows no effect of sterilisation on degradation rate of imazosulfuron. IPSN is thus probably formed via an abiotic process in soils (possibly hydrolysis). Half-lifes of imazosulfuron are 25-50 days at 20-30 °C and percentages of IPSN formed are 25-45%. The Committee made the conservative assumptions that, in the test soils, the half-life of imazosulfuron in the earthworm study was 100 days, 10% of the imazosulfuron molecules transform into IPSN and IPSN does not degrade. The time needed to form 0.4 mg/kg IPSN can be calculated from $M = f\ D\ (M1/M2)\ (1-\exp(-kt))$ where M is content IPSN (mg/kg), f is fraction IPSN formed (0.1), D is dose of parent compound (mg/kg), M1 and M2 are molar masses of IPSN and parent respectively (219.6 and 412.8 g/mol), k is degradation rate coefficient of imazosulfuron and t is time. This indicates that the required concentration would be formed within 1.1 days.

Committee considers that the existing studies provide an adequate margin of safety regarding the acute toxicity of IPSN to earthworms.

However, an analogous argument cannot be made for chronic risks to earthworms because an earthworm reproduction study has not been conducted with the parent compound. Nor can any conclusion be reached from other existing information (e.g. there is no established relation between the toxicity to earthworms of metabolites and their parent compound). Given the high proportions of IPSN that may be formed, and its persistence, chronic exposure is to be expected. Therefore, an appropriate earthworm reproduction study is required to enable an assessment of chronic risk from IPSN.

Ground-dwelling predatory arthropods

Tests with ground-dwelling predatory arthropods (*Poecilius cupreus* and *Aleochara bilineata*) indicated a low risk when the parent molecule was applied at the maximum proposed rate (50g a.s./ha). There was no information on the extent to which IPSN was formed under the test conditions, nor any other existing information on which to base an assessment. The Committee therefore considers that further information is required to assess the risk to ground-dwelling predatory arthropods. This might take the form of (a) a reasoned assessment of the levels of IPSN formed in the existing studies, (b) new studies with IPSN, or (c) new studies with the parent molecule in which relevant levels of IPSN are confirmed by measurement.

Soil macro-organisms

Effects of the parent molecule on other soil macro-organisms have not been tested. The Rapporteur Member State considered such tests unnecessary because the DT_{90}[7] of the parent molecule in field studies was <365 days, the trigger specified in Annex III point 10.6.2 for requiring additional data for soil organisms that contribute to organic matter breakdown (soil mesofauna and macrofauna). However, laboratory and lysimeter studies (summarised above) show that IPSN is very persistent in soil, and on the basis of these data the Committee considered it likely that the DT_{90} for IPSN exceeds 365 days. Since no existing information was available which could be used to assess the risks to soil macro-organisms, the Committee concluded that an appropriate study should be conducted.

Soil micro-organisms

Tests with soil micro-organisms were conducted with imazosulfuron in two soils (loamy sand and clay silt) and found no unacceptable effects after 28d. The duration of these studies was rather short for an assessment of IPSN given its slow rate of formation. However, the studies included application rates up to 500g a.s./ha, i.e. ten times the proposed maximum. The Committee considered that the amounts of IPSN formed at the highest application rates would have reached sufficient levels to conclude that significant effects are unlikely when imazosulfuron is applied at the proposed maximum rate. There are shortcomings in the study design used (European Commission, 2000). However, the Committee considered it unlikely that further studies with IPSN would give different results. The Committee concluded no further assessment of risks to soil micro-organisms is required.

[7] Period required for 90% dissipation.

Non-target terrestrial plants

The guidance document on terrestrial ecotoxicology (European Commission, 2000) states that where there is concern about risks to non-target plants, a qualitative risk assessment based on available data should be conducted. The draft evaluation report states that, in efficacy tests, imazosulfuron showed a long-lasting effect on rape, sugar beets and dicotyle weeds. In view of this, and of the data on persistence of IPSN in soils, the Committee considered that there is a concern about risks to non-target plants. Therefore, an appropriate assessment should be conducted.

4.3.2 Risks to aquatic organisms

The Committee estimated a worst-case (overspray and maximum percentage of IPSN formed in the water sediment studies, see section 4.2.7) concentration in surface water of about 0.4 μg/l and a sediment content of 0.002 mg/kg and therefore considered that the consequent risks should be assessed (SCP, 2000b).

The toxicity of IPSN to aquatic organisms has not been tested. The Committee therefore considered whether other information on structure of the metabolite or on ecotoxicity of the parent substance could be used to address the risk of IPSN. As for soil organisms, no firm conclusion could be reached based on the structure of the metabolite. Therefore, other lines of evidence regarding the ecotoxicity of IPSN were considered for each of the groups of organisms which are likely to be exposed to the metabolite in surface waters and sediments.

The Committee's opinion on aquatic risks is based on the worst-case PEC in water and sediment, without any allowance for risk mitigation measures. If such measures were to be applied, the assessment should be adjusted appropriately.

Higher aquatic plants

Of the aquatic organisms tested with the parent molecule, *Lemna* was the most sensitive with an EC_{50}[8] of 0.5 μg/L in a semi-static study. This study is unlikely to have included significant exposure to IPSN as it is formed slowly by hydrolysis (half-life = 400d at pH 7) whereas there is rapid photolysis that does not produce IPSN.

The Committee considers that all three parts (aromatic, pyrimidin and sulfonylurea bridge) of the parent molecule are necessary for the specific herbicidal action of a sulfonylurea such as imazosulfuron (Hay, 1990). Also, it is known that herbicide metabolites are usually less phytotoxic than the parent molecule. For these reasons, it is most likely that IPSN is less toxic to Lemna than is imazosulfuron. However, phytotoxicity of metabolites and breakdown products can be due to other non-specific actions as long as these compounds can be absorbed and taken up by the plant. Therefore, the possibility that the parent and metabolite are equally toxic (0.5 μg/L) cannot be excluded. In this case the TER[9] for the worst-case PEC (0.4 μg/L) would be 1.25. The Committee therefore considers that further information is required to address the risk from IPSN to higher aquatic plants. This may involve a more refined estimate of exposure, and/or testing the toxicity of IPSN to Lemna.

[8] Median effective concentration.
[9] Toxicity Exposure Ratio.

Aquatic invertebrates and fish

For the parent molecule, the most sensitive toxicity endpoints for Daphnia or fish were the semi-static 21d *Daphnia* NOECs[10] of 1.2 mg/L for both mortality and growth. It is unlikely that significant IPSN was formed in these tests due to (a) photolysis, and (b) the periodic renewal of the water in semi-static tests.

In the experience of the Committee, it is unusual for fish or Daphnia to be more sensitive to metabolites of a herbicide than to the parent molecule. Even if the toxicity of IPSN to fish or Daphnia were the same as the most sensitive endpoint for the parent molecule with these organisms (1.2 mg/L) then the TER based on the worst-case PEC (0.4 µg/L) for IPSN would be 3000. The Committee therefore considered that existing information indicates an adequate margin of safety for aquatic invertebrates and fish.

Sediment-dwelling organisms

The Committee estimated the worst-case (overspray and maximum percentage of IPSN formed in the water sediment studies, see section 4.2.7) PEC for IPSN in sediment to be 2 µg /kg. No sediment-dwelling organisms have been tested with the parent molecule, and the Committee has previously argued that toxicity to sediment-dwelling organisms cannot be inferred from data on Daphnia (SCP, 2000a). No other information was available to provide a basis for assessing the risk. The Committee therefore considered that the risk should be addressed either by a reasoned argument regarding exposure and/or toxicity, or by appropriate testing of sediment-dwelling organisms.

4.3.3 Risks for other organisms and other metabolites

The Committee notes that other metabolites were formed in some studies, sometimes at levels comparable to IPSN. Risks from these metabolites have not been considered. It might be possible to address these at the same time as IPSN, by conducting any new studies with the parent compound and measuring the levels of IPSN and other metabolites that are formed. For this strategy to succeed, the initial concentrations of parent molecule should be sufficiently high to provide an adequate safety margin for the metabolites, the levels of metabolites should be measured at several time points, and the test duration might need to be extended to ensure an appropriate period of exposure to the metabolites. This strategy may not be useful for aquatic risks, as the levels of metabolites formed in standard tests may not adequately represent those which could occur by drainage or runoff in the field.

The guidance document on terrestrial ecotoxicology states that the risk to mammals and birds from metabolites present in or on potential feed items should be fully assessed. The Committee considers that this should be done; some advice on how to proceed is given in the guidance document (European Commission, 2000).

4.4 Toxicological risk assessment

In metabolism studies of imazosulfuron in rats the main metabolite found was HMS, a demethylated derivative of the parent compound. Unidentified metabolites accounted from 6 to 11% of the administered dose. In plants, as in animals the main metabolite

[10] No Observed Effect Concentrations.

pathway resulted in HMS. Minor metabolites detected in plants were IPSN, ADPM and ADNG (N-glycoside of the ADPM). These three metabolites although not identified in rats are thought to occur in them at low levels according to the RMS report. At harvest no residues of either the parent compound or its metabolites were detected in edible parts of the plants.

The metabolite IPSN was not identified in the leachates of the lysimeter study and according to the experimental design (SCP/IMAZO/004) used in the study, this means its concentration was below 0.1 μg/L. Therefore assuming as a worst case a water concentration of 0.1 μg/L, given a 2 L/ day water consumption, the intake of IPSN would result in a maximum of 0.2 μg/person/day well below the threshold of toxicological concern of 1.5 μg/person/day (SCP 2000b). The Committee therefore considers that in this case no significant health risk is likely to arise.

HMS and IPSA are more polar than the parent compound. Their amounts in lysimeter leachates were at concentration that would result in an intake well below the threshold of toxicological concern. Therefore, also in this case, the Committee considers that no significant health risk is likely to arise.

In the lysimeter study, three unknown metabolites were detected in one of three lysimeters, in the third year only. They have an average sum of 0.07 μg/L (expressed as parent compound) in the lysimeter in which they occurred.

4.5 Overall Conclusion

In forming its opinion the SCP applied the principles and approaches which it expressed in its earlier opinion on the Guidance document on relevant metabolites (SCP, 2000b) and, where appropriate, approaches specified in the Guidance document on terrestrial ecotoxicology (European Commission, 2000). The Committee intends this opinion should be used as an example for future reference.

The Committee estimated a worst-case concentration in soil of 0.04 mg/kg IPSN after 10 years. Based on overspray and maximum percentage of IPSN formed in the water sediment studies, the Committee estimated a worst-case concentration in surface water of about 0.4 μg/L, and a content in aquatic sediments of 0.002 mg/kg. The ecotoxicity of IPSN has not been tested, so the Committee considered existing information. No conclusions could be reached based on the structure of the metabolite. Other lines of evidence regarding the ecotoxicity of IPSN were considered for each of the groups of organisms which are likely to be exposed to the metabolite in soil and water.

The Committee considered that existing studies provide an adequate margin of safety regarding the risks from IPSN to soil micro-organisms, aquatic invertebrates and fish, and the acute risks to earthworms.

The Committee considered that further information was required to assess other risks from IPSN, as follows:

1. An appropriate earthworm reproduction test to assess chronic risks to earthworms.

2. Further information to address risks to ground-dwelling predatory arthropods (e.g. a reasoned assessment based on existing studies, new studies with the parent in which formation of IPSN is measured or new studies with IPSN).

3. An appropriate study to address risks to soil macro-organisms.

4. An appropriate assessment of risks to non-target terrestrial plants, using existing data.

5. Further information to address risks to higher aquatic plants (e.g. a refined estimate of exposure, or a suitable study of the toxicity of IPSN to Lemna).

6. Further information to address risks to sediment-dwelling organisms (e.g. a reasoned argument regarding exposure and/or toxicity, or appropriate testing of sediment-dwelling organisms).

7. An appropriate assessment of the risks to mammals and birds from metabolites present in or on potential feed items.

The Committee's opinions on risks to aquatic and sediment-dwelling organisms are based on the worst-case (overspray and maximum percentage of IPSN formed in the water sediment studies) PEC in water and sediment, without any allowance for risk mitigation measures. If such measures were to be applied, the assessment should be adjusted appropriately.

The Committee notes that other metabolites were formed in some studies, sometimes at levels comparable to IPSN. Ecological and toxicological risks from these metabolites could be addressed by similar approaches to those used for IPSN.

The Committee noted that it might be possible to address risks from IPSN and other metabolites simultaneously, by conducting any new studies with the parent compound and measuring the levels of IPSN and other metabolites that are formed. Such a strategy is more likely to succeed for soil organisms than for aquatic organisms.

The metabolite IPSN was not identified in the leachates of the lysimeter study and according to the method used in the study, this means that in any case its concentration would have been below 0.1 µg/L. The Committee considers that no significant health risk is likely to arise from its eventual presence at levels below the limit of determination.

5. REFERENCES

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6. DOCUMENTS MADE AVAILABLE TO THE COMMITTEE

1. Imazosulfuron: Terms of reference (SCP/IMAZO/001 submitted by DG Health and Consumer Protection, 8 January 2000).
2. Imazosulfuron: Evaluation table, doc. 7456/VI/98 rev. 7 - 12.07.00 (SCP/IMZO/003 submitted by DG Health and Consumer Protection, 18 December 2000).
3. Imazosulfuron: Addendum 1 to the Monograph Volume 3, 15-06-2000 (SCP/IMAZO/004 submitted by DG Health and Consumer Protection, 18 December 2000).
4. Imazosulfuron: Danish comments, 30-06-1999 (SCP/IMAZO/005 submitted by DG Health and Consumer Protection, 18 December 2000).
5. Imazosulfuron, Draft evaluation report (volumes 1 to 4) prepared by Germany as Rapporteur Member State, May 1998.
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7. URA-96-098-00-H-0-WG: Acute toxicity to the rove beetle, *Aleochara bilineata* Gyll (Coleoptera, Staphilinidae) in the laboratory. Report n° URA-96-09800-032, Kühner, Ch, June 1996, 20 pages, submitted by Spiess-Urania Chemicals GmbH, 19 March 2001 (property of Spiess-Urania Chemicals GmbH).
8. Final report - Acute toxicity of URA-09800-H-0-WG on the compost worm of *Eisenia foetida*. Report n° URA-96-09800-045, Raddatz, April 1996, 19 pages, submitted by Spiess-Urania Chemicals GmbH, 19 March 2001 (property of Spiess-Urania Chemicals GmbH).
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