CONCLUSION ON PESTICIDE PEER REVIEW

Conclusion regarding the peer review of the pesticide risk assessment of the active substance chlorsulfuron

Issued on 26 November 2008

SUMMARY

Chlorsulfuron is one of the 84 substances of the third stage Part B of the review programme covered by Commission Regulation (EC) No 1490/2002[1]. This Regulation requires the European Food Safety Authority (EFSA) to organise upon request of the EU-Commission a peer review of the initial evaluation, i.e. the draft assessment report (DAR), provided by the designated rapporteur Member State and to provide within six months a conclusion on the risk assessment to the EU-Commission.

Greece being the designated rapporteur Member State submitted the DAR on chlorsulfuron in accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, which was received by the EFSA on 27 July 2007. The peer review was initiated on 03 October 2007 by dispatching the DAR for consultation of the Member States and the sole applicant DuPont. Subsequently, the comments received on the DAR were examined and responded by the rapporteur Member State in the reporting table. This table was evaluated by EFSA to identify the remaining issues. The identified issues as well as further information made available by the applicant upon request were evaluated in a series of scientific meetings with Member State experts in June – July 2008.

A final discussion of the outcome of the consultation of experts took place during a written procedure with the Member States in October 2008 leading to the conclusions as laid down in this report.

This conclusion was reached on the basis of the evaluation of the representative uses as a herbicide on wheat, barley, oats, rye and triticale. Full details of the GAP can be found in the attached list of end points.

[1] OJ No L 224, 21.08.2002, p. 25, as amended by Regulation (EC) No 1095/2007 (OJ L 246, 21.9.2007, p. 19)

The representative formulated product for the evaluation was "Chlorsulfuron 75 WG", a water dispersible granule (WG).

Only single methods for the determination of residues are available since a multi-residue-method like the German S19 or the Dutch MM1 is not applicable due to the nature of the residues.
Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that at least some quality control measurements of the plant protection product are possible. The specification could not be agreed, two impurities were found to be relevant but the maximum content has not been agreed. For the relevant impurities data gaps have been identified for spectra, storage and methods of analysis. A shelf life study was identified as a data gap for the product in water soluble bags.

With regard to its toxicological properties, chlorsulfuron was rapidly but not extensively absorbed after oral administration. Widely distributed in the rat body, it did not accumulate in any organ and was excreted mainly via urine as parent, with two minor metabolites. Of low acute toxicity, chlorsulfuron was not a skin irritant, slightly irritating to the eye and did not induce skin sensitisation. The short term toxicity was manifested by an increased testicular weight (rats), decreased body weight gain and haematological changes (dogs). Chlorsulfuron was not shown to have a genotoxic potential *in vivo*, but induced testicular interstitial cell tumours in the 2-year rat study leading to the proposed classification as **Carcinogen Category 3, R40** (Limited evidence of carcinogenic effects). In the reproductive toxicity studies, effects on the reproductive organs were observed without impact on the fertility parameters and were considered as related to general systemic toxicity. No effect in the offspring was observed up to the highest dose tested. Similarly in the developmental toxicity studies, some effects on the foetal development were considered as a result of maternal toxicity at the high dose level, and it was agreed that chlorsulfuron had no teratogenic properties.
Several metabolites/impurities were evaluated in the DAR and considered by the experts. The compound IN-A4097[2] was concluded to be a relevant groundwater metabolite and a relevant impurity. Based on the available information, there is no sufficient evidence demonstrating the absence of carcinogenic properties. The agreed ADI for IN-A4097 is 0.009 mg/kg bw/day based on the 90-day rat study with a safety factor of 1000. Based on acute toxicity results, the impurity IN-A4098[3] was considered as toxicologically relevant. As it is a potential metabolite, it was agreed that the reference values of the parent could be applied. Based on the available information, the other potential groundwater metabolites, not discussed by the experts, should also be considered as toxicologically relevant pending on the confirmation of the proposed classification of chlorsulfuron as Carcinogen Category 3 by ECHA.

[2] **IN-A4097:** 2-chlorobenzenesulfonamide
[3] **IN-A4098:** 4-methoxy-6-methyl-1,3,5-trazine-2-amine

The agreed **acceptable daily intake** (ADI) for chlorsulfuron is **0.2 mg/kg bw/day** based on the 2-year rat study, with the use of a safety factor of 100. The agreed **acceptable operator exposure level** (AOEL) is **0.43 mg/kg bw/day** based on the 1-year dog study, the application of a safety factor of 100 and a correction factor for oral absorption of 71%. It was agreed that no acute reference dose (ARfD) was needed for chlorsulfuron. The default value of 100% was agreed for dermal absorption in the absence of experimental values.
The operator exposure levels estimated with the UK and German models resulted in values below the AOEL even without the use of personal protective equipment. Similarly, estimated worker and bystander exposure levels were respectively below 5 and 1% of the AOEL for the representative use on cereals.

The metabolism of chlorsulfuron was investigated in cereals. Chlorsulfuron is metabolised extensively, mainly by hydroxylation followed by conjugation to glucose and by cleavage of the sulfonylurea linkage. Although the submitted residue trials were not carried out fully in accordance with the notified cGAP they were regarded as sufficient to propose an MRL for cereals taking into account that residues of chlorsulfuron in all grain samples were below LOQ.
Data on the metabolism in rotational crops show that no quantifiable residues of chlorsulfuron or the soil metabolite IN-A4098 are expected in rotational crops after application of chlorsulfuron according to the notified GAP. However, a data gap was set concerning the investigation of the possible presence of two further soil metabolites in rotational crops (IN-A4097 and IN-J998[4]).
The metabolite IN-A4097 which was found in the metabolism studies was regarded as toxicologically relevant. It was included in the proposed residue definition for risk assessment for products of plant and animal origin which should be carried out separately for chlorsulfuron and the metabolite. The risk assessment for the consumer for both was not peer reviewed. For IN-A4097 residue levels in cereal grain after application have not been analysed and can only be estimated on the basis of results from a metabolism study. According to provisional calculations the chronic exposure from intake of cereals is expected to be well below the ADI for chlorsulfuron and for IN-A4097. According to preliminary FOCUS calculations, concentrations of IN-A4097 are expected to exceed 0.1 µg/L in ground water. IN-A4097 is considered as a relevant metabolite according to draft guidance document SANCO/221/2000-rev.10 on the basis of the conclusions of the toxicological evaluation.

Degradation of chlorsulfuron was very limited in the particular soil used to investigate the route of degradation under aerobic conditions ($DT_{50\ lab\ 20\ °C}$ = 232 d). Only two metabolites exceeded 5 % AR at two consecutive data points: IN-JJ998, IN-A4098[5]. Other two minor metabolites were increasing in amount at the end of the study: IN-A4097 and IN-M6957[6]. Additionally, the applicant presented a

[4] **IN-JJ998:** N-[(N-carbamoylcarbamimidoyl)carbamoyl]-2-chlorobenzenesulfonamide
[5] **IN A4098:** 4-methoxy-6-methyl-1,3,5-triazine-2-amine
[6] **IN- M6957:** 2-chloro-N-[(4-hydroxy-6-methyl-1,3,5-triazin-2-yl)carbamoyl]benzenesulfonamide

position paper reviewing published scientific literature that contains up to 25 chlorsulfuron degradation rate determinations in soil (DT_{50} = 6.7 – 232 d). The submission of the original papers that support these data was identified as a data gap during the peer review. Furthermore, EFSA identified some shortcomings on the kinetic assessment of these data provided after the meeting of experts. Some of the papers were based on applicants' studies not directly available in the dossier. The submission and assessment of these studies has also been identified as a data gap. Taking into consideration the relatively low degradation of parent observed in the laboratory route study it may not be excluded that the trigger values for soil assessment and / or ground water exposure assessment are exceeded in less extreme soils by these or other metabolites. Soil metabolites reach significantly higher levels in some of the field studies available (IN-A4097 up to 77.5 % AR, IN-A4098 up to 65.9 % AR and IN-JJ998 up to 26.7 % AR). Metabolite IN-A4097 may be considered high to very high persistent in soil (DT_{50} = 175 – 436 d) under dark aerobic conditions according the available studies. Metabolite IN-A4098 may be considered moderated medium persistent in soil ($DT_{50\ lab}$ = 43.2 – 65.9 d) under dark aerobic conditions according to the available information as updated by the RMS after the meeting of experts. Metabolite IN-JJ998 may be considered medium to high persistent in soil (DT_{50} = 91.6 – 107.4 d) under dark aerobic conditions according the available information as updated by the RMS after the meeting of experts. Half lives of metabolites IN-A4098 and IN-JJ998 may not be considered fully peer reviewed.

The degradation of chlorsulfuron was also investigated under dark anaerobic conditions at 25 °C ($DT_{50\ lab\ 20\ °C\ anaerobic}$ = 78.2 d). Major metabolite IN-D5293[7] (max. 14 % AR after 56 d) not identified under aerobic conditions was found in the anaerobic study.

Half life of chlorsulfuron in the photolysis in soil study was calculated to be 62.2 d. A data gap was identified during the peer review to provide an estimation of soil photolysis half lives at different latitudes (35 – 55 °N). A specific photolysis metabolite (IN-V7160[8]) was identified in this study.

Field dissipation studies performed in California, Idaho (USA), Spain and Italy (2 sites) are available in the dossier. After the examination of these studies, the experts in the meeting agreed that the studies are not suitable to derive kinetic parameters for modelling purposes.

According the batch soil adsorption / desorption studies available chlorsulfuron may be considered to exhibit high to very high mobility in soil (K_{fOC} = 14.1 – 60.2 mL / g), IN-A4097 may be considered to exhibit very high mobility in soil (K_{fOC} = 21.2 – 48.2 mL / g), IN-A4098 may be considered to exhibit very high to medium mobility in soil (K_{fOC} = 16.7 – 225.5 mL / g) and IN-JJ998 may be considered to exhibit high to very high mobility (K_{fOC} = 14.7 – 114.0 mL / g). According estimations obtained using PCKOCWIN metabolites IN- B5528[9] and IN-V7160 are very highly mobile in soil and IN-M6957 may be considered low mobile in soil.

[7] **IN-D5293:** 2-chlorophenylsulfonylurea
[8] **IN-V7160**: 1-(4-methoxy-6-methyl-1,3,5-triazine-2-yl)urea
[9] **IN- B5528:** 4-amino-6-methyl-1,3,5-triazin-2-ol

Chlorsulfuron is stable to hydrolysis at pH 7 and 9 and it hydrolysis with a half life of 23.2 d at pH 5. Photolysis in water is not considered to contribute significantly to its environmental degradation. Chlorsulfuron was found not to be readily biodegradable.

Dissipation / degradation of chlorsulfuron in the aquatic environment were investigated in one study with one aerobic and one anaerobic water / sediment system. The experiment's design deviate significantly from the recommendations given by SETAC guidance and a data gap for an additional water sediment study has been identified by EFSA. The meeting of experts had already identified a data gap (considered not essential to finalize the EU risk assessment) for a new water / sediment study under acidic conditions.

PECs $_{SW/SED}$ presented in the DAR were not validated during the peer review due to the lack of adequate input parameters. Therefore, a new data gap was identified for new PEC $_{SW/SED}$.

Meeting of experts discussed the FOCUS GW calculations as presented in addendum 3.In these calculations, chlorsulfuron and metabolites IN-JJ998 and IN-A4097 exceeded the trigger of 0.1 µg / L in some of the scenarios simulated. Metabolite IN-A4097 also exceeds the trigger of 0.75 µg / L in some of the scenarios. Due to various deficiencies and data gaps, the calculations presented were not validated during the peer review and the ground water exposure assessment remains open.

Chlorsulfuron is not expected to volatilize significantly under normal environmental conditions. Half life in the atmosphere due to photochemical degradation has been estimated to be of 2.1 d.

For the representative use of chlorsulfuron a low risk was assessed for terrestrial vertebrates in a first-tier assessment.

Algae and aquatic plants were the most sensitive organisms. Risk assessment was driven by *Lemna gibba*, for which potential higher first-tier risk was identified. The higher tier TER calculations provided did not allow to identify a low risk. Furthermore, new PEC_{sw} FOCUS step 3 values were requested by the fate expert meeting. Therefore a data gap was identified to calculate FOCUS Step 3&4 TER values in order to address the risk to macrophytes and to identify the most appropriate mitigation measures.

Only if mitigation measures equivalent to an in-field non-spray buffer zone of 15 m (pre-emergence use) and 15 m plus a drift reduction ≥50% (post emergence use) are applied, the risk to terrestrial non-target plants was assessed as low. In order identify more realistic mitigation measures, EFSA proposed a data gap for the risk assessment for non target plants.

A low risk was assessed for bees, non-target arthropods, earthworm, soil non-target macro and micro-organisms and biological methods of sewage treatment.

Key words: chlorsulfuron peer review, risk assessment, pesticide, herbicide

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BACKGROUND

Commission Regulation (EC) No 1490/2002 laying down the detailed rules for the implementation of the third stages of the work program referred to in Article 8(2) of Council Directive 91/414/EEC and amending Regulation (EC) No 451/2000 as amended by Commission Regulation (EC) No 1095/2007, regulates for the European Food Safety Authority (EFSA) the procedure of evaluation of the draft assessment reports provided by the designated rapporteur Member State. Chlorsulfuron is one of the 84 substances of the third stage, part B, covered by the Regulation (EC) No 1490/2002 designating Greece as rapporteur Member State.

In accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, Greece submitted the report of its initial evaluation of the dossier on chlorsulfuron, hereafter referred to as the draft assessment report, received by EFSA on 27 July 2007. Following an administrative evaluation, the draft assessment report was distributed for consultation in accordance with Article 11(2) of the Regulation (EC) No 1095/2007 on 24 October 2007 to the Member States and the main applicant DuPont as identified by the rapporteur Member State.

The comments received on the draft assessment report were evaluated and addressed by the rapporteur Member State. Based on this evaluation, EFSA identified and agreed on lacking information to be addressed by the notifier as well as issues for further detailed discussion at expert level.

Taking into account the requested information received from the notifier, a scientific discussion took place in expert meetings in June – July 2008. The reports of these meetings have been made available to the Member States electronically.

A final discussion of the outcome of the consultation of experts took place during a written procedure with the Member States in October 2008 leading to the conclusions as laid down in this report.

During the peer review of the draft assessment report and the consultation of technical experts no critical issues were identified for consultation of the Scientific Panel on Plant Protection Products and their Residues (PPR).

In accordance with Article 11c(1) of the amended Regulation (EC) No 1490/2002, this conclusion summarises the results of the peer review on the active substance and the representative formulation evaluated as finalised at the end of the examination period provided for by the same Article. A list of the relevant end points for the active substance as well as the formulation is provided in appendix 1.

The documentation developed during the peer review was compiled as a **peer review report** comprising of the documents summarising and addressing the comments received on the initial evaluation provided in the rapporteur Member State's draft assessment report:

- the comments received,
- the resulting reporting table (rev 1-1, 11-04-2008)

as well as the documents summarising the follow-up of the issues identified as finalised at the end of the commenting period:

- the reports of the scientific expert consultation,
- the evaluation table (rev. 2-1, 23-10-2008).

Given the importance of the draft assessment report including its addendum (compiled version of August 2008) containing all individually submitted addenda) and the peer review report with respect to the examination of the active substance, both documents are considered respectively as background documents A and B to this conclusion.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Chlorsulfuron is the ISO common name for 1-(2-chlorophenylsulfonyl)-3-(4-methoxy-6-methyl-1,3,5-triazin-2-yl)urea (IUPAC).

Chlorsulfuron belongs to the class of triazinylsulfonylurea herbicides. Other examples of this group are iodosulfuron and metsulfuron. It is a systemic herbicide acting by absorption by foliage and uptake via the roots. It is used for the control of most broad-leaved weeds and some annual grasses in cereals.

The representative formulated product for the evaluation was "Chlorsulfuron 75 WG", a water dispersible granule (WG).

The evaluated representative uses are as a herbicide on wheat, barley, oats, rye and triticale. Full details of the GAP can be found in the attached list of end points.

SPECIFIC CONCLUSIONS OF THE EVALUATION

1. Identity, physical/chemical/technical properties and methods of analysis

The minimum purity of chlorsulfuron as manufactured should not be less than 950 g/kg this is in compliance with the FAO specification which is applicable to this DuPont source.

However, since clarification is required with respect to certain impurities to confirm the proposed maximum levels in the technical material, the specification for the technical material as a whole should be regarded as provisional. A new specification has been identified as a data gap.

The technical material contains IN-A4097[10] and IN-A4098[11] which have to be regarded as relevant impurities. The maximum content of these impurities has not been agreed.

The content of chlorsulfuron in the representative formulation is 750 g/kg (pure).

Beside the specification, the assessment of the data package revealed no issues that need to be included as critical areas of concern with respect to the identity, physical, chemical and technical properties of chlorsulfuron or the respective formulation. However, the following data gaps were identified:

- spectra for the relevant impurities
- method for the relevant impurities in the formulation
- Storage data where the relevant impurity content is analysed before and after storage
- Shelf life study for the formulation in water soluble bag material.

The main data regarding the identity of chlorsulfuron and its physical and chemical properties are given in appendix 1.

Sufficient test methods and data relating to physical, chemical and technical properties and analytical methods are available to ensure that at least limited quality control measurements of the plant protection product are possible.

Methods are available to monitor chlorsulfuron in products of plant origin (dry and watery matrices only). Analysis of plant matrices is by LC-MS/MS with a LOQ of 0.01 mg/kg. In soil chlorsulfuron is analysed by LC-MS/MS with a LOQ of 0.05 µg/kg. In a second method by LC-MS/MS chlorsulfuron and IN-A4098, IN-V7160[12] and IN-JJ998[13] are analysed with a LOQ of 0.2 µg/kg and IN-A4097 with a LOQ of 0.5 µg/kg. Chlorsulfuron in water is analysed by LC-MS/MS with a LOQ of 0.05 µg/L. It should be noted however, that the residue definition for ground water is provisional and therefore further methods may be required. In air chlorsulfuron is analysed by LC-MS/MS with a LOQ of 0.003 mg/m^3. A method of analysis for products of animal origin is not necessary as no

10 IN-A4097: 2-chlorobenzenesulfonamide
[11] IN-A4098: 4-methoxy-6-methyl-1,3,5-trazine-2-amine
[12] IN-V7160: 4-methoxy-6-methyl-1,3,5-trazine-2-yl)urea
[13] IN-JJ998: N-[(N-carbamoylcarbamimidoyl)carbamoyl]-2-chlorobenzenesulfonamide

MRLs will be set. As the active substance is not classified either toxic or very toxic methods of analysis for body fluids and tissues are not required.

2. Mammalian toxicology

Chlorsulfuron was discussed by the experts in mammalian toxicology in July 2008 (PRAPeR meeting 54, round 11).

Considering the revised technical specification provided in the addendum 1 to Annex C (June 2008), two impurities were considered as toxicologically relevant (see 2.8). However, the proposed levels in the technical specification didn't raise any toxicological concern since they were considered as covered by the levels tested within the toxicological batches.

EFSA notes: the revised technical specification has not been agreed by section 1, and the final proposal with agreed changes will have to be assessed again in comparison with the toxicological batches.

2.1. Absorption, Distribution, Excretion and Metabolism (Toxicokinetics)

Chlorsulfuron was rapidly absorbed after oral administration, but to a lower extent in females (~71%) than in males (~84%). Therefore the experts agreed to use a correction factor of 0.71 for the estimation of the systemic bioavailability of the compound. Widely and uniformly distributed within the rat body, chlorsulfuron did not show any potential for bioaccumulation. The excretion occurred mainly via urine, but also via feces (up to 27%). The main compound excreted was the parent, and only two minor metabolites were identified (IN-A4097 and IN-A4098). Based on that, the proposed metabolic pathway was hydrolytic cleavage of the sulfonylurea bridge of the parent.

2.2. Acute toxicity

In the available studies, chlorsulfuron was shown to be of low acute toxicity after oral (rat LD_{50} >5000 mg/kg bw) , dermal (rabbit LD_{50} >3400 mg/kg bw) and inhalation (rat LC_{50} >5.5 mg/L air, nose or head only exposure) exposure. The compound was not a skin irritant, induced a slight irritation in the rabbit eye but no skin sensitisation in a Maximization test (Magnusson & Kligman). Based on these results, no classification was required for the acute toxicity of chlorsulfuron.

2.3. Short term toxicity

The oral short-term toxicity of chlorsulfuron has been assessed in rats (two 90-day studies), mice (one 90-day study) and dogs (one 6-month and one 1-year study). In mice, no adverse effects were noted at doses up to 3716 mg/kg bw/day in the 90-day study. In rats, the adverse finding triggering the NOAEL in the first study (Dashiell, 1978) was an increased testicular weight at the high dose (373 mg/kg bw/day). Nevertheless the agreed overall NOAEL was 161 mg/kg bw/day, the highest dose without adverse effect in the second study (Wood, 1980).

The experts discussed the relevance of the increased testis weight observed in the 1-year dog study. Considering that the changes were not consistently dose related, were without histopathological correlation and did not occur in the 6-months study, the meeting agreed that this was not an adverse effect. Therefore, based on a reduced body weight gain and haematological changes in females in the 1-year dog study, the agreed overall NOAEL was 60.6 mg/kg bw/day supported by the 6-months study.

In the DAR, two additional short term studies with male rats were described as supplementary studies (B.6.8.2). In the first oral study, chlorsulfuron was administered at the single dose level of 2200 mg/kg bw/day during 2 weeks (5 days/week) and no NOAEL could be derived. In the second study by inhalation, the animals were exposed for two weeks (head-only, 6 h/day, 5 days/week) to aerosols containing up to 2.5 mg/L. Based on haematuria and crystalluria observed at 0.5 mg/L, the NOAEL was 0.1 mg/L for male rats (since females were not included in the study).

2.4. GENOTOXICITY

The genotoxic potential of chlorsulfuron was investigated *in vitro* for the induction of mutations and chromosome aberrations in bacterial and mammalian cells (Ames test, mammalian cell forward gene mutation assay, chromosome aberration assay in CHO cells). The results were negative but the studies were considered of limited validity, since they presented major shortcomings and limitations from the current guidelines. Nevertheless, chlorsulfuron did not induce DNA damage in the unscheduled DNA synthesis test with rat primary hepatocytes. Additionally, negative results were also obtained *in vivo* with a micronucleus test and an old dominant lethal assay, which is of limited validity according to current standards. Therefore the meeting concluded that chlorsulfuron does not show any evidence of a genotoxic potential in the available studies.

2.5. LONG TERM TOXICITY

The chronic toxicity and carcinogenicity of chlorsulfuron have been assessed in mice and rats.

In the DAR, the proposed NOAEL for the 2-year rat study was 4 mg/kg bw/day based on a statistically significant decrease in body weight (gain) in males. Considering that this decrease at the LOAEL was lower than 10% compared to controls, the experts agreed that 20 mg/kg bw/day was the NOAEL, based on an increased incidence in testicular tumours and body weight effects in males at the high dose (104 mg/kg bw/day). In the absence of any mechanistic data indicating the opposite, the increased incidence of unilateral testicular interstitial cell tumours was considered relevant for the risk assessment, leading to the proposed classification **Carcinogen Category 3, R40** (Limited evidence of a carcinogenic effect).

Similarly in the 2-year mouse study, the experts considered the slight decrease in body weight (gain) of both sexes at the high dose relevant and the agreed NOAEL was set 837 mg/kg bw/day. No increased incidence of tumours was observed in mice.

2.6. REPRODUCTIVE TOXICITY

The effects of chlorsulfuron on the **fertility** parameters have been investigated in a two-generation rat study (2005). In the DAR an additional three-generation study (1981) was considered unacceptable and was not taken into account for the risk assessment.

Effects in the parents were observed at the high dose level and consisted of decreased body weight gain and food efficiency during the pre-mating period, resulting in a parental NOAEL of 188.5 mg/kg bw/day.

Effects in the offspring were re-evaluated in the addendum (June 2008) and the meeting agreed with the RMS' conclusion that no relevant adverse effect was observed in the pups during lactation, leading to a NOAEL for the offspring of 578.5 mg/kg bw/day.

Effects on the reproductive organs included increased weight of the testis and epididymis in the high dose group, with an increased number of epididymal sperm per cauda. Based on these, the reproductive NOAEL was 188.5 mg/kg bw/day. The number of ovarian follicles in females of the high dose was below the concurrent control values and historical control data provided in the addendum (June 2008). However, the experts agreed that it was not a significant adverse effect in the absence of other findings in females.

Taking into account that the changes in the reproductive organs were only observed at high dose levels (in the presence of general systemic toxicity), were not accompanied by adverse effects on the fertility parameters, and were not supported by mechanistic data on hormone disruption, the experts agreed that the classification for reproductive toxicity with **R62** (Possible risk of impaired fertility) was not warranted. Considering that the slight decrease in pup body weight was not adverse, and that the transfer into milk is not supported by toxicokinetic data and physico-chemical properties, the experts agreed that the risk phrase **R64** (May cause harm to breastfed babies) as proposed in the DAR, was not needed.

Note after the written procedure: Possible androgenic effects have been discussed during the expert meeting. It was concluded that there was no clear indication of a significant androgenic effect from subchronic, chronic and reproductive studies.

The **developmental** toxicity of chlorsulfuron was assessed in rats and rabbits. With regard to the rat study, based on historical data provided in the addendum (June 2008), the experts agreed that the incidence of delayed ossification (partially ossified sternebrae) was within the historical range at all dose levels and occurred as a result of maternal toxicity at the high dose level (1500 mg/kg bw/day). Therefore the agreed developmental NOAEL was 500 mg/kg bw/day based on decreased foetal body weight at the high dose. The maternal NOAEL for rats was confirmed to be 165 mg/kg bw/day, based on the increased incidence of clinical signs (alopecia, vaginal discharge) and decreased body weight gain.

In the rabbit study, the agreed maternal NOAEL was 75 mg/kg bw/day, based on body weight loss and decreased adjusted body weight gains (final body weights minus the weight of the conception

products) at 200 mg/kg bw/day. The agreed developmental NOAEL was 200 mg/kg bw/day based on decreased body weight of the female foetuses (and equivocal delayed ossification).
Single incidences of malformations were observed in presence of maternal toxicity in both species, but not considered treatment-related. Based on the available studies, it was agreed that chlorsulfuron has no teratogenic properties.

2.7. NEUROTOXICITY

Chlorsulfuron does not have a structure related to compounds capable of inducing neurotoxicity. In all studies provided, no signs of neurotoxicity or histopathological changes with respect to brain, spinal cord or peripheral nerves were observed. Therefore, no specific neurotoxicity studies were considered necessary.

2.8. FURTHER STUDIES

Compound IN-A4097

Several toxicological studies were presented in the DAR for this compound, also identified as a minor rat metabolite (see 2.1). The acute oral toxicity study had many limitations and didn't allow deriving an LD_{50} value. In the indicative 2-week oral study (5 days/week), no NOAEL could be derived since adverse effects were observed at the lowest dose tested (750 mg/kg bw/day). From the 90-day oral study, the target organs were the liver, the kidney, the pancreas and the spleen (with haematological, clinical chemistry and histopathological changes) accompanied by body weight changes. The agreed NOAEL was 9.3 mg/kg bw/day. The *in vitro* genotoxic potential of IN-A4097 was investigated with an Ames test (only indicative), a gene mutation assay in CHO cells and a chromosome aberration assay in human lymphocytes. All the results were negative.
Based on these data showing a different toxicological profile than chlorsulfuron (and lower short term NOAEL), the experts agreed that IN-A4097 was a relevant impurity. Additionally, based on the available data, an acceptable daily intake (ADI) of 0.009 mg/kg bw/day was derived by the experts, applying an increased safety factor of 1000 to the NOAEL of the 90-day study. It was also agreed that no acute reference dose (ARfD) was needed for this metabolite, based on limited information indicating very low acute oral toxicity.

Compound IN-A4098

Several toxicological studies were presented in the DAR for this compound, also identified as a minor rat metabolite (see 2.1). In an acute oral study with rats, the proposed LD_{50} was 1600 mg/kg bw, which would result in a classification with **Xn, R22 Harmful if swallowed**. In an indicative 2-week study (5 days/week), no NOAEL could be derived since clinical signs of toxicity and histopathological changes were observed at 300 mg/kg bw/day (single dose tested). Negative results

were obtained in an Ames test, but the study was only considered as indicative due to major shortcomings.
Having a higher acute toxicity than chlorsulfuron, IN-A4098 was agreed to be a toxicologically relevant impurity. As a potential metabolite in products relevant for human intake, it was agreed that unless there was a specific concern (significant exposure of consumers), the reference values of the parent could be used for this metabolite.

Compound IN-JJ998
The *in vitro* genotoxic potential of IN-JJ998 was investigated with an Ames test, a gene mutation assay in CHO cells and a chromosome aberration assay in human lymphocytes. All the results were negative.

According to the Guidance Document on the assessment of the relevance of metabolites in groundwater (SANCO/221/2000 – rev.10), the available toxicological data did not give evidence that these metabolites (IN-A4097, IN-A4098, IN-JJ998) do not have the carcinogenic properties of chlorsulfuron (see 2.5). Therefore, they should be considered as toxicologically relevant groundwater metabolites. It is noted that this is dependent on the confirmation of the proposed classification for the parent (Carcinogenic Category 3; R40), in the context of the European Chemicals Agency (EChA) programme for classification and labelling under Directive 67/548/EEC.
EFSA note: The experts discussed and agreed the relevance of the groundwater metabolite IN-A4097, but the relevance of IN-A4098 and IN-JJ998 as potential groundwater metabolites has not been discussed during the meeting.

2.9. MEDICAL DATA

No occupational illnesses or symptoms associated with chlorsulfuron exposure were identified in the medical records of employees of the manufacturing, formulation and packaging facility. There have been no reported accidental poisonings with chlorsulfuron and there are no known specific human effects.

2.10. ACCEPTABLE DAILY INTAKE (ADI), ACCEPTABLE OPERATOR EXPOSURE LEVEL (AOEL) AND ACUTE REFERENCE DOSE (ARFD)

Acceptable daily intake (**ADI**)
The ADI proposed in the DAR is 0.04 mg/kg bw/day based on the 2-year rat study. Considering the revised and higher NOAEL for this study, the experts agreed that it was still the most relevant and agreed to derive an ADI of 0.2 mg/kg bw/day with the use of a safety factor of 100. With respect to the tumor effect level, the margin of safety is 520 (it was erroneously considered to be 2000 during the meeting).

Acceptable operator exposure level (**AOEL**)

The AOEL proposed in the DAR is 0.61 mg/kg bw/day based on the 1-year dog study. During the meeting, it was agreed to use the revised proposal made by the RMS in the addendum (June 2008), taking into account an additional correction factor of 0.71 for the limited enteral resorption.

Therefore the agreed systemic AOEL is 0.43 mg/kg bw/day based on the 1-year dog study with the use of a safety factor of 100 and a correction factor of 0.71 for enteral absorption.

EFSA note: With regard to the lowest level inducing tumours, the margin of safety of the AOEL is about 200. During the written procedure, one MS proposed to use a higher safety factor in order to increase this margin of safety.

Acute reference dose (**ARfD**)

The meeting of experts agreed that the setting of an ARfD is not needed for chlorsulfuron based on its toxicological profile of low acute toxicity.

2.11. DERMAL ABSORPTION

No dermal absorption studies were conducted with chlorsulfuron or the formulated product. Based on the physicochemical properties of chlorsulfuron and according to the Guidance Document on Dermal Absorption (SANCO/222/2000 rev.7, March 2004), the default value should be set at 100% for both the undiluted and diluted formulation.

2.12. EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

The representative plant protection product Chlorsulfuron 75 WG is a Water Dispersible Granule formulation containing 750 g/kg of chlorsulfuron (pure). It is an herbicide which is used in cereal crops (pre and post-emergence), and applied by means of tractor-mounted sprayers.

Operator exposure

According to the intended uses submitted by the applicant the maximum applied dose is 18.75 g a.s./ha in a spray volume of 200 to 600 L/ha. The exposure estimates were compared with the agreed AOEL in the addendum 2 to Volume 3 (August 2008) and the results are mentioned in the table below.

Estimated exposure presented as % of AOEL (0.43 mg/kg bw/day), according to calculations with the German and UK POEM model. The default for body weight of operator is 70 kg in the German model and 60 kg in the UK-POEM model.

Model	No PPE	With PPE[1]
UK POEM	37	3.5
German	5	2

PPE[1] (personal protective equipment): gloves during mixing/loading and application.

Worker exposure

In the DAR, no numerical estimate of the worker exposure during crop inspection was provided. In the first addendum (June 2008), data from Hoernicke and al. (1998) and EUROPOEM II were used and gave an estimated exposure level of 4.3% of the AOEL.

Bystander exposure

In the DAR, the bystander exposure levels have been calculated using drift data by Ganzelmeier (1995) and resulted in estimates lower than 1% of the proposed AOEL (initially lower than the agreed one by the experts). In the first addendum (June 2008), the use of the field crop study by Lloyd and Bell (1983) led to an estimated exposure still below 1% of the agreed AOEL.

3. Residues

The active substance chlorsulfuron was discussed at the PRAPeR experts meeting for residues (PRAPeR 55, round 11) in July 2008.

3.1. NATURE AND MAGNITUDE OF RESIDUES IN PLANT

3.1.1. PRIMARY CROPS

The nature of the residues in plants following the use of chlorsulfuron was studied in wheat and barley upon post-emergence application. Barley was treated by foliar application of phenyl-^{14}C labelled chlorsulfuron with an exaggerated rate (2.1N) compared to the cGAP. Samples were collected 1, 2 and 4 weeks after treatment and at maturity. The treated leaves and new growth were collected and analysed separately. Chlorsulfuron was extensively metabolised in the crop. Chlorsulfuron was identified only in treated leaves sampled one week after application (10% of TRR). The main metabolites in treated leaves were the glucose conjugate of 5-hydroxychlorsulfuron (IN -69182[14]) accounting for max. 81% and the glucose conjugate of 5-hydroxychlorsulfonamide (metabolite B[15]) accounting for max. 36%. Small amounts of chlorobenzensulfonamide (metabolite IN-A4097, 0.005 mg/kg) were identified in one leaf sample. In new growth, straw and mature grain 0.014-00.034 mg/kg TRR, 0.023 mg/kg TRR and 0.034 mg/kg TRR respectively were measured; chlorsulfuron or metabolites were not present in levels above LOQ (<0.005 mg/kg).

Wheat was treated by foliar application of phenyl- and triazine-^{14}C labelled chlorsulfuron, both at the critical application rate (ca. 1N) and an exaggerated rate (ca. 6N). After treatment at the 1N dose rate, TRR in forage declined from 1.2 mg/kg (day 0) to 0.03 mg/kg (day 19). Chlorsulfuron was only identified in forage sampled at day 0 (max. 69% of TRR). The main metabolite found in forage was

[14] Metabolite IN-69182: 2-chloro-5-(β-D-glucopyranosyloxy)-N-[[(4-methoxy-6-methyl-1,3,5-trazi-2-yl)amino]-carbonyl]benzenesulfonamide
[15] Metabolite B: 2-chloro-5-(β-D-glucopyranosyloxy)-benzenesulfonamide

IN-69182 (max. 49% of TRR). Further metabolites identified were metabolite B, 5-hydroxychlorsulfuron (IN-N5754[16]), O-desmethylchlorsulfuron (IN-M6957[17]) and the triazine-amine (IN-A4098[18]), all present at <0.01 mg/kg. After treatment at the 1N dose rate, TRR in straw and grain at maturity were very low (max. 0.003 mg/kg and 0.001mg/kg respectively).

Chlorsulfuron was applied at GS13 in the barley study and at GS14 to GS18 in the wheat study which is earlier than the latest notified use (GS 30). The RMS commented in the reporting table that the application timing is consistent with the notified use and that the main objective of metabolism studies, to generate sufficient metabolites to facilitate metabolite identification, was achieved.

The main metabolic pathway of chlorsulfuron in cereals starts with hydroxylation of the phenyl ring to form 5-hydroxychlorsulfuron (IN-N5754, only identified in wheat) which is followed by conjugation to glucose (IN-69182). Cleavage of the sulfonylurea linkage of IN-69182 produces the glucose conjugate of hydroxy chlorosulfonamide (metabolite B) and triazine amine (IN-A4098). Minor pathways include O-demethylation to form IN-M6957 and cleavage of the sulfonylurea linkage of chlorsulfuron or 5-hydroxychlorsulfuron producing IN-A4098 and 5-hydroxy chlorsulfonamide (IN-A5760) and its glucose conjugate (metabolite B) respectively.

The metabolism studies submitted show, that in cereals treated with chlorsulfuron according to the GAP, very little or no chlorsulfuron or metabolites are expected in straw or grain. Therefore, the residue definition for monitoring for cereals is proposed as chlorsulfuron only.

The PRAPeR 54 meeting discussed the toxicological relevance of metabolite IN-A4097. An ADI of 0.009 mg/kg bw/day was set. Metabolite IN-A4097 was identified in low concentrations in forage of barley in the metabolism study. The experts meeting concluded that the metabolite should be included in the residue definition for risk assessment for cereals as follows: chlorsulfuron; metabolite IN-A4097 separately.

The notifier submitted studies including a total of 16 residue trials on cereals conducted in Northern Europe. They were carried out at various application rates, GS has not been reported, but PHI is known. Four trials (two each on wheat and barley) were conducted in 1979-1980 with one application at 0.02 kg a.s./ha, which is in accordance with the application rate of the cGAP. PHI was approximately 100 days which the RMS considered as comparable to the notified cGAP in the DAR. Further 12 trials (11 on wheat and 1 on barley) were conducted in the years 1979 to 1981 with one

[16] Metabolite IN-N5754: 2-chloro-5-hydroxy-N-[[(4-methoxy-6-methyl-1,3,5-trazi-2yl)amino]-carbonyl]benzenesulfonamide
[17] Metabolite IN-M6957: 2-chloro-N-[[(4-hydroxy-6-methyl-1,3,5-trazin-2yl)amino]-carbonyl]benzenesulfonamide
[18] Metabolite: IN-A4098: 4-methoxy-6-methyl-1,3,5-trazine-2-amine

application each, with rates of 0.030 to 0.120 kg a.s./ha. Residues below the LOQ (0.01 mg/kg) were reported for all grain samples. Results for straw samples were reported for 9 of the trials. Residue concentrations were below the LOQ (0.05mg/kg) or at 0.05 mg/kg (for 1 trial with an application rate of 0.02 kg a.s./ha and one trial with an application rate of 0.04 kg a.s./ha). Studies on residue trials carried out in the United States of America were submitted as supplementary information. They were not taken into account for MRL proposals.

Further five trials on wheat were carried out in Southern Europe in 2001 with one application each at 0.014 to 0.016 kg a.s./ha at GS 30. For all grain and straw samples residues below the LOQ (<0.002 mg/kg and <0.01 mg/kg) respectively were found.

The expert meeting discussed the validity of some of the results from the study on stability of chlorsulfuron in wheat grain and straw during freezer storage. The experts concluded that stability of chlorsulfuron residues was sufficiently proven up to 36 months. Analysis in the submitted residue reials has been carried out within this time frame.

Taking into account that residues of chlorsulfuron in all grain samples were below the LOQ, the submitted residue trials are regarded as sufficient to propose an MRL for cereals at LOQ level.

The submitted residue trials did not cover the analysis of the metabolite IN A4097. Only the results of the metabolism study in barley allow the estimation of possible residue concentrations of the metabolite. IN-A4097 was found to be below LOQ (<0.005 mg/kg) in grain and straw and <0.005 – 0.005 mg/kg in forage samples. In Addendum 2 to Volume 3 of the DAR (August 2008), the RMS used residue levels of 0.005 mg/kg for calculations of dietary burden for livestock and chronic risk assessment. These calculations were not peer reviewed. EFSA notes that the metabolism study on barley did not reflect the cGAP. Therefore correction factors should be applied: a factor of 0.48 for the exaggerated application rate (2.1N), and a factor of 0.53 for correction of the molecular weight of the metabolite compared to chlorsulfuron. On the basis of this estimation, IN-A4097 concentrations <0.0013 mg/kg in cereal grain and straw and ≤0.0013 mg/kg in cereal forage are expected after application of chlorsulfuron at the cGAP. It is noted that the application of chlorsulfuron in the metabolism study was carried out earlier than the critical growth state which might lead to an underestimation of the residue level.

Field trials demonstrate that residues above LOQ (0.01 mg/kg) are not likely to occur in cereal grain to be processed. Therefore investigation of the effects of industrial processing and/or household preparation on the nature of the residue and on the residue levels is not required.

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

Whereas chlorsulfuron rapidly metabolises in soil, DT90 values are >100 d for the three main metabolites IN-4097, IN-A4098 and IN-JJ998.

Rotational crop studies have been carried out under glasshouse and field conditions respectively. In the glasshouse study, soil was treated with phenyl-^{14}C labelled chlorsulfuron at a rate equivalent to 70 g a.s./ha (3.7N). Wheat, sugar beet and oil-seed rape were planted after 4 and 12 months of aging. Whereas damage caused by the herbicide was generally reversible, rape did no yield seeds. TRR in parts of the plants used for human consumption were low (max. 0.004 mg/kg in wheat grain and 0.008 mg/kg in sugar beet). Higher TRR were found in forage foliage and straw (max. 0.041 mg/kg in wheat straw, 0.016 mg/kg in sugar beet foliage and 0.018 mg/kg in rape forage). Extracts of wheat straw and sugar beet were analysed. No chlorsulfuron was found in the organic fraction. Radioactive residues in the aqueous fraction were shown to be highly polar. Soil samples contained 0.012 and 0.009 mg/kg radioactive residues after aging of the residues for 4 and 12 months respectively.

In the field study, phenyl-^{14}C and triazine-^{14}C labelled chlorsulfuron respectively was applied on plots with spring wheat at a rate of 70 g a.s./ha (3.7N). After ageing of the residues in soil for 12 months, soy, rape and sugar beet were planted. The sugar beet plants died. TRR in sampled plant parts were low (max. 0.009 mg/kg in soybean straw, 0.003 mg/kg in soy beans, 0.004 in rape straw and 0.001 mg/kg in rape seed). TRR in soil samples after aging periods of 12, 18 and 25 months accounted for max 0.029 mg/kg, 0.018 mg/kg and 0.010 mg/kg. Chlorsulfuron was identified at max. 0.001 mg/kg. IN-A4097 and IN-A4098 were present at max. 0.003 mg/kg and 0.004 mg/kg respectively.

The meeting discussed if the possible presence of metabolite IN-A4098 in rotational crops was sufficiently investigated, as residues of triazine-^{14}C labelled chlorsulfuron in rotational crops were only studied after aging of the residues for 12 months. The experts concluded that model calculations on the basis of the results of the rotational crops studies and of PEC soil calculations for the metabolite show that no quantifiable residues of IN-A4098 are expected in rotational crops after application of chlorsulfuron at the cGAP on primary crops.

Furthermore, the meeting concluded that it was uncertain if the possible presence of the two other relevant soil metabolites (IN-A4097 and IN-JJ998) was investigated in the rotational crop studies. If this was not the case, the notifier should clarify if these metabolites are taken up by rotational crops and therefore add to the risk of the consumer. A respective data gap was formulated. The notifier has submitted related information in August 2008, but it could not be evaluated or peer reviewed at this stage.

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

Calculations of the dietary burden show that no significant intake of chlorsulfuron residues is expected for chicken, dairy and beef cattle, and pigs after feeding of cereal grain or straw treated according to the GAP. The calculation for chlorsulfuron (0.01 mg/kg (LOQ) in cereal grain and 0.05 mg/kg (HR) in cereal straw) included in the DAR showed a maximum intake for beef cattle of 0.035 mg/kg DM/day. The RMS provided the results for the intake calculation for the metabolite IN-A4097 (for residue levels of 0.005 mg/kg in cereal grain and straw, see section 3.1.1). The highest intake was calculated for beef cattle (0.000125 g/kg bw/day). EFSA carried out dietary burden calculations taking account of correction factors as suggested in section 3.1.1. The estimated intake for beef cattle was 0.002 g/kg DM/day.

Although no significant residues in livestock feed are expected, the notifier has submitted metabolism studies on chlorsulfuron in lactating goats and laying hens. The studies have been reported and evaluated in the DAR. The meeting of experts agreed on the residue definition for livestock.

Lactating goats were administered phenyl-^{14}C and triazine-^{14}C labelled chlorsulfuron respectively at dosing levels of approximately 25 mg/kg feed for three consecutive days. The majority of the administered radioactivity was excreted, mainly through faeces. Chlorsulfuron was the only radioactive component identified in the urine and accounted for approximately 70% of TRR. In faeces two major radioactive components were identified, chlorsulfuron and IN-M6957. In milk radioactive residues of approximately 0.05 mg/kg were found, chlorsulfuron and triazine IN-A4098 were identified. Kidney contained TRR at concentrations of max. 0.16 mg/kg, chlorsulfuron and IN-A4097. The TRR in liver accounted for max. 0.05 mg/kg, IN-A4097 was identified. TRR in muscle samples were max. 0.03 mg/kg.

Laying hens were administered phenyl-^{14}C at dosing levels of 1.1 and 47 mg/kg diet respectively for 14 days or triazine-^{14}C labelled chlorsulfuron at dosing levels of 1.0 and 45 mg/kg diet for 5 days. Most of the radioactive residues were found in excreta. Approximately 90% of the extracted radioactivity was identified as chlorsulfuron. The main metabolite (up to 12%) which was found in excreta extracts could not be identified. TRR was found to be ≤0.01 mg/kg in eggs from the low dose studies and max. 0.11 mg/kg in the high dose studies. Chlorsulfuron, IN-V7160 and IN-A4098 could be identified in extracts of different eggs at the high dose level. TRR was <0.01 mg/kg in most of the tissues of the low dose study with low concentrations of radioactivity found in kidney and muscle. In the high dose group, highest radioactive residues were found in kidney (0.5 mg/kg) and liver (0.15 mg/kg). In liver extracts from the high dose group chlorsulfuron, IN-A4097, IN-M6957, IN-A5760[19], A4098 and IN-V7160 were found. In extracts of muscle chlorsulfuron, IN-A4097, IN-V7160 and IN-A4098 were identified. Residues in fat could not be identified. No information concerning

[19] IN-A 5760: 2-chloro-5-hydroxybenzenesulfonamide

metabolites formed in kidney is included in the DAR. EFSA notes that this information might be required for further uses, especially regarding the risk assessment for metabolite IN-A4097.

After oral administration of chlorsulfuron to goats or hens, residues are rapidly excreted, mainly as chlorsulfuron and smaller amounts of IN-M6957 (only identified in faeces of goats). Only small amounts of residues are transferred into tissues, milk or eggs. However, a more extensive metabolism was observed in these compartments. Cleavage of the sulfonylurea linkage of chlorsulfuron to produce IN-A4097 and IN-V7160 is the primary metabolic pathway. Two further metabolites (IN-A5760 and IN-A4098) which were only identified in hen tissues can be formed by further metabolism of the primary metabolites or from chlorsulfuron through alternative pathways.

Taking into account that no quantifiable residues are expected on the basis of the intended uses, the following residue definition for food of animal origin for monitoring is suggested: chlorsulfuron only.

The expert meeting agreed on the following residue definition for food of animal origin for the risk assessment: chlorsulfuron; metabolite IN-A4097 separately. (For the discussion see section 3.1.1).

3.3. CONSUMER RISK ASSESSMENT

The PRAPeR 54 meeting discussed the toxicological relevance of metabolite IN A4097, which was considered as a relevant groundwater metabolite. Classification category R40 for chlorsulfuron was proposed. The meeting concluded that there was not enough evidence to exclude that the metabolite was carcinogenic. An ADI of 0.009 mg/kg bw/day was set for IN A4097.

An intake calculation on the basis of the ADI of 0.2 mg/kg for chlorsulfuron set by the PRAPeR 54 meeting with the EFSA PRAPeR model was provided by the RMS but was not peer-reviewed. It showed that the WHO Cluster diet B and Danish model for children are the most critical models (TMDI = 0.1% ADI).
The consumer risk assessment for the metabolite IN-A4097 was also not peer reviewed. In Addendum 2 to Volume 3 of the DAR (August 2008), the RMS provided calculations of the chronic risk for the intake of barley only (residues of 0.005 mg/kg) on the basis of EFSA PRAPeR model. They showed the highest TMDI values for the Irish adult (0.1% ADI) and the WHO Cluster diet E and F (0.0% ADI). Calculations on the basis of EFSA PRAPeR model carried out for EFSA for intake of wheat, rye, barley and oats (estimated residues of 0.0013 mg/kg) showed the highest TMDI values for the Danish model (0.1%ADI) and the WHO Cluster diet B (0.1%ADI). EFSA notes that for future uses it might be necessary to further investigate the possible presence of IN-A4097 in cereal grain and with regard to the setting of MRLs in feeding stuffs, also in cereal feeding stuff (see also above concerning rotational crops).

EFSA notes that the intake calculations can only be regarded as provisional. They were not peer reviewed and the risk assessment for the metabolite IN-A4097 is not based on results of residue trials but only on estimated values from a metabolism study.

The experts meeting discussed if potential exposure from chlorsulfuron through drinking water has to be taken into account. The results of preliminary FOCUS ground water calculations show that the PECgw for IN-A4097 is expected to exceed 0.1 µg/L. Maximum concentrations of up to 1.452 µg/L were reached for spring applications and concentrations of up 1.637 µg/L for autumn calculations. On the basis of the conclusions of PRAPeR 54 toxicology meeting (see above) IN-A4097 has to be regarded as relevant metabolite according to stage 3 step 3 of the assessment following the draft guidance document SANCO/221/2000-rev.10.

3.4. PROPOSED MRLS

Based on the results of the submitted residue trials (see section 3.1.1) an MRL of 0.01 mg/kg for cereals (wheat, rye, triticale, barley and oats) is proposed. MRLs for products of animal origin are not necessary for the representative use.

4. Environmental fate and behaviour

Fate and behaviour of chlorsulfuron in the environment was discussed in the PRAPeR meeting of experts PRAPeR 52 (June-July 2008) on basis of the DAR (July 2007) and the addendum 1 (June 2008). After the experts meeting EFSA received addendum 2 (August 2008) from the RMS. If not otherwise stated, the fate and behaviour experiments were performed by duplicate with chlorsulfuron ^{14}C labelled at the phenyl and chlorsulfuron ^{14}C labelled at the triazine ring.

4.1. FATE AND BEHAVIOUR IN SOIL

4.1.1. ROUTE OF DEGRADATION IN SOIL

Route of degradation of chlorsulfuron in soil under dark aerobic conditions at 20 °C was investigated in one soil (pH 8.3. OC 2.1 %, clay 21.2 %). Degradation of chlorsulfuron was very limited in this particular soil with more than 65 % AR remaining as chlorsulfuron at the end of the study (120 d) and presenting the longest half life (DT_{50} = 232 d) of all the 25 degradation experiments listed by the applicant. In this experiment, only two metabolites exceeded 5 % AR at two consecutive data points: **IN-JJ998** (max. 7.2 % AR after 120 d), **IN-A4098** (max. 8.2 % AR after 120 d). Other two metabolites were increasing in amount at the end of the study: **IN-A4097** (max. 3.3 % AR after 120 d) and **IN-M6957** (max. 4.0 % AR after 120 d). Taking into consideration the relatively low degradation of the parent chlorsulfuron observed in this study, it may not be excluded that the trigger values for soil assessment and / or ground water risk assessment are exceeded in less extreme soils by these or other metabolites. In fact, among the additional information presented by the RMS after the meeting and reproduced in addendum 2, there is data from a Du Pont chlorsulfuron soil metabolism

study that has not been submitted in the dossier but was used as background for one of the published papers listed.[20] In this experiment (performed on a Keyport silt loam soil at 25 °C; pH 6.4, OC 1.6 %) degradation occurred at a faster rate (DT_{50} = 12.2 d) and the two main metabolites IN-A4098 and IN-A4097 reached levels of about 40 % AR (DAT ~ 120 – 180) and about 50 % AR (DAT ~ 60 – 180) respectively (see Addendum 2 p. 189). Since fit is not possible to derive kinetic formation fractions for the metabolites from the study available in the dossier e, a new data gap has been identified after the experts' meeting to submit and kinetically assess the DuPont soil metabolism study, which was used as background data to support paper Streck, H.J. (1998)[14] in order to derive formation fractions of the metabolites. Furthermore, amount of these metabolites also reach significantly high levels in some of the field studies available performed with radio labelled material (IN-A4097 up to 77.5 % AR, IN-A4098 up to 65.9 % AR and IN-JJ998 up to 26.7 % AR).

In a separated study, degradation of chlorsulfuron (^{14}C labelled either at the phenyl or at the triazine ring) was also investigated under dark anaerobic conditions at 25 °C in four anaerobic systems (3 soils and one sediment: pH 5 – 8.4; OC 2.2 – 4.4 %; clay 1 – 31 %). In these experiments, anaerobic conditions were set at the moment of the application and degradation under anaerobic conditions was not preceded by an aerobic phase. Major metabolite **IN-D5293**[21] (max. 14 % AR after 56 d) not identified under aerobic conditions was found under anaerobic ones. Experts in the meeting agreed that some MSs may have field anaerobic conditions under the conditions of use for the EU representative use (cereals). Therefore, a new data gap was identified to address major anaerobic soil metabolite IN-D5293 with respect to soil and ground water compartments. This data gap was considered not essential to finalize EU risk assessment.

Photolysis of chlorsulfuron (^{14}C labelled either at the phenyl or at the triazine ring) in one soil (pH 8.0, OC 1.2 %, clay 29 %) was investigated under simulated sun light (Suntest) at 25 °C. In this experiment, photolysis enhanced degradation of chlorsulfuron. Formation of metabolite **IN-V7160** (max. 7 % AR after 31 d [end of the study] 12 h cycles) was significantly enhanced by photolysis.

4.1.2. PERSISTENCE OF THE ACTIVE SUBSTANCE AND THEIR METABOLITES, DEGRADATION OR REACTION PRODUCTS

In the study that investigates aerobic route of degradation in soil, summarized in the section above, chlorsulfuron was high persistent in soil ($DT_{50\ lab\ 20\ °C}$ = 232 d). Additionally, the applicant presented a position paper reviewing published scientific literature that contains up to 25 chlorsulfuron degradation rate determinations in soil. However, the individual scientific papers quoted in this review were not provided in the dossier. The submission of the original papers was identified as a data gap during the peer review. Additionally, the peer review noted that an assessment of each individual experiment with enough background information to assess its relevance and adequacy for

[20] Streck, H. J. 1998, Fate of chlorsulfuron in the environment. 1. Laboratory evaluations. *Pesticide Science,* **53:** 29-51.
[21] **IN-D5293:** 2-chlorophenylsulfonylurea

the EU environmental risk assessment was missing both in the dossier and in the DAR. The fact that all the articles quoted had been published in peer reviewed journals, and therefore scientifically validated, does not necessary imply the adequacy of these data for the EU risk assessment. Before the meeting, the applicant presented a position paper to the RMS to address the clarification required including reanalysis of kinetic data according FOCUS kinetics. This position paper had not been evaluated and summarized by the RMS in an addendum at the time when the meeting of experts took place and therefore it was not possible to peer review it. After the meeting, the RMS reproduced the applicant's position paper in addendum 2 without additional comments or assessment. EFSA did a brief examination of the data presented and the following shortcomings were identified (Table 7, pg 157 – 159):

- Some typos were found in the list of recalculated DT_{50}'s: ref. 3 soil Flanagan half life is stated 16.7 and should be 6.7 d; ref.8 soil Halbury half life is stated 4.5 and should be 45 d.
- For ref. 9 soil Colorado pH 6.2, it is stated that the slow phase DFOP DT_{50} is reported as recalculated DT_{50}, but the fast phase is quoted instead (DT_{50} = 4.5 d). The correct slow phase DT_{50} is 115.52 d.
- For ref. 2. soil Nebraska pH 7.5 applicant choose the SFO fit for modelling purposes (DT_{50} recalculated = 56.8 d, poor visual fit with a plot of residuals indicating a non-random error). On the EFSA's opinion, second phase DFOP DT_{50} (DT_{50} = 101.11 d) should be used instead.
- For ref. 6 the recalculated DT_{50} values presented have been derived on basis of data from only one of the soil horizons. In the EFSA's opinion these values should be disregarded for the derivation of modelling end points.
- Ref. 4 refers to a study performed on a volcanic soil. Further examination of background data and possible experts' discussion would be needed to decide its inclusion or not as representative EU soil.

Taking into consideration the above observations, chlorsulfuron may be considered to exhibit low to high persistence in soil (DT_{50} = 6.7 – 232 d) under aerobic conditions. The geometric mean half life would be 47.12 d (*versus* the half life of 28.2 d proposed by the applicant) and the normalized half life would be 51.35 (*versus* the normalized half life of 32 d proposed by the applicant). However, these half lives should be considered only as indicative since they are not peer review and the original background reports and papers have not been directly examined. Tabulated data used to perform the kinetic analysis is not provided and individual values can not be validated. From the position paper (Streck and Mackay, 2008) reproduced in addendum 2 (p 137 – 209), it becomes apparent that published papers in references 1, 3 and 7 used as background information, the studies are performed and owned by the applicant. These studies are not available in the dossier and would have to be submitted. Since the background route study in ref. 7 has already been required in the context of the

route of degradation, a new data gap is identified here for the DuPont studies used as background information of papers of Beyer, EM *et al.* (1987)[22] and paper of Joshi, M.M. *et al.* (1985)[23].

Rate of degradation of soil metabolite IN-A4097 under dark aerobic conditions at 20 °C was investigated in one study with five soils (pH 5.2 – 8.1; OC 0.8 – 2.2 %; clay 6.8 – 30.4 %). This metabolite is high to very high persistent under these conditions (DT_{50} = 175 – 436 d).

Rate of degradation of soil metabolite IN-A4098 under dark aerobic conditions at 20 °C was investigated in one study with three soils (pH_{CaCl2} 5.7 – 7.7; OC 1.45 – 2.38 %; clay 8 – 14 %). Further kinetic evaluation of this study was required during the peer review for non linear fitting of the data. Before the meeting of experts, the applicant presented a position paper with additional kinetic evaluation. However, this information was neither summarized nor assessed by the RMS before the meeting and therefore it has not been peer reviewed. After the meeting, the RMS reproduced the applicant's position paper in addendum 2. EFSA briefly examined it and found the SFO half lives were adequately derived. According this new fitting, this metabolite may be considered moderate to medium persistent in soil ($DT_{50\ lab}$ = 43.2 – 65.9 d). These values result on a normalized geometric mean value of 54.4 d, above the end point originally used in the assessments presented in the DAR (DT_{50} = 39 d; 23 d).

Rate of degradation of soil metabolite IN-JJ998 under dark aerobic conditions at 20 °C was investigated in one study with five soils (pH 6.2 – 8.5; OC 1.0 – 2.8 %; clay 7.0 – 36.6 %). Further kinetic evaluation of this study was required during the peer review for non linear fitting of the data. Before the meeting of experts, the applicant presented a position paper with additional kinetic evaluation. However, it was neither summarized nor assessed by the RMS before the meeting and therefore it has been not peer reviewed. After the meeting the RMS reproduced the applicant's position paper in addendum 2. EFSA briefly examined it and found that the SFO half lives were adequately derived. According to this new fitting, this metabolite may be considered medium to high persistent in soil (DT_{50} = 91.6 – 107.4 d). These results are only slightly different to the values presented in the DAR. Following the FOCUS kinetic recommendations, the applicant proposes to use the second phase DFOP DT_{50} = 121 as persistence end point for this metabolite. Modelling geometric mean half life proposed in the DAR ($DT_{50\ lab\ soil\ geometric\ mean}$ = 74 d) would remain invariable after the new kinetic assessment.

Rate of degradation of chlorsulfuron in soil under anaerobic conditions was investigated in the same study summarized in the route section. The meeting of experts agreed that only the value obtained with at least five data points (Baron's Alberta, Canada) should be retained in the list of end point ($DT_{50\ lab\ 20\ °C\ anaerobic}$ = 78.2 d).

[22] Beyer, E.M., Duffy, M.J., Hay. J.V., Schlueter, D.D. 1987. Chapter 3. Sulfunylureas, Herbicides, in *Chemistry, degradation and Mode of Action, Volume 3,* ed. P.C. Kearney, D.D. Kaufman, Marcel Dekker, Inc. New York and Base. Pp. 117-189.

[23] Joshi, M.M., Brown, H.M., Romesser, J.A. 1985. Degradation of chlorsulfuron by soil microorganisms. *Weed Science,* **34**: 328 – 332.

Half life of chlorsulfuron in soil due to photolysis study was calculated to be 62.2 d (12 h) with respect to a half life of 355 d (12 h) in the dark control. During the peer review, the applicant was requested to provide an estimation of the photolysis in soil half lives at different latitudes (35 – 55 °N) representative of EU situations. Since the information provided was found to be not satisfactory by the meeting of experts, a data gap was identified for this estimation.

Field dissipation studies performed in California, Idaho (USA), Spain and Italy (2 sites) are available in the dossier. The meeting of experts discussed the suitability of the available field studies to derive degradation kinetic parameters of chlorsulfuron to use in the modelling for fate and behaviour. All the field trials presented were performed on bare soil, where the product was applied on the surface. Soil aerobic metabolites IN-A4097, IN-A4098 and IN-JJ998 and the soil photolysis metabolite IN-V7160 were analyzed in these studies. The meeting noted that photolysis contributed to the degradation of chlorsulfuron in these field trials and that most of the compounds were highly mobile. A detailed assessment of the suitability of field studies to derive kinetic parameters (as required by FOCUS kinetics, CBS check list) was missing in the DAR. Therefore, the experts agreed that the derived half lives are not suitable kinetic degradation parameters for modelling purposes. The experts also noted that, in the DAR, it was not transparently reported how the formation fractions and half lives of metabolites were derived (individual data points and graphical representations not available). With respect to formation fractions, it was noted that in some cases these were below of the maximum observed in field studies, which is in contradiction to the theoretical grounds of kinetics. A different route of degradation was proposed for alkaline and acidic soils; however, the meeting could not confirm any pH dependence on the degradation of chlorsulfuron in soil from the data available. Further details on the normalization procedure were presented by the RMS in addendum 1. However, the end points derived were not validated by the experts due to shortcomings in the transparency of the report and the fundamental reasons given above. During the written procedure on the conclusion, two MSs expressed some discrepancies between the draft EFSA conclusion and the conclusions drawn in the expert meetings. In opinion of these MSs the field dissipation studies could be used to obtain kinetic parameters on basis of a detailed assessment according FOCUS kinetics guidance criteria. Nevertheless, no MS has disagreed with the meeting conclusions on the lack of transparency on the kinetic analysis and the lack of experiments representing Northern EU conditions (see below).

With respect to the use of the field dissipation half lives for PEC soil calculations, the experts discussed if the available field data could represent dissipation of chlorsulfuron under Northern EU conditions. The applicant claimed that the study in Idaho (USA) could be considered representative of Northern – EU. The experts noted that no information was available to assess this later point, but considered that data from a single field trial could not be considered representative enough (at least data on four sites representative of Northern EU would be needed).

Potential accumulation in soil had been addressed in the dossier by four field accumulation trials on wheat in Southern EU (Spain, Italy [2 sites] and Greece). To the applicant's opinion accumulation studies were not triggered. Nevertheless, not enough field data representative for Northern European conditions are available. The experts agreed that soil exposure assessment for Northern EU could not

be finalized based on field studies. Therefore, the PEC soil used in the ecotoxicological risk assessment was not agreed and the calculation of new PECs soil were proposed. However, in the DAR PEC soil using the worst case laboratory half life over ten years of continuous use are provided (0.037 mg / kg). This PEC soil has been used by EFSA to finalize the soil risk assessment.

4.1.3. MOBILITY IN SOIL OF THE ACTIVE SUBSTANCE AND THEIR METABOLITES, DEGRADATION OR REACTION PRODUCTS

Batch soil adsorption / desorption studies are available for chlorsulfuron in four soils (pH 5.4 – 8.0; OC 0.8 – 4.3 %, clay 8 – 14 %) and for metabolites IN-A4097 in five soils (pH 5.2 – 8.1; OM 1.4 – 4.3 %, clay 6.8 – 30 .4 %), IN-A4098 in seven soils (2 different studies: pH 5.3 – 7.7; OC 0.5 – 3.0; 4.4 – 30.8 %) and IN-JJ998 in five soils (pH 6.2 – 8.5; OC 1.1 – 1.3; clay 7.0 – 21.5). According these studies chlorsulfuron may be considered to exhibit high to very high mobility in soil (K_{fOC} = 14.1 – 60.2 mL / g), IN-A4097 may be considered to exhibit very high mobility in soil (K_{fOC} = 21.2 – 48.2 mL / g), IN-A4098 may be considered to exhibit very high to medium mobility in soil (K_{fOC} = 16.7 – 225.5 mL / g) and IN-JJ998 may be considered to exhibit high to very high mobility (K_{fOC} = 14.7 – 114.0 mL / g).

Additionally, the applicant presented Koc estimations obtained using PCKOCWIN for metabolites IN-B5528[24], IN-M6957 and photolysis metabolite IN-V7160. According these estimations IN- B5528 and IN-V7160 are very highly mobile in soil and IN-M6957 may be considered low mobile in soil.

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

Hydrolysis of chlorsulfuron was investigated in aqueous buffered solutions (pH 5,7, and 9) at 25 °C under dark conditions. Chlorsulfuron is stable at pH 7 and 9 and hydrolyses with a half life of 23.2 d at pH 5. Main hydrolysis metabolites are IN-A4097 (max. 33 % AR), IN-A4098 (max. 17 % AR), IN-F5475[25] (max. 9 % AR), IN-M6957 (14 % AR) and triazine ring-opened acetyltriuret chlorsulfuron[26] (max. 18 % AR).

Aqueous photolysis of chlorsulfuron was investigated in aqueous buffered solutions (pH 5,7, and 9) irradiated with natural sunlight (Wilmington, Delaware, 90 m above see, 39 ° 46’ 28” N, 16-06-1989 to 24-07-1989) at 25 °C. Degradation was only observed at pH 5 with a rate slightly higher than the one observed in the dark control. The degradation rate attributed directly to the effect of photolysis (once hydrolysis is subtracted) was calculated to correspond to a half-life of 100 d. Therefore,

[24] IN-B5528: 4-amino-6-methyl-1,3,5-triazin-2-ol

[25] IN- F5475: 6-methyl-1,3,5-triazine-2,4-diol;
N-(carbamoylcarbamoyl)acetamide

[26] triazine ring-opened acetyltriuret chlorsulfuron: N'-acetyl-N-[(E)-amino({[(2-chlorophenyl)sulfonyl]carbamoyl}amino)methylidene]carbamimidic acid

photolysis in water is not considered to contribute significantly to the environmental degradation of chlorsulfuron.

Chlorsulfuron was found not to be readily biodegradable according the available test (OECD 301B).

Dissipation / degradation of chlorsulfuron in the aquatic environment were investigated in one study with one aerobic water / sediment system (pH_{water} 8.1; pH_{sed} 7.8; OC 5.3 %, clay 6) and an anaerobic system (pH_{water} 7.5; pH_{sed} 8.3; OC 1.7 %, clay 27%). The proportion of sediment/water used in these experiments was 1/4 w/w (on dry sediment basis) in the lower limit of the recommendations given by SETAC guidance (1 / 4 – 1 / 10 w/w).[27] Under these conditions, chlorsulfuron is degraded relatively rapid in the aerobic system ($DT_{50\ whole\ system}$ = 26 d) and is very high persistent under anaerobic conditions ($DT_{50\ whole\ system}$ = 375 d). Only one aerobic water / sediment is available in the dossier. The meeting of experts identified a data gap (considered not essential to finalize the EU risk assessment) for a new water / sediment study under acidic conditions.

Two major metabolites were identified both in the aqueous and the sediment phases of the aerobic water system: **IN-M6957** (max. $_{water}$ 22.2 % AR; max. $_{sed.}$ 21.6 % AR) and **IN-JJ998** (max. $_{water}$ 11.4 % AR; max. $_{sed.}$ 16.5 % AR).

PECs $_{SW/SED}$ presented in the DAR were not validated during the peer review due to the lack of adequate input parameters. Therefore, a new data gap was identified for new PEC $_{SW/SED}$. In case new Step 4 calculations are needed to finalize the risk assessment, the effect of spray drift mitigation and run off mitigation should be presented separately. EFSA PPR Panel Opinion on FOCUS Landscape and the FOCUS Landscape guidance document must be followed.[28,29] If mitigation of run off needs to be modelled, it should be transparently reported how the effect of vegetative buffer strips is incorporated in the model.

4.2.2. POTENTIAL FOR GROUND WATER CONTAMINATION OF THE ACTIVE SUBSTANCE THEIR METABOLITES, DEGRADATION OR REACTION PRODUCTS

Potential ground water contamination by chlorsulfuron and soil metabolites IN-A4097, IN-A4098, IN-M6957, IN-JJ998, IN-V7160 and IN-B5528 was addressed in the dossier by estimation of 80th percentile concentration in the leachate at 1m depth, calculated with FOCUS GW modelling PELMO 3.3.2. Additional calculations performed with FOCUS GW PEARL were presented in the addendum 3 (June 2008) to fulfil requirements imposed by EFSA PPR panel opinion on FOCUS GW.[30] The Meeting of experts discussed the FOCUS calculations as presented in addendum 3. Based on the

[27] In the DAR this proportion is mistakenly reported on basis of wet sediment weight as 1 / 0.6 – 1 / 2.4 w/w.

[28] Opinion of the Scientific Panel on Plant protection products and their residues (PPR) related on the Final Report of the FOCUS Working Group on Landscape and Mitigation Factors in Ecological Risk Assessment. The EFSA Journal (2006) 437, 1-30.

[29] Landscape and mitigation factors in aquatic ecotoxicological risk assessment, The Final report of the FOCUS Working Group on Landscape and Mitigation Factors in Ecological Risk Assessment. SANCO/10422/2005, version 2.0, September 2007.

[30] Opinion of the Scientific Panel on Plant Health, Plant Protection Products and their Residues on a request of EFSA related to FOCUS groundwater models.The EFSA Journal (2004) 93, 1-20.

results of field studies the applicant proposed different degradation pathways and formation fractions of metabolites for acidic and alkaline soils. Based on the results of laboratory degradation studies published in the scientific literature, the applicant also claimed that a strong positive correlation was found between soil pH and half life of chlorsulfuron in soil. However, no apparent pH dependence is observed in the field dissipation half lives. The applicant presented calculations using the geometric mean of normalized published laboratory half lives of chlorsulfuron (labelled as Tier 1 calculations, only PELMO) and with geometric mean of the normalized half lives of chlorsulfuron in field studies (labelled as Tier 2 calculations, PELMO and PEARL). For metabolites IN-JJ998, IN-A4097 and IN-A4098 geometric mean of laboratory half lives were used in the modelling. For metabolites IN-M6957, IN-V7160 and IN-B5528 half lives derived from the field dissipation studies were used in the modelling. Standard arithmetic mean K_{foc} or estimated K_{foc} (for minor and photolysis metabolites) were used as input parameters. In the calculations named Tier 1, chlorsulfuron and metabolites IN-JJ998, IN-A4097 exceeded the trigger of 0.1 µg / L in some of the scenarios simulated. Metabolite IN-A4097 also exceeds the trigger of 0.75 µg / L in some of the scenarios of both calculations (named Tier 1 and Tier 2).

Among all the degradation parameters used in these simulations, only the degradation half lives for the metabolite IN-A4097 have been completely validated during the peer review. Neither degradation half life of chlorsulfuron nor formation fractions of metabolites has been confirmed. Additionally, normalization procedures had not been transparently reported by the time the meeting took place. The presumed pH dependence of chlorsulfuron degradation and the pH dependence of the formation fractions of the metabolites could not be confirmed by the meeting of experts. As previously indicated, the meeting of experts did not consider available field studies adequate to derive modelling kinetic parameters, therefore neither the calculations named as “Tier 1”, which use field studies to determine metabolite formation fractions, nor the ones named “Tier 2” can be considered reliable for EU risk assessment. Furthermore, the half life for chlorsulfuron based on published laboratory studies used in the calculations named as “Tier 1” was not confirmed by the meeting.

Therefore, a new data gap was identified for new FOCUS PEC GW modelling with adequate kinetic input parameters when available.

4.3. FATE AND BEHAVIOUR IN AIR

Based on its physical and chemical properties, chlorsulfuron is not expected to volatilize significantly under normal environmental conditions. Half life in the atmosphere due to photochemical degradation has been estimated to be 2.1 days (see section B2 in the DAR).

5. Ecotoxicology

Chlorsulfuron was discussed at the PRAPeR expert meeting for ecotoxicology (PRAPeR 53 – sub-group 2) in July 2008 on the basis of the Draft Assessment Report (DAR) and the addendum 1 (B.9).

The supported use evaluated was to control a wide range of broad-leaf and grass weeds in cereal crops (winter, spring), pre and post-emergence. The representative product was "Chlorsulfuron 75 WG", with a maximum application rate of 18.75 g a.s./ha (once per growing season).
The risk assessment was conducted according to the following guidance documents: Risk Assessment for Birds and Mammals. SANCO/4145/2000 September 2002; Aquatic Ecotoxicology, SANCO/3268/2001 rev.4 final, October 2002; Terrestrial Ecotoxicology, SANCO/10329/2002 rev.2 final, October 2002; Risk Assessment for non-target arthropods, ESCORT 2, March 2000, SETAC.

5.1. RISK TO TERRESTRIAL VERTEBRATES

The submitted studies with chlorsulfuron indicated a low acute and short-term toxicity to birds. No mortality was observed at the highest tested doses: acute LD_{50} >5000 mg a.s. /kg bw (*Anas platyrhynchos* and *Colinus virginianus*) and the lowest short-term LC_{50} >634 mg a.s. /kg bw /day (*A. platyrhynchos*). The lowest long-term toxicity (reproduction) NOEL was 28 mg a.s. /kg bw/day (*C. virginianus*).
On the basis of mammalian toxicity data, the acute LD_{50} was >5545 mg a.s./kg (rat) and the long-term toxicity (reproductive) NOAEL was 75 mg a.s./kg bw/day (rat).
The TERs were calculated for large herbivorous birds, small herbivorous mammal, insectivorous birds and insectivorous mammals. All the first-tier TERs were above the Annex VI trigger of 10 and 5 indicating a low risk to birds and mammals.
The risk of secondary poisoning (i.e. earthworm-eating birds and mammals, fish-eating birds and mammals) was considered to be low (log P_{ow} = -0.99).
Overall, on the basis of available data, it was concluded that the risk to terrestrial vertebrates was low for the representative use of chlorsulfuron.

5.2. RISK TO AQUATIC ORGANISMS

Studies with technical chlorsulfuron and its metabolite on fish, invertebrates, algae and non-target plants were provided and peer reviewed. Metabolites were less toxic than the active substance in invertebrate, algae and plant tests, except the metabolite IN-JJ998, for which the chronic toxicity to *Daphnia magna* was comparable to that of chlorsulfuron.
The formulated product ("Chlorsulfuron 75 WG") was tested on algae and aquatic plants, showing a similar toxicity as the active substance, based on the content of the active substance.
Algae and aquatic plants were the most sensitive organisms. The endpoint driving the risk assessment was observed in a study with technical chlorsulfuron and *Lemna gibba* (14-day E_bC_{50} = 0.35 µg/L). The endpoint of 0.11 µg/L from *Lemna minor* study was not supported for risk assessment by the experts of member states because the study was considered not valid (measurements of the analytical concentrations were not performed during the test).

For algae, the lowest endpoint was observed in a study with *Selenastrum capricornutum* and the formulated product (72-h EC_{50} was 66 µg/L). Since the criterion for coefficient of variation was partially not met, the validity of a study on *Anabaena flos-aquae* with technical chlorsulfuron as well as the validity of studies on *S. capricornutum* with the metabolite IN-JJ998 and the technical chlorsulfuron, was discussed at the experts meeting. For the study on *S. capricornutum* with technical chlorsulfuron raw data were provided by the applicant and reported in addendum 1 (June 2008). The experts recognised that such studies were conducted when the coefficient of variation was not yet considered as a validity criterion. Nevertheless for biomass the quality criteria were met; therefore, it was concluded to consider these studies as valid.

Chlorsulfuron is of low acute toxicity to fish and aquatic invertebrates: no mortality was observed at the highest tested concentrations: 96-h LC_{50} >122 mg/L (*Oncorhynchus mykiss*) and the EC_{50} >112 mg/L (*Daphnia magna*). NOECs of 32 mg/L (77-d flow-through reproduction test, *O. mykiss*) and of 12 mg/L (21-d reproduction test, *D. magna)*, were observed in chronic toxicity studies.

Chlorsulfuron and its major metabolite TERs were calculated based on FOCUS Step 2 PEC_{sw} values. A potential high risk to aquatic plants for the active substance was identified (TER = 0.114). The other TERs were above the Annex VI triggers.
FOCUS Step 3 and on FOCUS Step 4 modelling was provided to refine the risk to *L. gibba*. However, the PRAPeR experts' meeting 52 considered the $PEC_{sw/sed}$ not valid and requested new calculations based on adequate input parameters (see section 4.2.1). Nevertheless, on the basis of available calculations, TERs were below the Annex VI trigger of 10, ranging from 0.144 to 4.487 for all Step 3 scenarios, except R1-pond (TER of 29.17). The Step 4, including a non-spray buffer zone of 5 m, was only conducted for R1-stream, R3-stream, R4-stream and D3-ditch whereas 14 scenarios were considered at the Step 3. The TERs were still below the trigger of 10, except for the D3-ditch (TER = 10.61). Therefore a data gap was identified to provide a new risk assessment for *Lemna*.
The new TER calculations should be based on global maximum PEC as agreed by the experts, due to the uncertainty of the persistence of chlorsulfuron in water (see data gap in section 4.2.1 for two new water/sediment studies). Originally, the RMS had considered the 14-d twa-PEC more appropriate to take into account the recovery, since in the study with *Lemna* a recovery was observed at concentrations of chlorsulfuron less or equal to 1 µg/L.
Furthermore, EFSA recommended to conduct the FOCUS Step 4 modelling for all the scenarios which do not pass the Step 3, in order to address the risk to aquatic plants and thus to identify appropriate mitigation measures (i.e. mitigation measures equivalent to a non-spray buffer zone >5).

5.3. RISK TO BEES

Acute contact and oral toxicity studies were conducted with technical and formulated product ("Chlorsulfuron 75 WG") showing similar toxicity of the a.s. when formulated (contact LD_{50} > 100 µg a.s./bee and >135.1 µg product/bee). The HQ values were below the Annex VI trigger of 50 indicating a low risk to bees from the representative uses evaluated.

5.4. RISK TO OTHER ARTHROPOD SPECIES

Standard laboratory tests were conducted with formulated chlorsulfuron and the indicator species *Aphidius rhopalosiphi* and *Typhlodromus pyri*. No effects on mortality nor on reproduction were observed at the tested rate of 75 g product/ha (equivalent to 56.25 g a.s./ha, 3-fold the proposed use). The in field HQ values were calculated as <0.33 and the off-field HQs were <0.0092 indicating a low risk for non-target arthropods.

5.5. RISK TO EARTHWORMS

The acute and chronic toxicity to earthworms was tested with the formulated product and the metabolites IN-A4097, IN-A4098 and IN-JJ998. No acute effects were observed at the highest tested concentrations (14-d LC_{50} > 750 mg a.s./kg soil for product and > 1000 for metabolites). Chronic testing was performed with formulated chlorsulfuron and its metabolites. The NOEC for the product was 187.5 mg a.s./kg soil and the lowest value observed for metabolites was 0.2 mg /kg soil (IN-A4098). The TERs were calculated on the basis of the plateau PECs soil and they were above the Annex VI triggers of 10 and 5, indicating a low risk to earthworms for chlorsulfuron and its metabolites. However, since the PRAPeR 52 identified a data gap for new PEC_{soil} values (see section 4.1.2), EFSA recalculated TERs for chlorsulfuron based on worst-case PEC =0.371 mg a.s. /kg. The outcome of the risk assessment was not changed (TERa = 2016; TERlt = 5054).

5.6. RISK TO OTHER SOIL NON-TARGET MACRO-ORGANISMS

Studies assessing the effects (mortality and reproduction) on collembola (*Folsomia candida*) from major soil metabolites were provided. The lowest endpoint was observed for IN-A4098 (NOEC = 0.225 mg/kg soil). TERs calculated on the basis of plateau PECs soil were above the trigger of 5, indicating a low risk. However, according to the data gap identified by the PRAPeR 52 to provide new PEC_{soil} values (see section 4.1.2), TERs should be amended accordingly. The outcome of the risk assessment is not expected to change, since the TER values calculated on the basis of the available PEC_{soil} are approximately 8-fold the trigger.

Effects on organic matter breakdown (litter bag studies) were assessed for chlorsulfuron 75 WG and the metabolite IN-A4097 by field studies conducted in two different locations in Spain (Almacelles and Llida, respectively). No impact on straw degradation was observed in both studies. The extrapolation between southern and northern Europe conditions was discussed at the meeting and

forwarded to the fate experts. An answer was provided by EFSA after the meeting clarifying that such extrapolation is not possible. Therefore, the provided studies on the effects on the decomposition of organic matter in the field cannot be considered suitable for the indented uses in northern Europe.

Overall, on the basis of available data it was concluded that the risk to soil non-target macro-organisms was low. Further data on the effects on organic matter breakdown in field should be provided for northern Europe use.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

No effects of >25 % on soil respiration and nitrification were observed in tests with technical chlorsulfuron and major soil metabolites up to concentrations equivalent to 5-times the application rate proposed, indicating a low risk to soil non-target micro-organisms for the representative uses evaluated.

5.8. RISK TO OTHER NON-TARGET-ORGANISMS (FLORA AND FAUNA)

Herbicidal effects of the formulation "Chlorsulfuron 75 WG" on vegetative vigour and emergence were investigated in tests with 6 dicotyl plant species and with 4 monocotyl plant species. The lowest ER_{50} values were observed for pea (*Pisum sativum*) ER_{50} = 1.09 g a.s./ha and for sugar beet (*Beta vulgaris*) ER_{50} = 0.09 g a.s./ha. The first-tier TERs were 2.1 and 0.2 for pre- and post-emergence treatment based on PECs from spray drift at 1 m distance. TER were calculated above the trigger of 5 with the application of an in-field no-spray buffer zone of 15 m for the pre-emergence application and with an additional drift reduction equal or greater than 50% for the post emergence application. At the meeting the proposed trigger of 1 was not accepted, due to the uncertainty resulting from low representativeness of the sugar beet endpoint for other terrestrial plants.
The probabilistic risk assessment conducted by the RMS on the basis of a species sensitivity distribution approach (HR_{05} = 0.64 g a.s./ha) was not accepted by the experts: the HR_{05} was considered not reliable because of the poor fit of the data.
Overall, it was concluded that on the basis of available data, a potential high risk to terrestrial non-target plants could be excluded only if mitigation measures are applied. EFSA considered the proposed 15 m of in-field no-spray buffer zone quite extensive and probably not practicable. As additional drift reduction nozzles were necessary to achieve a low risk, EFSA suggested a data gap for the applicant to further address the risk in order to reduce the necessary risk mitigation measures.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

Technical chlorsulfuron did not inhibit the respiration of activated sewage sludge at the highest tested concentration of 100 mg a.s./L. It is not expected that the concentrations of chlorsulfuron in biological sewage treatment plants would reach a concentration of more than 100 mg a.s./L if the

product is applied according to the GAP and therefore the risk to biological methods of sewage treatment was considered to be low.

6. Residue definitions

Soil

The definitions given below were considered provisional by the meeting of experts pending the outcome of further evaluation of laboratory and field studies.

Definition for risk assessment: chlorsulfuron, IN-A4097, IN-A4098, IN-JJ998 and IN-V7160 (photolysis metabolite) and IN-D5293 (for anaerobic conditions).
Definition for monitoring: chlorsulfuron

Water

Ground water

The definitions given below were considered provisional by the meeting of experts pending the outcome of further evaluation of laboratory and field studies.

Definition for exposure assessment: chlorsulfuron, IN-A4097, IN-A4098, IN-JJ998, IN-M6957 and IN-V7160 (photolysis metabolite) and IN-D5293 (for anaerobic conditions).
Definition for monitoring: chlorsulfuron, IN-A4097, IN-JJ998 (preliminary pending further data and assessment).

Surface water

The definitions given below were considered provisional by the meeting of experts pending the outcome of further evaluation of laboratory and field studies.

Definition for risk assessment: chlorsulfuron, IN-A4097, IN-A4098, IN-JJ998, IN-M6957 and IN-V7160 (photolysis metabolite) and IN-D5293 (for anaerobic conditions).

Definition for monitoring: chlorsulfuron

Air

Definition for risk assessment: chlorsulfuron
Definitions for monitoring: chlorsulfuron

Food of plant origin

Definition for risk assessment: chlorsulfuron and IN-A4097 separately (cereals only)

Definition for monitoring: chlorsulfuron (cereals only)

Food of animal origin

Definition for risk assessment: chlorsulfuron and IN-A4097 separately

Definition for monitoring: chlorsulfuron

Overview of the risk assessment of compounds listed in residue definitions for the environmental compartments

Soil

Compound (name and/or code)	**Persistence**	**Ecotoxicology**
chlorsulfuron	low to high persistent (DT_{50} = 6.7 – 232 d)	**Risk assessed as low**
IN-A4097	high to very high persistent (DT_{50} = 175 – 436 d)	**Risk assessed as low**
IN-A4098	moderated medium persistent ($DT_{50\ lab}$ = 43.2 – 65.9 d)	**Risk assessed as low**
IN-JJ998	medium to high persistent (DT_{50} = 91.6 – 107.4 d)	**Risk assessed as low**
IN-V7160 (photolysis metabolite)	No information available	No information available
IN-D5293 (for anaerobic conditions)	No information available	No information available

Ground water

Compound (name and/or code)	Mobility in soil	> 0.1 µg / L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological activity
chlorsulfuron	high to very high mobile (K_{fOC} = 14.1 – 60.2 mL / g)	Data gap There are solid indications that the 0.1 µg / L trigger will be exceeded for at least some scenarios		Yes	yes
IN-A4097	very high mobile (K_{fOC} = 21.2 – 48.2 mL / g)	Data gap There are solid indications that the 0.1 µg / L and 0.75 µg / L trigger will be exceeded for at least some scenarios		Yes (Experts' decision related to the proposal Carc.cat.3 R40 for chlorsufuron. Proposed classification to be considered in the ECHA process under Directive 67/548/EEC)	no
IN-A4098	very high to medium mobile (K_{fOC} = 16.7 – 225.5 mL / g)	Data gap		Yes (EFSA's proposal after the meeting, pending confirmation of classification Carc.cat.3 R40 for chlorsulfuron in	no

Compound (name and/or code)	Mobility in soil	> 0.1 µg / L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological activity
				the ECHA process under Directive 67/548/EEC)	
IN-JJ998	high to very high mobile (K_{foc} = 14.7 – 114.0 mL / g)	Data gap There are solid indications that the 0.1 µg / L trigger will be exceeded for at least some scenarios		Yes (see above for IN-A4098)	no
IN-M6957	low mobile on basis of PCKOWIN calculation	No information available		Yes (see above for IN-A4098)	no
IN-V7160 (photolysis metabolite)	very high mobile on basis of PCKOWIN calculation	No information available		Yes (see above for IN-A4098)	no
IN- B5528	very highly mobile on basis of PCKOWIN	No information available		Yes (see above for IN-A4098)	No information available

Compound (name and/or code)	Mobility in soil	> 0.1 µg / L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological activity
	calculation				
IN-D5293 (for anaerobic conditions)	No data available	No information available		Yes (see above for IN-A4098)	No information available

Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Chlorsulfuron (water and sediment)	Potential high risk to aquatic plants. Data gap to further address the risk and identified appropriate mitigation measures.
IN-A4097 (water only)	Risk assessed as low
IN-A4098 (water only)	Risk assessed as low
IN-JJ998 (water and	Risk assessed as low

sediment)	
IN-M6957 (water and sediment)	Risk assessed as low
IN-V7160 (photolysis metabolite)	Risk assessed as low
IN-D5293 (for anaerobic conditions)	No information available

Air

Compound (name and/or code)	**Toxicology**
chlorsulfuron	low acute toxicity by inhalation (rat LC_{50} >5.5 mg/L)

LIST OF STUDIES TO BE GENERATED, STILL ONGOING OR AVAILABLE BUT NOT PEER REVIEWED

- A revised specification (relevant for all uses evaluated, data gap identified by meeting of experts June 2008, proposed submission date unknown, refer to chapter 1)
- Spectra of the relevant impurities (relevant for all uses evaluated, data gap identified by EFSA September 2008, proposed submission date unknown, refer to chapter 1)
- Storage study where the relevant impurities are analysed before and after storage (relevant for all uses evaluated, data gap identified by EFSA September 2008, proposed submission date unknown, refer to chapter 1)
- Method of analysis for the relevant impurities in the formulation (relevant for all uses evaluated, data gap identified by EFSA September 2008, proposed submission date unknown, refer to chapter 1)
- Shelf life study for the formulation in water soluble bag material (relevant for all uses evaluated, data gap identified by meeting of experts June 2008, proposed submission date unknown, refer to chapter 1).
- Should the proposed classification of chlorsulfuron as Carcinogenic category 3 R40 be confirmed in the context of the European Chemicals Agency (EChA) programme for classification and labelling under Directive 67/548/EEC this would, in line with the guidance document on groundwater metabolites, require that, for those metabolites with the potential to contaminate groundwater, convincing evidence must be provided that the metabolites will not lead to the risk of carcinogenicity (relevant for all representative uses evaluated; data gap identified by PRAPeR 54 for IN-A4097 and by EFSA after the meeting for the other metabolites; no submission date proposed by the notifier; refer to point 2.8)
- Clarification if the presence of the soil metabolites IN-A4097 and IN-JJ998 was investigated in the rotational crop studies. If this was not the case, the notifier should clarify if these metabolites are taken up by rotational crops and therefore add to the risk of the consumer. (relevant for all representative uses evaluated; submitted in August 2008; refer to point 3.1.2).
- A data gap has been identified after the experts' meeting to submit and kinetically assess the DuPont soil metabolism study used as background data to support paper Streck, H.J. (1998)[14] in order to derive formation fractions of the metabolites (relevant for all representative uses evaluated; no submission date proposed by the notifier; refer to point 4.1.1)
- A data gap was identified to address major anaerobic soil metabolite IN-D5293 with respect to soil and ground water compartments (relevant for all representative uses evaluated; this data gap was not considered essential to finalize EU risk assessment; refer to point 4.1.1).
- A data gap was identified for the DuPont studies used as background information of papers of Beyer, EM *et al.* (1987) and paper of Joshi, M.M. *et al.* (1985).
- A data gap was identified for an estimation of the photolysis in soil half lives at different latitudes (35 – 55 °N) representative of EU situations (relevant for all representative uses; RMS

informed EFSA that some information has been submitted in August 2008, not evaluated and not peer reviewed; refer to point 4.1.2).

- A data gap was identified for the submission and incorporation in the dossier of the background scientific papers quoted in position paper: Streck, H.J. Chlorsulfuron (DPX-W4189): *Rate of degradation in aerobic soils (2003)*(relevant for all representative uses evaluated; no submission date proposed by the notifier; refer to point 4.1.2)
- A data gap has been identified for at least an additional aerobic water / sediment system performed following the recommendations of SETAC guidance in an acidic system. (not essential to finalize the EU risk assessment; no submission date proposed by the notifier; refer to point 4.2.1)
- A data gap was identified for new PEC $_{SW/SED}$. In case new Step 4 calculations are needed to finalize the risk assessment, effect of spray drift mitigation and run off mitigation should be presented separately. EFSA PPR Panel Opinion on FOCUS Landscape and the FOCUS Landscape guidance document must be followed. If run off mitigation needs to be assumed, it should be transparently reported how the effect of vegetative buffer strips is incorporated in the model (relevant for all representative uses evaluated; no submission date proposed by the notifier; refer to point 4.2.1).
- A data gap was identified for new FOCUS PEC GW modelling for chlorsulfuron and metabolites IN-A4097, IN-A4098, IN-JJ998 and IN-V7160 with adequate kinetic input parameters when available (relevant for all representative uses evaluated; no submission date proposed by the notifier; refer to point 4.2.2)
- A data gap was identified to further address the risk to aquatic non-target plants (relevant for all representative uses evaluated; no submission date proposed by the notifier; refer to point 5.2).
- Effects on organic matter decomposition in field (relevant for use on northern Europe; no submission date proposed by the notifier; refer to point 5.6).
- A data gap was identified to further address the risk to terrestrial non-target plants (relevant for all representative uses evaluated; no submission date proposed by the notifier; refer to point 5.8).

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

This conclusion was reached on the basis of the evaluation of the representative uses as a herbicide on wheat, barley, oats, rye and triticale. Full details of the GAP can be found in the attached list of end points.

The representative formulated product for the evaluation was "Chlorsulfuron 75 WG", a water dispersible granule (WG).

Only single methods for the determination of residues are available since a multi-residue-method like the German S19 or the Dutch MM1 is not applicable due to the nature of the residues.
Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that at least some quality control measurements of the plant protection product are possible. The specification could not be finalised, two impurities were found to be relevant but the maximum content has not been agreed. For the relevant impurities data gaps have been identified for spectra, storage and methods of analysis. A shelf life study was identified as a data gap for the product in water soluble bags.

With regard to its toxicological properties, chlorsulfuron was rapidly but not extensively absorbed after oral administration. Widely distributed in the rat body, it did not accumulate in any organ and was excreted mainly via urine as parent, with two minor metabolites. Of low acute toxicity, chlorsulfuron was not a skin irritant, slightly irritating to the eye and did not induce skin sensitisation. The short term toxicity was manifested by an increased testicular weight (rats), decreased body weight gain and haematological changes (dogs). Chlorsulfuron was not shown to have a genotoxic potential *in vivo*, but induced testicular interstitial cell tumours in the 2-year rat study leading to the proposed classification as **Carcinogen Category 3, R40** (Limited evidence of carcinogenic effects). In the reproductive toxicity studies, effects on the reproductive organs were observed without impact on the fertility parameters and were considered as related to general systemic toxicity. No effect in the offspring was observed up to the highest dose tested. Similarly in the developmental toxicity studies, some effects on the foetal development were considered as a result of maternal toxicity at the high dose level, and it was agreed that chlorsulfuron had no teratogenic properties.
Several metabolites/impurities were evaluated in the DAR and considered by the experts. The compound IN-A4097[31] was concluded to be a relevant groundwater metabolite and a relevant impurity. Based on the available information, there is no sufficient evidence demonstrating the absence of carcinogenic properties. The agreed ADI for IN-A4097 is 0.009 mg/kg bw/day based on the 90-day rat study with a safety factor of 1000. Based on acute toxicity results, the impurity IN-A4098[32] was considered as toxicologically relevant. As it is a potential metabolite, it was agreed that the reference values of the parent could be applied. Based on the available information, the other potential groundwater metabolites, not discussed by the experts, should also be considered as toxicologically relevant pending on the confirmation of the proposed classification of chlorsulfuron as Carcinogen Category 3 by ECHA.
The agreed **acceptable daily intake** (ADI) for chlorsulfuron is **0.2 mg/kg bw/day** based on the 2-year rat study, with the use of a safety factor of 100. The agreed **acceptable operator exposure level** (AOEL) is **0.43 mg/kg bw/day** based on the 1-year dog study, the application of a safety factor of 100 and a correction factor for oral absorption of 71%. It was agreed that no acute reference dose

[31] **IN-A4097:** 2-chlorobenzenesulfonamide
[32] **IN-A4098:** 4-methoxy-6-methyl-1,3,5-trazine-2-amine

(ARfD) was needed for chlorsulfuron. The default value of 100% was agreed for dermal absorption in the absence of experimental values.
The operator exposure levels estimated with the UK and German models resulted in values below the AOEL even without the use of personal protective equipment. Similarly, estimated worker and bystander exposure levels were respectively below 5 and 1% of the AOEL for the representative use on cereals.

The metabolism of chlorsulfuron was investigated in cereals. Chlorsulfuron is metabolised extensively, mainly by hydroxylation followed by conjugation to glucose and by cleavage of the sulfonylurea linkage. Although the submitted residue trials were not carried out fully in accordance with the notified cGAP they were regarded as sufficient to propose an MRL for cereals taking into account that residues of chlorsulfuron in all grain samples were below LOQ.
Data on the metabolism in rotational crops show that no quantifiable residues of chlorsulfuron or the soil metabolite IN-A4098 are expected in rotational crops after application of chlorsulfuron according to the notified GAP. However, a data gap was formulated concerning the investigation of the possible presence of two further soil metabolites in rotational crops.
The metabolite IN-A4097 which was found in the metabolism studies was regarded as toxicological relevant. It was included in the proposed residue definition for risk assessment for products of plant and animal origin which should be carried out separately for chlorsulfuron and the metabolite. The risk assessment for the consumer was not peer reviewed. For IN-A4097 residue levels in cereal grain after application have not been analysed and can only be estimated on the basis of results from a metabolism study. According to provisional calculations the chronic exposure from intake of cereals is expected to be well below the ADIs for chlorsulfuron and IN-A4097. According to preliminary FOCUS calculations concentrations of IN-A4097 are expected to exceed 0.1 µg/L in ground water. IN-A4097 is considered as relevant metabolite according to draft guidance document SANCO/221/2000-rev.10 on the basis of the conclusions of the toxicological evaluation.

Degradation of chlorsulfuron was very limited in the particular soil used to investigate the route of degradation under aerobic conditions ($DT_{50\ lab\ 20\ °C}$ = 232 d). Only two metabolites exceeded 5 % AR at two consecutive data points: IN-JJ998[33], IN-A4098[34]. Other two minor metabolites were increasing in amount at the end of the study: IN-A4097 and IN-M6957. Additionally, the applicant presented a position paper reviewing published scientific literature that contains up to 25 chlorsulfuron degradation rate determinations in soil (DT_{50} = 6.7 – 232 d). The submission of the original papers that support these data was identified as a data gap during the peer review. Furthermore, EFSA identified some shortcomings on the kinetic assessment of these data provided after the meeting of experts. Some of the papers were based on applicants' studies not directly available in the dossier.

[33] **IN-JJ998:** N-[[(Aminocarbonyl)aminoiminomethy]-aminocarbonyl]-2-chlorobenenesulfonamide
[34] **IN-A4098:** 4-methoxy-6-methyl-1,3,5-trazine-2-amine

The submission and assessment of these studies has also been identified as a data gap. Taking into consideration the relatively low degradation of parent observed in the laboratory route study it may not be excluded that the trigger values for soil assessment and / or ground water exposure assessment are exceeded in less extreme soils by these or other metabolites. Soil metabolites reach significantly higher levels in some of the field studies available (IN-A4097 up to 77.5 % AR, IN-A4098 up to 65.9 % AR and IN-JJ998 up to 26.7 % AR). Metabolite IN-A4097 may be considered high to very high persistent in soil (DT_{50} = 175 – 436 d) under dark aerobic conditions according the available studies. Metabolite IN-A4098 may be considered moderated medium persistent in soil ($DT_{50\ lab}$ = 43.2 – 65.9 d) under dark aerobic conditions according the available information as updated by the RMS after the meeting of experts. Metabolite IN-JJ998 may be considered medium to high persistent in soil (DT_{50} = 91.6 – 107.4 d) under dark aerobic conditions according the available information as updated by the RMS after the meeting of experts. Half lives of metabolites IN-A4098 and IN-JJ998 may not be considered fully peer reviewed.

Degradation of chlorsulfuron was also investigated under dark anaerobic conditions at 25 °C ($DT_{50\ lab\ 20\ °C\ anaerobic}$ = 78.2 d). Major metabolite IN-D5293[35] (max. 14 % AR after 56 d) not identified under aerobic conditions was found in the anaerobic study.

Half life of chlorsulfuron in the photolysis in soil study was calculated to be 62.2 d. A data gap was identified during the peer review to provide an estimation of soil photolysis half lives at different latitudes (35 – 55 °N). A specifically photolysis metabolite (IN-V7160) was identified in this study.

Field dissipation studies performed in California, Idaho (USA), Spain and Italy (2 sites) are available in the dossier. After the examination of these studies, the experts in the meeting agreed that the studies are not suitable to derive kinetic parameters for modelling purposes.

According the batch soil adsorption / desorption studies available chlorsulfuron may be considered to exhibit high to very high mobility in soil (K_{fOC} = 14.1 – 60.2 mL / g), IN-A4097 may be considered to exhibit very high mobility in soil (K_{fOC} = 21.2 – 48.2 mL / g), IN-A4098 may be considered to exhibit very high to medium mobility in soil (K_{fOC} = 16.7 – 225.5 mL / g) and IN-JJ998 may be considered to exhibit high to very high mobility (K_{fOC} = 14.7 – 114.0 mL / g). According estimations obtained using PCKOCWIN metabolites IN- B5528 and IN-V7160 are very highly mobile in soil and IN-M6957 may be considered low mobile in soil.

Chlorsulfuron is stable to hydrolysis at pH 7 and 9 and it hydrolysis with a half life of 23.2 d at pH 5. Photolysis in water is not considered to contribute significantly to its environmental degradation. Chlorsulfuron was found not to be readily biodegradable.

Dissipation / degradation of chlorsulfuron in the aquatic environment were investigated in one study with one aerobic and one anaerobic water / sediment systems. The experiments design deviate significantly from the recommendations given by SETAC guidance and a data gap for an additional water sediment study has been identified by EFSA. The meeting of experts had already identified a

[35] **IN-D5293:** 2-chlorophenylsulfonylurea

data gap (considered not essential to finalize the EU risk assessment) for a new water / sediment study under acidic conditions.
PECs $_{SW/SED}$ presented in the DAR were not validated during the peer review due to the lack of adequate input parameters. Therefore, a new data gap was identified for new PEC $_{SW/SED}$.
Meeting of experts discussed the FOCUS GW calculations as presented in addendum 3.In these calculations, chlorsulfuron and metabolites IN-JJ998, IN-A4097 exceeded the trigger of 0.1 µg / L in some of the scenarios simulated. Metabolite IN-A4097 also exceeds the trigger of 0.75 µg / L in some of the scenarios. Due to various deficiencies and data gaps, the calculations presented were no validated during the peer review and the ground water exposure assessment remains open.
Chlorsulfuron is not expected to volatilize significantly under normal environmental conditions. Half life in the atmosphere due to photochemical degradation has been estimated to be of 2.1 d.

For the representative use of chlorsulfuron a low risk was assessed for terrestrial vertebrates in a first-tier assessment.
Algae and aquatic plant were the most sensitive organisms. Risk assessment was driven by *Lemna gibba*, for which potential higher first-tier risk was identified. The provided higher tier TER calculations did not allow to identify a low risk. Furthermore, new PEC_{sw} FOCUS step 3 values were requested by the fate expert meeting. Therefore data gap was identified to calculate FOCUS Step 3&4 TERs in order to address the risk to macrophytes and to identify the most appropriate mitigation measures.
Only if mitigation measures equivalent to an in-field non-spray buffer zone of 15 m (pre-emergence use) and 15 m plus a drift reduction ≥50% (post emergence use) are applied, the risk to terrestrial non-target plants was assessed as low. In order identify more realistic mitigation measures, EFSA proposed a data gap for the risk assessment for non target plants
A low risk was assessed for bees, non-target arthropods, earthworm, soil non-target macro and micro-organisms and biological methods of sewage treatment.

Particular conditions proposed to be taken into account to manage the risk(s) identified

- mitigation measures to protect non-target aquatic and terrestrial plants

Critical areas of concern

- There is no finalised specification.
- The risk assessment for the consumer could not be finalised.
- Environmental exposure assessment could not be finalized for any of the compartments including ground water. Available information indicates that chlorsulfuron and metabolites IN-

JJ998 and IN-A4097 may exceed 0.1 µg / L in some scenarios. Metabolite IN-A4097 could also exceed 0.75 µg / L in some scenarios. These metabolites are considered toxicologically relevant., pending on the confirmation of classification Carcinogenic category 3 for chlorsulfuron in the ECHA process under Directive 67/548/EEC,

- Risk to aquatic organisms (macrophytes) not finalized.

APPENDIX 1 –THE LIST OF ENDPOINTS

Identity, Physical and Chemical Properties, Details of Uses, Further Information

Active substance (ISO Common Name) ‡	Chlorsulfuron
Function (*e.g.* fungicide)	Herbicide
Rapporteur Member State	Greece
Co-rapporteur Member State	-

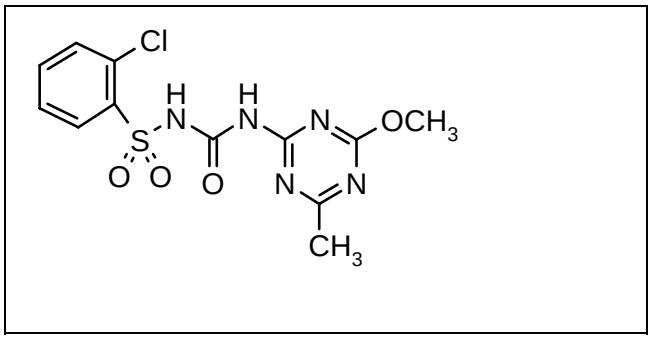
Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	1-(2-chlorophenylsulfonyl)-3-(4-methoxy-6-methyl-1,3,5-triazin-2-yl)urea
Chemical name (CA) ‡	2-chloro-N-[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino]carbonyl]benzenesulfonamide
CIPAC No ‡	391
CAS No ‡	64902-72-3
EC No (EINECS or ELINCS) ‡	265-268-5
FAO Specification (including year of publication) ‡	FAO Specification 391/TC (2003): 950 g/kg *(only applicable for the material of DuPont)*
Minimum purity of the active substance as manufactured ‡	950 g/kg
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	2-Chlorobenzenesulfonamide (IN-A4097) max. content: open 4-methoxy-6-methyl-1,3,5-triazin-2-amine (IN-A4098) max. content: open
Molecular formula ‡	$C_{12}H_{12}ClN_5O_4S$
Molecular mass ‡	357.8 g/mol

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

Structural formula ‡



‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	Melting range: 171.5 – 174 °C (98.0% technical)
Boiling point (state purity) ‡	Not applicable
Temperature of decomposition (state purity)	Pure a.s. (98.5%): 150 °C
Appearance (state purity) ‡	Pure a.s. (98.5%): white crystalline solid with a slight organic solvent (xylene) odour
	Technical a.s. (98.0%): same as above
Vapour pressure (state temperature, state purity) ‡	3.1×10^{-9} Pa at 25 °C (99.1% pure)
Henry's law constant ‡	Calculated values at 20 °C: $H = 5.0 \times 10^{-10}$ Pa × m^3 × mol^{-1} at pH 5 $H = 3.5 \times 10^{-11}$ Pa × m^3 × mol^{-1} at pH 7 $H = 3.2 \times 10^{-12}$ Pa × m^3 × mol^{-1} at pH 9
Solubility in water (state temperature, state purity and pH) ‡	Pure a.s. (99.4%): at 20 °C and pH 5: 0.876 g/L pH 7: 12.5 g/L pH 9: 134 g/L
Solubility in organic solvents ‡ (state temperature, state purity)	At 20 °C (99.93% technical): *Solvent* — *Solubility (g/L)* n-hexane — 0.0024 isopropanol — 1.6 toluene — 2.8 methanol — 15 acetonitrile — 21 ethyl acetate — 25 acetone — 37 dichloromethane — 140
Surface tension ‡ (state concentration and temperature, state purity)	The surface tension of a 90% saturated aqueous solution of chlorsulfuron (97.18% technical): 73.1 ± 0.9 mN/m at 20.5 ± 0.06 °C.

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

Partition co-efficient ‡ (state temperature, pH and purity)	At 25 °C: pH 5: P_{ow} = 2.13 and log P_{ow} = 0.33 pH 7: P_{ow} = 0.102 and log P_{ow} = -0.99 pH 9: P_{ow} = 0.0387 and log P_{ow} = -1.41 Radiochemical purity of carbonyl ^{14}C-chlorsulfuron: 96% Chemical purity of chlorsulfuron: ≈ 100%
Dissociation constant (state purity) ‡	pK_a = 3.4 (99.93% technical)
UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	**UV/vis –spectrum**

pH	λ_{max}		ε ($Lmol^{-1}cm^{-1}$)	
	Rep1	Rep2	Rep1	Rep2
<2	202	202	42725	42378
	222	222	23968	23968
	205	205	33462	32420
	222	222	23852	23968
~5	236	236	26399	26399
	237	237	26284	26284
~7	236	236	26399	26399
	204	203	30915	31725
	236	236	26284	26284
≥10	236	236	26399	26399
	203	203	33462	34041
	237	237	26052	26052

No absorbance maxima (λ_{max}) above 290 nm were observed at any pH, for aqueous solutions of chlorsulfuron, at concentrations of 10.3 and 30.9 µg/mL.

Flammability ‡ (state purity)	Not highly flammable (97.18%, technical) Chlorsulfuron has no self-ignition temperature (97.18% technical)
Explosive properties ‡ (state purity)	Chlorsulfuron is not expected to have explosive properties (97.18% technical)

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

Oxidising properties ‡ (state purity)	Chlorsulfuron is not expected to have oxidizing properties (expert's statement)

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

Summary of representative uses evaluated (*chlorsulfuron*)

Crop and/or situation (a)	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
			Type (d-f)	Conc. of a.s. (i)	method kind (f-h)	Growth stage & season (j)	number (k)	interval between applications (min)	kg a.s./hL min max	water L/ha min max	g a.s./ha min max		
Cereals Wheat (winter) (soft & durum) Barley Oats	F	Broad-leaved and grass weeds	WG	750	Tractor-mounted/ trailed boom sprayer, hydraulic nozzles	Pre-emergence or Post-emergence (BBCH 11-30)	1	N/A	1.88-9.38 or 1.63-7.5	200-600	11.25-18.75 or 9.75 -15	None [1)]	[1] [2] [3}
Cereals Wheat (winter, spring) Barley (winter, spring) Oats (spring) Rye (winter) Triticale (winter)	F	Broad-leaved and grass weeds	WG	750	Tractor-mounted/ trailed boom sprayer, hydraulic nozzles	Pre-emergence or Post-emergence (BBCH 12-30)	1	N/A	2.81-9.38 or 0.94-9.38	200-400	11.25-18.75 or 3.75-18.75	None [1)]	Maximum seasonal application rate in Estonia is 3.75 g a.s./ha (post-emergence) [1] [2] [3]

[1] The specification can not be finalised.
[2] Consumer risk assessment provisionally.
[3] Environmentla risk assessment including groundwater exposure assessment cannot be finalized.

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

) Do not treat later than Growth Stage BBCH 30. PHI is covered by conditions of use and/or growing period between application and harvest.

Remarks:
(a) For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (e.g., fumigation of a structure)
(b) Outdoor or field use (F), glasshouse application (G) or indoor application (I)
(c) e.g., biting and suckling insects, soil-born insects, foliar fungi, weeds
(d) e.g., wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(e) GCPF Codes - GIFAP Technical Monograph No. 2, 1989
(f) All abbreviations must be explained
(g) Method, e.g., high volume spraying, low volume spraying, spreading, dusting, drench
(h) Kind, e.g., overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated.
(i) g/kg or g/L
(j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
(k) The minimum and maximum number of application possible under practical conditions of use must be provided
(l) PHI - minimum pre-harvest interval
(m) Remarks may include: Extent of use/economic importance/restrictions

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

Methods of Analysis

Analytical methods for the active substance (Annex IIA, point 4.1)

Technical as (analytical technique)	HPLC-UV_{254nm}: Acceptable, validated method for the determination of a.s. in chlorsulfuron technical. It is the CIPAC method 391/TC/(M)/- with a slight modification on the column used.
Impurities in technical as (analytical technique)	- HPLC-UV_{230nm} - HPLC/UV_{230nm} - GC/FID - Karl Fischer's titration method - Determination of weight percent inorganic ions (salts) by high temperature:
Plant protection product (analytical technique)	HPLC-UV_{254nm}: Acceptable, fully validated method in the representative formulation (Chlorsulfuron 75 WG) It is the CIPAC method 391/TC/(M)/-.

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		Chlorsulfuron
Food of animal origin		Chlorsulfuron
Soil[1)]		Chlorsulfuron
Water	surface	Chlorsulfuron
	drinking/ground[1)]	Chlorsulfuron IN-A4097, IN-JJ998 (provisional)
Air		Chlorsulfuron

Analytical methods for residues (Annex IIA, point 4.2)

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	**Doc No.: DuPont 8054**: Substrates: wheat grain, barley grain, corn grain, tomato Analysis: LC/MS/MS Determined analyte: chlorsulfuron

Appendix 1 – list of endpoints

	LOQ: 0.01 mg/kg **Doc No.: Dupont-5367 (ILV study)** Substrates: wheat (grain, forage, straw) Analysis: LC/MS Determined analyte: chlorsulfuron LOQ: 0.01 mg/kg (wheat) LOQ: 0.05 mg/kg (forage and straw)
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	No MRLs are proposed; therefore no analytical method is required.
Soil (principle of method and LOQ)	**Doc No: DuPont-5082**: Substrates: soil Analysis: LC/MS/MS Determined analyte: Chlorsulfuron LOQ: 0.05 µg/kg **Doc No: DuPont-6154**: Substrates: soil Analysis: LC/MS/MS Determined analyte: Chlorsulfuron, IN-A4097, IN-A4098, IN-V7160 and IN-JJ998 LOQ: 0.2 µg/kg (Chlorsulfuron, IN-A4098, IN-V7160 and IN-JJ998) LOQ: 0.5 µg/kg (IN-A4097)
Water (principle of method and LOQ)	**Doc No: DuPont-5491**: Substrates: Drinking water: tap and well water, Surface water: pond, river and surface water Analysis: LC/MS/MS Determined analyte: Chlorsulfuron LOQ: 0.05 µg/L
Air (principle of method and LOQ)	**Doc No: DuPont-4560:** Substrates: air Analysis: LC/MS/MS Determined analyte: chlorsulfuron LOQ: 0.003 mg/m^3
Body fluids and tissues (principle of method and LOQ)	Not required because chlorsulfuron is not classified as toxic or highly toxic.

Appendix 1 – list of endpoints

Classification and proposed labelling with regard to physical and chemical data (Annex IIA, point 10)

	RMS/peer review proposal
Active substance	RMS proposal: None

Appendix 1 – list of endpoints

Impact on Human and Animal Health

Absorption, distribution, excretion and metabolism (toxicokinetics) (Annex IIA, point 5.1)

Rate and extent of absorption ‡	Rapidly absorbed (> 80% of total urinary excreted radioactivity within 24 hrs). Oral absorption up to 71% within 72h (based on urine, cage rinse, total tissues/organs or carcass in females).
Distribution ‡	Widely and uniformly distributed.
Potential for accumulation ‡	No evidence of accumulation.
Rate and extent of excretion ‡	Rapid, primarily *via* urine (52-95%) and secondarily *via* faeces (4-27%), up to 97% within 72 hrs.
Metabolism in animals ‡	Hydrolytic cleavage of the sulfonylurea bridge of the parent compound. Two minor metabolites identified (up to 3% in urine, up to 8.5% in faeces) : 2-chlorobenzenesulfonamide (IN-A4097) and 2-amino-4-methoxy-6-methyl-1,3,5-triazine (IN-A4098).
Toxicologically relevant compounds ‡ (animals and plants)	Parent compound and metabolites.
Toxicologically relevant compounds ‡ (environment)	Parent compound and metabolites.

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	> 5000 mg/kg bw	
Rabbit LD_{50} dermal ‡	> 3400 mg/kg bw	
Rat LC_{50} inhalation ‡	> 5.5 mg/L air (4h, nose or head only, aerosol)	
Skin irritation ‡	Non-irritant	
Eye irritation ‡	Slightly irritant (no classification proposed)	
Skin sensitisation ‡	Non-sensitiser (M&K test)	

Appendix 1 – list of endpoints

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Decreased body weight gain (rats, dogs), increased testicular weight (rats), haematological changes (dogs)	
Relevant oral NOAEL ‡	60.6 mg/kg bw/day (1-year dog) 161 mg/kg bw/day (90-day rat) 3716 mg/kg bw/day (90-day mouse)	
Relevant dermal NOAEL ‡	No data - not required	
Relevant inhalation NOAEL ‡	0.1 mg/L (male rats, head-only, 6h/d, 5 d/wk, 2-week)	

Genotoxicity ‡ (Annex IIA, point 5.4)

No evidence of a genotoxic potential for chlorsulfuron.	

Long term toxicity and carcinogenicity (Annex IIA, point 5.5)

Target/critical effect ‡	Testicular tumours (rats), decreased body weight (gain) (rats)	
Relevant NOAEL ‡	20 mg/kg bw/day (2-year rat) 837 mg/kg bw/day (2-year mouse)	
Carcinogenicity ‡	Unilateral testicular interstitial cell tumours (rats)	**Carc. Cat. 3; R40**

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	Parents: decreased bwg Offspring: no relevant adverse effect Reproductive: increased epididymides and testes weight, increased number of epididymal sperm	
Relevant parental NOAEL ‡	188.5 mg/kg bw/day	
Relevant reproductive NOAEL ‡	188.5 mg/kg bw/day	
Relevant offspring NOAEL ‡	578.5 mg/kg bw/day	

Appendix 1 – list of endpoints

Developmental toxicity

Developmental target / critical effect ‡	Decreased foetal body weight in the presence of substantial maternal toxicity in both rats and rabbits.	
Relevant maternal NOAEL ‡	Rat: 165 mg/kg bw/day Rabbit: 75 mg/kg bw/day	
Relevant developmental NOAEL ‡	Rat: 500 mg/kg bw/day Rabbit: 200 mg/kg bw/day	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	No data available - not required
Repeated neurotoxicity ‡	No data available - not required
Delayed neurotoxicity ‡	No data available - not required

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	No data available
Studies performed on metabolites or impurities ‡	Metabolite IN-A4097: *90-day feeding, rat*: NOAEL 9.3 mg/kg bw/day) Target organs: Liver, kidney, pancreas, spleen Effects: Haematological & clinical chemistry changes, decreased bw gain, microscopic kidney, liver, spleen and pancreatic pathology. *Ames, gene mutation and chromosome aberration tests* : Non mutagenic Agreed ADI: 0.009 mg/kg bw/day (90-d rat, safety factor 1000) Metabolite IN-A4098: *Acute oral toxicity (rats)*: LD_{50} = 1600 mg/kg b.w. *Ames test*: Non mutagenic Metabolite IN-JJ998: *Ames test, gene mutation and chromosome aberration tests*: Non mutagenic

Medical data‡ (Annex IIA, point 5.9)

Appendix 1 – list of endpoints

– No occupational illnesses or symptoms during manufacturing, formulation and packaging – No accidental poisonings reported.

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	0.2 mg/kg bw/day	2-yr rat	100
AOEL ‡	0.43 mg/kg bw/day	1-yr dog	100 + correction for oral absorption of 71%
ARfD ‡	Not established – not required		

Dermal absorption‡ (Annex IIIA, point 7.3)

100% (No data available)

Exposure scenarios (Annex IIIA, point 7.2)

Operator

The estimated exposure levels for the intended use of Chlorsulfuron 75 WG on cereals at a maximum total dose of 0.025 kg product/ha (18.75 g a.i./ha) are below the AOEL even when no PPE is considered.		
Model	no PPE	with PPE*
UK POEM	37	3.5
German BBA	5	2
PPE*: gloves during mix/loading and application		

Workers

Estimated exposure level up to 4.3% of the AOEL.

Bystanders

Exposure estimates below 1% of the AOEL

Classification and proposed labelling with regard to toxicological data (Annex IIA, point 10)

RMS/peer review proposal

Appendix 1 – list of endpoints

Chlorsulfuron	Carc. Cat. 3; R40 Limited evidence of a carcinogenic effect.

EFSA Scientific Report **(2008) 201, 1-107**
Conclusion on the peer review of chlorsulfuron

Appendix 1 – list of endpoints

Metabolism in plants (Annex IIA, point 6.1 and 6.7, Annex IIIA, point 8.1 and 8.6)

Plant groups covered	Cereals (C) (wheat, barley)
Rotational crops	Sugar beet, rapeseed, soybean
Metabolism in rotational crops similar to metabolism in primary crops?	Yes
Processed commodities	Not relevant
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Not relevant
Plant residue definition for monitoring	Chlorsulfuron (cereals only)
Plant residue definition for risk assessment	Chlorsulfuron and IN-A4097 separately (cereals only)
Conversion factor (monitoring to risk assessment)	Not applicable

Metabolism in livestock (Annex IIA, point 6.2 and 6.7, Annex IIIA, point 8.1 and 8.6)

Animals covered	Goats, hens (a)
Time needed to reach a plateau concentration in milk and eggs	Not relevant. (a)
Animal residue definition for monitoring	Chlorsulfuron
Animal residue definition for risk assessment	Chlorsulfuron and IN-A4097 separately
Conversion factor (monitoring to risk assessment)	Not relevant.
Metabolism in rat and ruminant similar (yes/no)	Not relevant. (a)
Fat soluble residue: (yes/no)	Not relevant. (a)

(a) Metabolism studies are not required as no significant residues in livestock feed (≥ 0.1 mg/kg of the total diet as received) are expected after application of chlorsulfuron according to the notified GAP. Studies have been reported, but not evaluated in the DAR. Discussions of the experts meeting were restricted to the setting of residue definitions.

Residues in succeeding crops (Annex IIA, point 6.6, Annex IIIA, point 8.5)

Decision concerning the requirement of field studies in rotational crops is pending. (a)

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

EFSA Scientific Report **(2008) 201, 1-107**
Conclusion on the peer review of chlorsulfuron

Appendix 1 – list of endpoints

(a) Results of the crop metabolism studies show that no quantifiable residues of chlorsulfuron or the metabolite IN-A4098 are expected in rotational crops after application of chlorsulfuron according to the notified GAP. However, a data gap was formulated concerning the investigation of the possible presence of the IN-A4097 and IN-JJ998 in rotational crops.

Stability of residues (Annex IIA, point 6 introduction, Annex IIIA, point 8 Introduction)

Freezer storage stability study indicated that residues of chlorsulfuron in wheat grain and straw are stable for 36 months.

Residues from livestock feeding studies (Annex IIA, point 6.4, Annex IIIA, point 8.3)

CHLORSULFURON

	Ruminant:	Poultry:	Pig:
	Conditions of requirement of feeding studies		
Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no - If yes, specify the evel)	No	No	No
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)	Not Required	Not Required	Not Required
	Feeding studies (Specify the feeding rate in cattle and poultry studies considered as relevant) Residue levels in matrices : Mean (max) mg/kg		
Muscle	-	-	-
Liver	-	-	-
Kidney	-	-	-
Fat	-	-	-
Milk	-		
Eggs		-	

IN-A4097

	Ruminant:	Poultry:	Pig:
	Conditions of requirement of feeding studies		
Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no - If yes, specify the evel)	No	No	No

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)	Not Required	Not Required	Not Required
	Feeding studies (Specify the feeding rate in cattle and poultry studies considered as relevant) Residue levels in matrices : Mean (max) mg/kg		
Muscle	-	-	-
Liver	-	-	-
Kidney	-	-	-
Fat	-	-	-
Milk	-		
Eggs		-	

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

Summary of residues data according to the representative uses on raw agricultural commodities and feedingstuffs (Annex IIA, point 6.3, Annex IIIA, point 8.2)

Crop	Northern or Mediterranean Region, field or glasshouse, and any other useful information	Trials results relevant to the representative uses (a)	Recommendation/comments	MRL estimated from trials according to the representative use	HR (c)	STMR (b)
Cereal grain (wheat, triticale, rye, barley, oats)	Mediterranean Region	5 x <0.002 mg/kg	GS at application date not reported, PHI: approximately 100 days	0.01* mg/kg	<0.002 mg/kg	<0.002 mg/kg
Cereal grain (wheat, triticale, rye, barley, oats)	Northern Region	2 x <0.01 mg/kg (wheat) 2 x <0.01 mg/kg (barley)	GS 30 application rate lower than cGAP (0.014-0.016 mg/kg)	0.01* mg/kg	<0.01 mg/kg	<0.01 mg/kg
Cereal straw	Mediterranean Region	5 x <0.01 mg/kg	GS at application date not reported, PHI: approximately 100 days	-	<0.01 mg/kg	<0.01 mg/kg
Cereal straw	Northern Region	0.05 mg/kg	GS 30 application rate lower than cGAP (0.014-0.016 mg/kg)	-	0.05 mg/kg	0.05 mg/kg

(a) Numbers of trials in which particular residue levels were reported *e.g.* 3 x <0.01, 1 x 0.01, 6 x 0.02, 1 x 0.04, 1 x 0.08, 2 x 0.1, 2 x 0.15, 1 x 0.17

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

(b) Supervised Trials Median Residue *i.e.* the median residue level estimated on the basis of supervised trials relating to the representative use
(c) Highest residue

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

Consumer risk assessment (Annex IIA, point 6.9, Annex IIIA, point 8.8)

CHLORSULFURON	
ADI	0.2 mg/kg b.w./day
TMDI (% ADI) according to WHO European diet	≤ 0.1% (EFSA model, WHO cluster B) **(a)**
TMDI (% ADI) according to national (to be specified) diets	≤ 0. 1% EFSA model, DK child) **(a)**
IEDI (WHO European Diet) (% ADI)	
NEDI (specify diet) (% ADI)	
Factors included in IEDI and NEDI	
ARfD	Not relevant
IESTI (% ARfD)	Not relevant
NESTI (% ARfD) according to national (to be specified) large portion consumption data	Not relevant
Factors included in IESTI and NESTI	Not relevant

(a) Not peer reviewed.

IN-A4097	
ADI	0.009 mg/kg
TMDI (% ADI) according to WHO European diet	**(a)**
TMDI (% ADI) according to national (to be specified) diets	
IEDI (WHO European Diet) (% ADI)	
NEDI (specify diet) (% ADI)	
Factors included in IEDI and NEDI	
ARfD	
IESTI (% ARfD)	
NESTI (% ARfD) according to national (to be specified) large portion consumption data	
Factors included in IESTI and NESTI	

(a) Not peer reviewed. See EFSA conclusion.

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

Processing factors (Annex IIA, point 6.5, Annex IIIA, point 8.4)

Crop/ process/ processed product	Number of studies	Processing factors		Amount transferred (%) (Optional)
		Transfer factor	Yield factor	
Not relevant				

Proposed MRLs (Annex IIA, point 6.7, Annex IIIA, point 8.6)

Cereals (wheat, barley, oats, rye, triticale)	0.01* mg/kg

When the MRL is proposed at the LOQ, this should be annotated by an asterisk after the figure

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

Route of degradation (aerobic) in soil (Annex IIA, point 7.1.1.1.1)

Mineralization after 100 days ‡	Phenyl labeled: 5.5%AR 120 d Triazine labeled: 1.9%AR 120 d
Non-extractable residues after 100 days ‡	Phenyl: 9.0% AR 120 d Triazine: 8.1% AR 120 d
Metabolites requiring further consideration ‡ - name and/or code, % of applied (range and maximum)	IN-A4097 Range 3.3% AR to 77.5% AR (in radiolabelled field studies) IN-A4098 Range 8.2% AR to 65.9% AR (in radiolabelled field studies) IN-JJ998 Range 7.2% AR to 26.7% AR (in radiolabelled field studies)

Route of degradation in soil - Supplemental studies (Annex IIA, point 7.1.1.1.2)

Anaerobic degradation ‡

Mineralization after 100 days	No data available
Non-extractable residues after 100 days	14 % after 21 d, [^{14}C-phenyl]-label (n= 3) 2.3 % after 56 d, [^{14}C-triazine]-label (n= x)
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	IN-A4097: 11-17 % at 21-56 d (n= 3) IN-A4098: *11* % at *112* d (n= *1*) [^{14}C-phenyl] & [^{14}C-triazine] labels IN-D5293: 3.1-14 % (n= *x*) at 7-56 d (n=3)

Soil photolysis ‡

Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	IN-V7160: 6.3-7.0 % at 21-31 d (n=1) Observed for [^{14}C-triazine] labelled chlorsulfuron only

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

Rate of degradation in soil (Annex IIA, point 7.1.1.2, Annex IIIA, point 9.1.1)

Laboratory studies ‡

Parent	Aerobic conditions

Recalculated DT_{50} Values for Chlorsulfuron Laboratory Aerobic Soil Degradation – Persistence Endpoints

Indicative values may be found in addendum 2 to the DAR, not peer reviewed

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

Recalculated DT_{50} Values for Chlorsulfuron Laboratory Aerobic Soil Degradation – Modelling Endpoints

Note: the following values have been briefly reviewed by EFSA but not peer reviewed. Tabulated experimental data would be needed for the independent confirmation of the calculated values. A data gap is pending for the submission of the published scientific literature and three applicant's study reports mentioned on it.

Soil Origin	pH	OC (%)	Texture	Exper. Temp.	Original DT_{50} (days)	Recalc. DT_{50} (days)	Norm. DT_{50} (days)	Chi^2 Error (%)	Chosen Kinetic Model	R^2
Illinois	5.7	2.8	silt loam	20	22.7	37.4	31.1	13	SFO	0.9258
North Dakota	7.5	3.3	silt loam	20	168.7	228.9	190.5	3	SFO	0.9250
Nebraska	5.6	1.4	silty clay loam	25	18.9	11.4	10.4	9	SFO	0.9787
Nebraska	7.5	1.4	silty clay loam	25	101.5	101.11	92.4	12	DFOP Slow phase DT_{50}	0.9904
Illinois	5.9	2.9	silt loam	30	10.4	35.0	60.0	6	SFO	0.9633
Delaware	6.5	0.6	sandy loam	30	14.5	16.0	27.4	8	SFO	0.9782
North Dakota	8.0	2.9	silt loam	30	67.9	6.7	11.47	15	SFO	0.9666
Italy	6.0	1.7	loamy sand	25	40.2	30.3	35.0	3	DFOP Slow phase DT_{50}	0.9981
Italy	7.6	1.1	silt loam	25	67.0	45.7	52.8	3	DFOP Slow phase DT_{50}	0.9969
Delaware	6.4	1.6	silt loam	25	29.0	12.2	14.1	17	SFO	0.9415
Victoria	7.1	0.5	sandy loam	25	27.6	18.9	21.8	5	SFO	0.9831
South Australia	7.8	1.0	clay loam	25	49.3	45	52	7	SFO	0.9220
South Australia	7.9	1.2	sandy loam	25	68.2	46.2	53.4	4	SFO	0.9773
Victoria	8.5	2.0	clay	25	89.9	59.5	68.8	3	SFO	0.9804
South Australia	8.7	1.6	sandy loam	25	60.9	47.5	54.9	2	SFO	0.9918
Colorado	8.1	0.8	silty clay loam	20	77.0	151.2	123.6	5	SFO	0.9624
Colorado	7.7	0.8	loam	20	38.5	137.7	112.6	6	SFO	0.9357
Colorado	7.1	0.8	clay loam	20	57.8	110.9	90.7	9	SFO	0.9238
Colorado	6.2	0.9	clay	20	99.0	115.52	94.98	4	DFOP Slow Phase DT_{50}	0.9935
Warwick	7.1	1.2	sandy loam	20	20.9	32.2	23.3	6	SFO	0.9790
Aragón	8.3	1.2	loam	20	232.0	232.3	187.4	2	SFO	0.9629
Geomean	-	-	-	-	41.3	**47.12**	**51.35**	-		-

Metabolites

Method of calculation	First-order kinetics using linear and non-linear regression and graphical interpolation.

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

Laboratory studies (range or median, with n value, with r^2 value)	**IN-A4097:** DT_{50lab} (20°C, 10 kPa, aerobic): 175 - 436 days (5 soils), r^2 >0.78 Geometric mean for use in FOCUS modelling, 312 days

Peer review degradation half lives are not avialble for IN-A4098 and IN-JJ998

Field studies ‡

Parent & IN-V7160		Aerobic conditions							
				Soil properties			Statistical evaluation		
Analyte	**Test site (reference)**	**Application season**	**Application rate g a.s./ha**	**Soil type**	**% Organic carbon**	**pH**	**$DissT_{50}$ (days)**	**$DissT_{90}$ (days)**	**r^2**
Chlorsulfuron (DPX-W4189)	Madera, California (AMR 1417-89)	Spring	30	Sandy loam-loamy sand	0.2	6.3-6.9	29.0	96.3	0.957
	Moscow, Idaho (AMR 2266-91)	Spring	30	Silt loam-silty clay loam	1.3-0.6	6.1-6.9	11.2	37.1	0.941
	Almacelles, Spain (DuPont-5195)	Spring	30	Clay loam	0.8-<0.05	8.5-8.7	70.1	232.9	0.960
	Pesaro, Italy (DuPont-5728)	Fall	30	Silty clay loam	1.1-0.9	7.8-8.0	2.5	8.3	0.980
	Catania, Italy (DuPont-5729)	Fall	30	Loam-clay loam	0.9-0.5	7.9-8.2	68.3	226.7	0.915
						Average	36.2	120.3	-
						Median	29.0	96.3	
						Geometric Mean	22.8	75.7	
						n	*5*	*5*	
IN-V7160	Almacelles, Spain (DuPont-5195)	Spring	30 (a.s.)	Clay loam	0.8-<0.05	8.5-8.7	7.6	25.2	0.960

All DT_{50} and DT_{90} values calculated using **single first-order kinetics**. PRAPeR 52 experts meeting agreed that due to photolysis and potential. Leaching the values can only be considered dissipation DT50s representative of Southern EU conditions, not suitable as input parameters for environmental modeling.

pH dependence ‡ (yes / no) (if yes type of dependence)	No
Soil accumulation and plateau concentration ‡	Spain, Italy, and Greece 4 sites Accumulation was investigated field trials in alkaline soils of southern Europe. Average DT_{50} and DT_{90} values were similar in cropped field soil accumulation studies to those seen in bare ground field soil dissipation studies.

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

Laboratory studies ‡

Parent	Anaerobic conditions						
Soil type	X[1]	pH	t. °C / % MWHC	DT_{50} /DT_{90} (d)	DT_{50} (d) 20°C pF2/10kPa	St. (r^2)	Method of calculation
Silt loam		8.4	25 °C / -	78.2 / 260	- / -	0.769	Non-linear regression (Model Manager v.1.0)
Geometric mean/median				78.2 / 260			

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Parent ‡							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Loam	0.8	8.0	0.27	58.1	0.28	60.2	0.90
Sandy loam	1.1	6.6	0.08	12.5	0.09	14.1	0.85
Silt loam	1.9	5.7	0.33	29.9	0.38	34.4	0.88
Silt loam	4.3	5.4	0.85	34.0	0.91	36.4	0.91
Arithmetic mean/median					0.42	36.3	0.89
pH dependence, Yes or No			No				

Metabolite IN-A4097‡							
Soil Type	OM %	Soil pH (water)	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Sandy loam	4.3	6.7	0.65	29.7	0.47	21.2	0.903
Loam	1.4	5.2	0.28	35.2	0.21	26.2	0.913
Clay loam	1.9	8.0	0.46	38.7	0.29	23.9	0.862
Clay loam	1.7	8.1	0.85	71.1	0.43	35.5	0.811

[1] X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

Sandy loam	1.9	6.1	0.84	76.5	0.53	48.2	0.870
Arithmetic mean/median					0.39	31.0	0.872
pH dependence (yes or no)			No				

Metabolite IN-A4098‡							
Soil Type	OC %	Soil pH (water)	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Silt loam	1.2	7.7	0.2	17.1	0.2	18.8	1.05
Sandy loam	2.3	5.7	0.8	34.4	0.7	29.7	0.94
Silt loam	2.6	6.4	0.5	18.3	0.4	16.7	0.96
Silt loam	1.1	5.3	2.1	187.3	2.4	214	0.84
Sandy loam	0.5	6.3	0.5	98.9	0.6	133.8	0.78
Silty clay loam	3.0	5.7	6.9	228.1	6.8	225.5	0.84
Sand	0.6	6.2	0.2	37.8	0.3	45.5	0.87
Arithmetic mean/median					1.63	97.7	0.90
pH dependence (yes or no)			No				

Metabolite IN-JJ998‡							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Sandy clay loam	1.3	8.4	0.231	25.7	0.07	14.7	0.73
Silty clay loam	1.3	8.5	0.832	48.9	0.42	42.4	0.85
Clay loam	1.2	8.2	1.47	70.2	0.53	44.4	0.77
Silt loam	1.2	6.2	2.65	156	1.14	114.0	0.82
Loamy sand	1.1	6.2	3.54	73.8	1.41	50.4	0.80
Arithmetic mean/median					0.79	0.72	53.2
pH dependence (yes or no)			No				

Metabolites IN-B5528, IN-M6957 and IN-V7160, calculation

K_{oc} (mL/g)		
IN-B5528	**IN-M6957**	**IN-V7160**
22.8	544.4	10.0

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

PCKOCWIN (Syracuse Research Corp., North Syracuse, New York), *Environ. Sci. Technol.*, **26,** 1560-1567.

Mobility in soil (Annex IIA, point 7.1.3, Annex IIIA, point 9.1.2)

Column leaching ‡	No data, justification given
Aged residues leaching ‡	No data, justification given
Lysimeter/ field leaching studies ‡	No data, justification given

PEC (soil) (Annex IIIA, point 9.1.3)

Parent Method of calculation	Crop: Cereals DT_{50lab} 232 days (worst case from lab studies) SFO kinetics 5 cm soil depth, soil bulk density 1.5 g/cm^3
Application data	Chlorsulfuron 18.75 g a.s./ha; no interception to plants; 10 years of continuous application

	PECsoil (mg/kg)	TWA
0	0.0371	
1	0.0370	0.0371
2	0.0369	0.0370
4	0.0366	0.0369
7	0.0363	0.0368
14	0.0356	0.0364
21	0.0348	0.0360
28	0.0341	0.0356
50	0.0319	0.0345
100	0.0275	0.0321

Metabolite IN-A4097 IMethod of calculation	Crop: cereals DT_{50lab} 436 days (worst case from laboratory studies)

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

	Max. 77.5% w/w observed formation from parent in field study DT_{50} parent observed in relevant field study = 21 d Kinetic conversion observed in relevant field study = 0.75 Molecular weight of parent = 357.78 g/mol Molecular weight of metabolite = 191.64 g/mol SFO kinetics 5 cm soil depth, soil bulk density 1.5 g/cm^3
Application data	Chlorsulfuron 18.75 g a.s./ha; no interception to plants; 10 years of continuous application

PECsoil (mg/kg)		TWA
0	0.0213	
1	0.0213	0.0213
2	0.0212	0.0213
4	0.0212	0.0213
7	0.0211	0.0213
14	0.0208	0.0213
21	0.0206	0.0213
28	0.0204	0.0212
50	0.0197	0.0210
100	0.0182	0.0205

Metabolite IN-A4098 Method of calculation	Crop: cereals DT_{50lab} 65.9 days (worst case from laboratory studies) Max. 69.9% w/w observed formation from parent in field study DT_{50} parent observed in relevant field study = 13 d Kinetic conversion observed in relevant field study = 0.65 Molecular weight of parent = 357.78 g/mol Molecular weight of metabolite = 140.15 g.mol SFO kinetics 5 cm soil depth, soil bulk density 1.5 g/cm^3
Application data	Chlorsulfuron 18.75 g a.s./ha; no interception to plants; 10 years of continuous application

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

PECsoil (mg/kg)		TWA
0	0.0044	
1	0.0043	0.0044
2	0.0043	0.0044
4	0.0042	0.0044
7	0.0041	0.0044
14	0.0038	0.0044
21	0.0035	0.0043
28	0.0033	0.0043
50	0.0026	0.0042

Metabolite IN-JJ998 Method of calculation	Crop: cereals DT50lab 107 days (worst case from laboratory studies) Max. 26.7% w/w observed formation from parent in field study DT50 parent observed in relevant field study = 24 d DT50 IN-M6957 observed in relevant field study = 5 d Kinetic conversion observed in relevant field study (parent to IN-M6957)= 0.65 Kinetic conversion observed in relevant field study (IN-M6957 to IN-JJ998)= 1.00 Molecular weight of parent = 357.78 g/mol Molecular weight of IN-M6957 = 343.75 g.mol Molecular weight of IN-JJ998 = 335.73 g/mol SFO kinetics 5 cm soil depth, soil bulk density 1.5 g/cm3
Application data	Chlorsulfuron 18.75 g a.s./ha; no interception to plants; 10 years of continuous application

PECsoil (mg/kg)		TWA
0	0.0073	
1	0.0072	0.0073
2	0.0072	0.0073
4	0.0071	0.0073

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

7	0.0070	0.0073
14	0.0067	0.0073
21	0.0064	0.0073
28	0.0061	0.0072
50	0.0053	0.0072
100	0.0038	0.0068

Metabolite IN-M6957 Method of calculation	Crop: cereals $DT_{50field}$ 8 days (worst case from field studies) Considered valid estimation for Southern EU Max. 5.6% w/w observed formation from parent in field study DT_{50} parent observed in relevant field study = 13 d Kinetic conversion observed in relevant field study = 0.22 Molecular weight of parent = 357.78 g/mol Molecular weight of IN-M6957 = 343.75 g.mol SFO kinetics 5 cm soil depth, soil bulk density 1.5 g/cm^3
Application rate	Chlorsulfuron 18.75 g a.s./ha; no interception to plants; 10 years of continuous application

PECsoil (mg/kg)		TWA
0	0.0015	
1	0.0014	0.0015
2	0.0012	0.0015
4	0.0010	0.0015
7	0.0008	0.0015
14	0.0004	0.0014
21	0.0002	0.0014
28	0.0001	0.0013
50	0.0000	0.0010
100	0.0000	0.0006

Metabolite IN-V7160 Method of calculation	Crop: cereals $DT_{50field}$ 96 days (worst case from field studies) Considered valid estimation for Southern EU Max. 5.0% w/w observed formation from parent in field study

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

	DT_{50} parent observed in relevant field study = 26 d Kinetic conversion observed in relevant field study = 0.16 Molecular weight of parent = 357.78 g/mol Molecular weight of IN-V7160 = 183.17 g.mol SFO kinetics 5 cm soil depth, soil bulk density 1.5 g/cm^3
Application rate	Chlorsulfuron 18.75 g a.s./ha; no interception to plants; 10 years of continuous application

PECsoil (mg/kg)		TWA
0	0.0014	
1	0.0014	0.0014
2	0.0014	0.0014
4	0.0013	0.0014
7	0.0013	0.0014
14	0.0012	0.0014
21	0.0012	0.0014
28	0.0011	0.0014
50	0.0010	0.0013
100	0.0007	0.0013

Metabolite IN-B5528 Method of calculation	Crop: cereals $DT_{50field}$ 25 days (worst case from field studies) Considered valid estimation for Southern EU Max. 5.7% w/w observed formation from parent in field study DT_{50} parent observed in relevant field study = 13 d DT50 IN-M6957 observed in relevant field study = 8 d Kinetic conversion observed in relevant field study (parent → IN-M6957)= 0.22 Kinetic conversion observed in relevant field study (IN-M6957 → IN-B5528)= 0.51 Molecular weight of parent = 357.78 g/mol Molecular weight of IN-M6957 = 343.75 g.mol Molecular weight of IN-B5528 = 126.12 g/mol SFO kinetics 5 cm soil depth, soil bulk density 1.5 g/cm^3
Application rate	Chlorsulfuron 18.75 g a.s./ha; no interception to plants; 10 years of continuous application

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

PECsoil (mg/kg)		TWA
0	0.0012	
1	0.0011	0.0012
2	0.0011	0.0012
4	0.0011	0.0012
7	0.0010	0.0012
14	0.0008	0.0012
21	0.0007	0.0012
28	0.0005	0.0011
50	0.0003	0.0011
100	0.0001	0.0008

Route and rate of degradation in water (Annex IIA, point 7.2.1)

Hydrolytic degradation of the active substance and metabolites > 10 % ‡	pH 5: 25°C: Chlorsulfuron DT_{50} = 23.2 days Metabolites: IN-A4097, IN-A4098, IN-M6957, triazine ring-opened acetyltriuret chlorsulfuron - stable
	pH 7: 25°C: Chlorsulfuron stable Metabolites: stable
	pH 9: 25°C: Chlorsulfuron stable Metabolites: stable
Photolytic degradation of active substance and metabolites above 10 % ‡	Direct photolysis in aqueous solutions is not a major degradation mechanism for chlorsulfuron. A DT_{50} value of 18.8 days was observed at pH 5 in light. When hydrolysis degradation is discounted the half life due solely to photolysis is 100d.
Quantum yield of direct phototransformation in water at ☒ > 290 nm	No data available.
Readily biodegradable ‡ (yes/no)	No data submitted, substance considered not ready biodegradable.

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

Degradation in water / sediment

Only one of the systems available was under aerobic conditions.

Parent	Distribution **Phenyl label**: Total 6.8% (100 d) & 82.5% (120 d), n=2 Water 4.4% (100 d) & 73.0% (120 d), n=2 Sediment 2.4% (100 d) & 9.5% (120 d), n=2 **Triazine label**: Total 6.7% (100 d) & 82.1% (120 d), n=2 Water 4.4% (100 d) & 73.4% (120 d), n=2 Sediment 2.3% (100 d) & 8.7% (120 d), n=2

Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	St. (r^2)	DT_{50}-DT_{90} water	St. (r^2)	DT_{50}-DT_{90} sed	St. (r^2)	Method of calculation
Mill Stream Pond Loamy sand **Aerobic**	8.1	7.8	-	26-87	0.994	21-69	0.996	-	-	Non-linear first-order Model Manager v. 1.0
Geometric mean/median				Data gap for a second study identified		Data gap for a second study identified		-		

Metabolite IN-JJ998	Distribution **Phenyl label:** Total 27.4% (100 d) & 2.7% (120 d), n=2 Water 11.4% (100 d) & 1.8% (120 d), n=2 Sediment 16.0% (100 d) & 0.9% (120 d), n=2 **Triazine label:** Total 27.2% (100 d) & 2.9% (100 d), n=2 Water 10.7% (100 d) & 1.8% (120 d), n=2 Sediment 16.5% (100 d) & 1.1% (120 d), n=2

Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	St. (r^2)	DT_{50}-DT_{90} water	r^2	DT_{50}-DT_{90} sed	St. (r^2)	Method of calculation

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

Mill Stream Pond Loamy sand	8.1	7.8	-	-	-	-	-	-	-	
Cavrini Farm Pond Loam	7.5	8.3	-	-	-	-	-	-	-	
Geometric mean/median				-		-		-		

Metabolite	Distribution
IN-M6957	**Phenyl label:** Total 38.1% (71 d) & 5.2% (120 d), n=2 Water 22.2% (71 d) & 4.4% (120d), n=2 Sediment 18.2% (50 d) & 0.8% (120 d), n=2 **Triazine label:** Total 42.5% (50 d) & 4.9% (100 d), n=2 Water 20.9% (50 d) & 4.3% (100 d), n=2 Sediment 21.6% (50 d) & 0.8% (120 d), n=2

Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	St. (r^2)	DT_{50}-DT_{90} water	r^2	DT_{50}-DT_{90} sed	St. (r^2)	Method of calculation
Mill Stream Pond Loamy sand	8.1	7.8	-	73-241	0.994	94-312	0.996	-	-	Non-linear first-order
Geometric mean/median				73-241		94-312		-		

Mineralization and non extractable residues					
Water / sediment system	pH water phase	pH sed	Mineralization x % after n d. (end of the study).	Non-extractable residues in sed. Max x % after n d	Non-extractable residues in sed. Max x % after n d (end of the study)
Mill Stream Pond Loamy sand	8.1	7.8	0.7% after 100d	25.6% after 100d	25.6% after 100d
Cavrini Farm Pond Loam	7.5	8.3	2.9% after 120d	6.8% after 120d	6.8% after 120d

PEC (surface water) (sediment) (Annex IIIA, point 9.2.3)

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

Method of calculation	FOCUS Surface Water Working Group: FOCUS surface water calculations are provided as a tiered scheme: Step 1 & 2: worst-case loading Step 3: Worst-case loadings as calculated for 10 soil and climate scenarios across the EU (Step 3a; degradation of chlorsulfuron based upon laboratory endpoints; Step 3b; degradation of chlorsulfuron based upon field endpoints) Step 4: Inclusion of mitigation options such as buffer zones and reduced use rates at the Member State Level
Application rate	18.75 g a.s./ha autumn applications; no plant interception 15 g a.s./ha spring application; 25% plant interception
Main routes of entry	Drift, drainflow, runoff, erosion, inflow from upstream catchment

Input parameters for chlorsulfuron and its metabolites for use in FOCUS surface water and sediment modelling at Steps 1 and 2 are summarised below. Whereas some of the input parameters refer to not agreed end points the Step 2 calcualtions are considered by EFSA to represent a conservative estimation of the $PEC_{SW/SED}$.

	Parameter	Unit	Value	Remarks
Chlorsulfuron	Molecular weight	g mol^{-1}	357.78	Step 1 & 2
	Solubility in water	mg L^{-1}	31800	Step 1 & 2
	Kfoc	Kg L^{-1}	36	Step 1 & 2
	Half-life total system	d	375	Step 1
	Half-life water layer	d	375	Step 2; total system half-life used
	Half-life sediment layer	d	375	Step 2; total system half-life used
	Half-life soil	d	95	Step 2; worst-case for alkaline soils
IN-M6957	Max. % water/sediment	% of parent	22.2	Step 1 & 2
	Max. % soil	% of parent	5.6	Step 1 & 2
	Molecular weight	g mol^{-1}	343.75	Step 1 & 2
	Solubility in water	mg L^{-1}	31800	Step 1 & 2, same as parent
	Kfoc	Kg L^{-1}	36	Step 1 & 2
	Half-life total system	d	73	Step 1
	Half-life water layer	d	73	Step 2
	Half-life sediment layer	d	73	Step 2

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

	Half-life soil	d	6	Step 2
IN-JJ998	Max. % water/sediment	% of parent	16.5	Step 1 & 2
	Max. % soil	% of parent	26.7	Step 1 & 2
	Molecular weight	g mol^{-1}	335.73	Step 1 & 2
	Solubility in water	mg L^{-1}	31800	Step 1 & 2, same as parent
	Kfoc	Kg L^{-1}	53	Step 1 & 2
	Half-life total system	d	300	Step 1, worst-case (EU, 2002)
	Half-life water layer	d	300	Step 2, worst-case (EU, 2002)
	Half-life sediment layer	d	300	Step 2, worst-case (EU, 2002)
	Half-life soil	d	74	Step 2
IN-A4097	Max. % water/sediment	% of parent	2.5	Step 1 & 2
	Max. % soil	% of parent	77.5	Step 1 & 2
	Molecular weight	g mol^{-1}	191.64	Step 1 & 2
	Solubility in water	mg L^{-1}	31800	Step 1 & 2, same as parent
	Kfoc	Kg L^{-1}	31	Step 1 & 2
	Half-life total system	d	300	Step 1, worst-case (EU, 2002)
	Half-life water layer	d	300	Step 2, worst-case (EU, 2002)
	Half-life sediment layer	d	300	Step 2, worst-case (EU, 2002)
	Half-life soil	d	233	Step 2

	Parameter	Unit	Value	Remarks
IN-A4098	Max. % water/sediment	% of parent	3.9	Step 1 & 2
	Max. % soil	% of parent	69.9	Step 1 & 2
	Molecular weight	g mol^{-1}	140.15	Step 1 & 2
	Solubility in water	mg L^{-1}	31800	Step 1 & 2, same as parent
	Kfoc	Kg L^{-1}	98	Step 1 & 2
	Half-life total system	d	300	Step 1, worst-case (EU, 2002)
	Half-life water layer	d	300	Step 2, worst-case (EU, 2002)
	Half-life sediment layer	d	300	Step 2, worst-case (EU, 2002)

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

	Half-life soil	d	23	Step 2
IN-V7160	Max. % water/sediment	% of parent	1.0	Step 1 & 2
	Max. % soil	% of parent	7.6	Step 1 & 2
	Molecular weight	g mol^{-1}	183.17	Step 1 & 2
	Solubility in water	mg L^{-1}	31800	Step 1 & 2, same as parent
	Kfoc	Kg L^{-1}	10	Step 1 & 2
	Half-life total system	d	300	Step 1, worst-case (EU, 2002)
	Half-life water layer	d	300	Step 2, worst-case (EU, 2002)
	Half-life sediment layer	d	300	Step 2, worst-case (EU, 2002)
	Half-life soil	d	18	Step 2
IN-B5538	Max. % water/sediment	% of parent	0.5	Step 1 & 2
	Max. % soil	% of parent	5.7	Step 1 & 2
	Molecular weight	g mol^{-1}	126.12	Step 1 & 2
	Solubility in water	mg L^{-1}	31800	Step 1 & 2, same as parent
	Kfoc	Kg L^{-1}	21	Step 1 & 2
	Half-life total system	d	300	Step 1, worst-case (EU, 2002)
	Half-life water layer	d	300	Step 2, worst-case (EU, 2002)
	Half-life sediment layer	d	300	Step 2, worst-case (EU, 2002)
	Half-life soil	d	25	Step 2

PEC_{sw} in Step 1 & 2 for a maximum application rate of 18.75 g a.s./ha in cereals	Chlorsulfuron	IN-A4097	IN-A4098	IN-M6957	IN-JJ998	IN-V7160	IN-B5528
Step 1							
Max. PEC water (µg/L)	6.12	2.49	1.52	0.39	1.51	0.24	0.12
Max. PEC sediment (µg/kg)	2.20	0.77	1.48	0.12	0.78	0.02	0.03
Step 2 Northern EU							
Max. PEC water (µg/L)	3.06	1.23	0.67	0.17	0.75	0.10	0.06
Max. PEC sediment (µg/kg)	1.10	0.38	0.66	0.06	0.39	0.01	0.01
Step 2 Southern EU							
Max. PEC water (µg/L)	2.48	0.99	0.54	0.15	0.61	0.08	0.04
Max. PEC sediment (µg /kg)	0.89	0.31	0.53	0.05	0.32	0.01	0.01

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

PEC (groundwater) (Annex IIIA, point 9.2.1)

Method of calculation and type of study (*e.g.* modeling, monitoring, lysimeter)	FOCUS groundwater scenarios (2000) Model: FOCUS PELMO 3.3.2
Application rate	Autumn application 18.75 g a.s./ha; no plant interception Spring application 15 g a.s./ha; 25% plant interception

Input parameters

Input parameters proposed by the applicant were not agreed during the Peer Review. Data gaps outstanding to confirm some of the degradation half lives. Data gap outstanding to caluculate reliable formation fractions ofr metabolites.

$PEC_{(gw)}$

Due to the outstanding data gaps, available PEC GW were not validated by the PRAPeR 52 experts meeting. Available calculations indicate potential exceedance of 0.1 µg / L trigger by chlrosulfuron, IN-AD4097 and IN-JJ998 in one or more calculations and scenarios. Metabolite IN-AD4097 could also exceed the trigger of 0.75 µg / L in some situations.

Fate and behaviour in air (Annex IIA, point 7.2.2, Annex III, point 9.3)

Direct photolysis in air ‡	No data, not required due to low volatility
Quantum yield of direct phototransformation	No data, no direct phototransformation is expected to occur
Photochemical oxidative degradation in air ‡	No data, the Henry's law constants of chlorsulfuron (pH 5: 5.0×10^{-10} Pa-m^3 mol^{-1}, pH 7: 3.5×10^{-11} Pa-m^3 mol^{-1}, pH 9: 3.2×10^{-12} Pa-m^3 mol^{-1}) are significantly less than 3×10^{-2} Pa-m^3 mol^{-1}, suggesting little potential for volatilisation in the environment.
Volatilisation ‡	No data. The vapour pressure of chlorsulfuron was 3.0×10^{-9} Pa, making it essentially non-volatile from plant or soil surfaces.
Metabolites	No data available, not required.

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

PEC (air)

Method of calculation	Method of Lyman et al. (1982)

$PEC_{(a)}$

Maximum concentration	The predicted volatilisation loss of chlorsulfuron from a treated field into air was predicted to be 1.7×10^{-9} % loss within 24 hours. This rate of loss is likely to result in negligible concentrations in air (PEC_{air}) due to the combination of a low rate of loss as well as the dilution effects of moving air. The concentration in air was, therefore, not calculated.

Residues requiring further assessment

Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology).	Provisional depending on the outcome of further evaluation of the lab and field degradation studies (especially for IN-M6957, IN-B5528, IN–V7160): Soil: Chlorsulfuron, IN-A4097, IN-A4098, IN-JJ998 and IN-V7160 (photolysis) and IN-D5293 (for anaerobic conditions) Groundwater: Chlorsulfuron IN-A4097, IN-A4098, IN-JJ998, IN-M6957 and IN-V7160 (photolysis) and IN-D5293 (for anaerobic conditions) Surface water: Chlorsulfuron, IN-A4097, IN-A4098, IN-JJ998, IN-M6957, IN-V7160 (photolysis) and IN-D5293 (for anaerobic conditions) Sediment: Chlorsulfuron, IN-JJ998 and IN-M6957 Air: Chlorsulfuron

Monitoring data, if available (Annex IIA, point 7.4)

Soil (indicate location and type of study)	No data available
Surface water (indicate location and type of study)	No data available

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

Ground water (indicate location and type of study)	No data available
Air (indicate location and type of study)	No data available

Points pertinent to the classification and proposed labelling with regard to fate and behaviour data

Not readily biodegradable

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

6 Effects on Non-target Species

Effects on terrestrial vertebrates (Annex IIA, point 8.1, Annex IIIA, points 10.1 and 10.3)

Species	Test substance	Time scale	End point (mg/kg bw/day)	End point (mg/kg feed)
Birds ‡				
Bobwhite quail	a.s.	Acute	LD_{50} >5000	
Mallard duck	a.s	Acute	LD_{50} >5000	
Mallard duck	a.s.	Short-term	LC_{50} >634	
Bobwhite quail	a.s.	Long-term	NOEL = 28	
Mammals ‡				
Rat	a.s.	Acute	LD_{50} >5545	
Rat	a.s.	Long-term	NOAEL = 75	
Additional higher tier studies ‡: none				

Toxicity/exposure ratios for terrestrial vertebrates (Annex IIIA, points 10.1 and 10.3)

Cereals (early and late), 18.75 g a.s./ha

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

Indicator species/Category[2]	Time scale	ETE	TER[1]	Annex VI Trigger[3]
Tier 1 (Birds)				
Large herbivorous bird	Acute	1.17	>4274	10
Insectivorous bird	Acute	1.01	>4950	10
Large herbivorous bird	Short-term	0.63	>1006	10
Insectivorous bird	Short-term	0.57	>1121	10
Large herbivorous bird	Long-term	0.33	84	5
Insectivorous bird	Short-term	0.57	49	10
Higher tier refinement (Birds): not necessary				
Tier 1 (Mammals)				
Small herbivorous mammal	Acute	3.70	1499	10
Insectivorous mammal	Acute	0.17	33529	10
Small herbivorous mammal	Long-term	1.05	72	5
Insectivorous mammal	Long-term	0.06	1245	5
Higher tier refinement (Mammals): not necessary				

[1] in higher tier refinement provide brief details of any refinements used (e.g., residues, PT, PD or AV)
[2] for cereals indicate if it is early or late crop stage
[3] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance (e.g. many single species data), it should appear in this column.

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

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1] (mg/L)
Laboratory tests ‡				
Fish				
Oncorhynchus mykiss	Chlorsulfuron	96 hr (static)	Mortality, LC_{50}	>122, measured; limit test
Oncorhynchus mykiss	IN-A4097	96 hr (static)	Mortality, LC_{50}	>124, measured
Oncorhynchus mykiss	IN-A4098	96 hr (static)	Mortality, LC_{50}	>0.93, measured; limit test
Oncorhynchus mykiss	IN-JJ998	96 hr (static)	Mortality, LC_{50}	>96, measured

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1] (mg/L)
Oncorhynchus mykiss	IN-M6957	96 hr (static)	Mortality, LC_{50}	>120, measured
Oncorhynchus mykiss	Chlorsulfuron	77 day (ELS, flow through)	Growth, NOEC	32 mg/L, measured
Aquatic invertebrate				
Daphnia magna	Chlorsulfuron	48 h (static)	Mortality, EC_{50}	>112, measured
Daphnia magna	IN-A4097	48 h (static)	Mortality, EC_{50}	>129, measured
Daphnia magna	IN-A4098	48 h (static)	Mortality, EC_{50}	>99, measured
Daphnia magna	IN-JJ998	48 h (static)	Mortality, EC_{50}	>102, measured
Daphnia magna	IN-M6957	48 h (static)	Mortality, EC_{50}	>122, measured
	Chlorsulfuron	21 d (static)	Growth, NOEC	12, measured
Algae				
Selenastrum capricornutum.	Chlorsulfuron	72 h (static)	EC_{50} (cell count)	0.068 mg/L, nominal,
Selenastrum capricornutum.	Chlorsulfuron 75WG	72 h (static)	EC_{50} (cell count)	0.066 mg/L, nominal,
Selenastrum capricornutum.	IN-A4097	72 h (static)	EC_{50} (all parameters)	>131 mg/L, measured, (all parameters)
Selenastrum capricornutum.	IN-A4098	72 h (static)	EC_{50} (all parameters)	>10, nominal limit test
Selenastrum capricornutum.	IN-JJ998	72 h (static)	EC_{50} (all parameters)	>70, nominal, limit test
Selenastrum capricornutum.	IN-M6957	72 h (static)	E_bC_{50} (area under the growth curve)	26.4, measured
Anabaena flos-aquae	Chlorsulfuron	120 h (static)	EC_{50} (cell count)	0.609, measured

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1] (mg/L)
Higher plant				
Lemna gibba	Chlorsulfuron	14 d (static)	Fronds, E_bC_{50}	0.00035 mg/L, nominal (biomass)
Lemna gibba	Chlorsulfuron 75WG	14 d (static)	Fronds, EC_{50}	0.00046mg/L, nom. (number)
Lemna gibba	IN-JJ998	14 d (static)	Fronds, EC_{50}	>100 mg/L, nominal
Lemna gibba	IN-A4097	14 d (static)	Fronds, EC_{50}	26.5 mg/L, meas. (number.)
Lemna gibba	IN-A4098	14 d (static)	Fronds, EC_{50}	>10 mg/L, nominal; limit test (biomass/number.)
Lemna gibba	IN-M6957	14 d (static)	Fronds, EC_{50}	5.26 mg/L, nom. (biomass)
Lemna gibba	IN-V7160	14 d (static)	Fronds, EC_{50}	>100 mg/L, nom (biomass/frond no.)
Microcosm or mesocosm tests				
Indicate if not required				

[1] indicate whether based on nominal ($_{nom}$) or mean measured concentrations ($_{mm}$). In the case of preparations indicate whether end points are presented as units of preparation or a.s.

Toxicity/exposure ratios for the most sensitive aquatic organisms (Annex IIIA, point 10.2)

FOCUS Step 2

Cereals (early and late), 18.75 g a.s./ha

Test substance	N/S[1]	Organism[2]	Toxicity end point (mg/L)	Time scale	PEC[3] (mg/L)	TER	Annex VI Trigger[4]
a.s.	N	Fish	>122	Acute	0.00306	>39869	100

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

Test substance	N/S[1]	Organism[2]	Toxicity end point (mg/L)	Time scale	PEC[3] (mg/L)	TER	Annex VI Trigger[4]
a.s.	N	Fish	32	Chronic	0.00306	10458	10
a.s.	N	Aquatic invertebrates	> 112	Acute	0.00306	36601	100
a.s.	N	Aquatic invertebrates	12	Chronic	0.00306	3922	10
Product	N	Algae	0.066	Chronic	0.00306	21.57	10
a.s.	N	Higher plants[5]	0.00035	Chronic	0.00306	**0.114**	10
IN-A4097	N	fish	>124	Acute	0.00123	>100813	100
IN-A4097	N	Aquatic invertebrates	>129	Acute	0.00123	>104878	10
IN-A4097	N	Aquatic invertebrates	39.3	Chronic	0.00123	31951	100
IN-A4097	N	Algae	>131	Chronic	0.00123	>106504	10
IN-A4097	N	Higher plants[5]	26.5	Chronic	0.00123	21545	10
IN-A4098	N	fish	>93	Acute	0.00067	>138806	10
IN-A4098	N	Aquatic invertebrates	>99	Acute	0.00067	>147761	100
IN-A4098	N	Aquatic invertebrates	97	Chronic	0.00067	144776	10
IN-A4098	N	Algae	>10	Chronic	0.00067	>14925	100
IN-A4098	N	Higher plants[5]	>10	Chronic	0.00067	>14925	10
IN-JJ998	N	fish	>96	Acute	0.00017	>564706	10
IN-JJ998	N	Aquatic invertebrates	>102	Acute	0.00017	>600000	10
IN-JJ998	N	Aquatic invertebrates	11.7	Chronic	0.00017	68824	100
IN-JJ998	N	Algae	>70	Chronic	0.00017	>411765	10
IN-JJ998	N	Higher plants[5]	>100	Chronic	0.00017	>588235	100
IN-M6957	N	fish	>120	Acute	0.00075	>160000	10
IN-M6957	N	Aquatic invertebrates	>122	Acute	0.00075	>162667	10
IN-M6957	N	Aquatic invertebrates	57.7	Chronic	0.00075	76933	10
IN-M6957	N	Algae	26.4	Chronic	0.00075	35200	100
IN-M6957	N	Higher plants[5]	5.26	Chronic	0.00075	7013	10
IN-V7160	N	Higher plants[5]	>100	Chronic	0.0001	>1000000	10

[1] indicate whether Northern of Southern
[2] include critical groups which fail at Step 1.
[3] maximum.

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

[4] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance, it should appear in this column. E.g. if it is agreed during the risk assessment of mesocosm, that a trigger value of 5 is required, it should appear as a minimum requirement to MS in relation to product approval.
[5] only required for herbicides
[6] consider the need for PEC_{sw} and PEC_{sed} and indicate which has been used

Refined aquatic risk assessment using higher tier FOCUS modelling.

FOCUS Step 3

Cereals (early and late), 18.75 g a.s./ha

Test substance	Scenario[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity end point (mg/L)	PEC[4]	TER	Annex VI trigger[5]
a.s.	D1	Ditch	*Lemna*	Chronic	0.00035	0.001116	**0.314**	10
	D1	Stream	*Lemna*	Chronic	0.00035	0.000794	**0.441**	10
	D2	Ditch	*Lemna*	Chronic	0.00035	0.002427	**0.144**	10
	D2	Stream	*Lemna*	Chronic	0.00035	0.001515	**0.231**	10
	D3	Ditch	*Lemna*	Chronic	0.00035	0.000118	**2.966**	10
	D4	Pond	*Lemna*	Chronic	0.00035	0.000141	**2.482**	10
	D4	Stream	*Lemna*	Chronic	0.00035	0.000169	**2.071**	10
	D5	Pond	*Lemna*	Chronic	0.00035	0.000137	**2.555**	10
	D5	Stream	*Lemna*	Chronic	0.00035	0.000156	**2.244**	10
	D6	Ditch	*Lemna*	Chronic	0.00035	0.000827	**0.423**	10
	R1	Pond*	*Lemna*	Chronic	0.00035	0.000012	29.167	10
	R1	Stream	*Lemna*	Chronic	0.00035	0.000783	**0.447**	10
	R3	Stream	*Lemna*	Chronic	0.00035	0.001203	**0.291**	10
	R4	Stream	*Lemna*	Chronic	0.00035	0.000078	**4.487**	10

FOCUS Step 4

Scenario	Water body type	Test organism	Time scale	Toxicity end point	Buffer zone distance	PEC(mg a.s./L)	TER	Annex VI trigger
D3	Ditch*	*Lemna gibba*	14d	0.00035	5 m	0.000033	10.61	10

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

Scenario	Water body type	Test organism	Time scale	Toxicity end point	Buffer zone distance	PEC(mg a.s./L)	TER	Annex VI trigger
R1	Stream	*Lemna gibba*	14d	0.00035	5 m	0.000686	**0.51**	10
R3	Stream	*Lemna gibba*	14d	0.00035	5 m	0.001105	**0.32**	10
R4	Stream	*Lemna gibba*	14d	0.00035	5 m	0.000036	**9.72**	10

Bioconcentration

logPO/W	
Bioconcentration factor (BCF) ‡	No study was required due to the low log Kow, which is below the trigger value of 3 (pH = 7: log Kow = -0.99). Chlorsulfuron has a low potential for bioconcentration.
Annex VI Trigger for the bioconcentration factor	
Clearance time (days) (CT50)	
(CT90)	
Level and nature of residues (%) in organisms after the 14 day depuration phase	

Effects on honeybees (Annex IIA, point 8.3.1, Annex IIIA, point 10.4)

Test substance	Acute oral toxicity (LD_{50} µg/bee)	Acute contact toxicity (LD_{50} µg/bee)
a.s. ‡	>130 µg a.s./bee	>100 µg a.s./bee
Preparation[1]	>135.1 µg product/bee	>135.1 µg product/bee
Metabolite 1		
Field or semi-field tests: none. Not required due to the low contact and oral toxicity of Chlorsulfuron 75WG and chlorsulfuron to bees.		

[1] for preparations indicate whether end point is expressed in units of a.s. or preparation

Hazard quotients for honey bees (Annex IIIA, point 10.4)

Cereals (early and late), 18.75 g a.s./ha

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

Test substance	Route	Hazard quotient	Annex VI Trigger
Chlorsulfuron 75WG	Contact	<0.14	50
Chlorsulfuron 75WG	oral	<0.19	50

Effects on other arthropod species (Annex IIA, point 8.3.2, Annex IIIA, point 10.5)

Laboratory tests with standard sensitive species

Species	Test Substance	End point	Effect (LR_{50} g/ha[1])
Typhlodromus pyri ‡	Chlorsulfuron 75WG	Mortality (adult and protonymphs)	>56.25
Aphidius rhopalosiphi ‡	Chlorsulfuron 75WG	Mortality (adult and protonymphs)	>56.25

[1] for preparations indicate whether end point is expressed in units of a.s. or preparation

Cereals (early and late), 18.75 g a.s./ha

Test substance	Species	Effect (LR_{50} g/ha)	HQ in-field	HQ off-field[1]	Trigger
	Typhlodromus pyri	>56.25	<0.33	<0.0092	2
	Aphidius rhopalosiphi	>56.25	<0.33	<0.0092	2

[1] indicate distance assumed to calculate the drift rate

Effects on earthworms, other soil macro-organisms and soil micro-organisms (Annex IIA points 8.4 and 8.5. Annex IIIA, points, 10.6 and 10.7)

Test organism	Test substance	Time scale	End point[1]
Earthworms			
	Chlorsulfuron 75WG	Acute 14 days	LC_{50} >750 mg a.s./kg d.w.soil
	Chlorsulfuron 75WG	Chronic 8 weeks	NOEC 187.5 mg a.s./kg d.w.soil
	IN-A4097	Acute 14 days	LC_{50} >1000 mg/kg d.w.soil
	IN-A4098	Acute 14 days	LC_{50} >1000 mg/kg d.w.soil
	IN-JJ998	Acute 14 days	LC_{50} >1000 mg/kg d.w.soil

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

Test organism	Test substance	Time scale	End point[1]
	IN-A4097	Chronic 8 weeks	NOEC 25 mg/kg d.w.soil
	IN-A4098	Chronic 8 weeks	NOEC 0.2 mg/kg d.w.soil
	IN-JJ998	Chronic 8 weeks	NOEC 500 mg/kg d.w.soil
Collembola			
Folsomia candida	IN-A4097	Chronic	NOEC0.90mg/kg d.w.soil (mg a.s/ha)
Folsomia candida	IN-A4098	Chronic	NOEC 0.225 mg/kg d.w.soil (mg a.s/ha)
Folsomia candida	IN-JJ998	Chronic	NOEC 0.275 mg/kg d.w.soil (mg a.s/ha)
Soil micro-organisms			
Nitrogen mineralisation	Chlorsulfuron 75WG		<25% at 0.025 mg chlorsulfuron/kg dry soil and 0.125 mg chlorsulfuron/kg dry soil
	IN-A4098		<25% at 0.041 mg IN-A4098/kg dry soil and at 0.204 mg IN-A4098/kg dry soil
	IN-A4097		<25% at 0.025 mg IN-A4097/kg dry soil and at 0.125 mg IN-A4097/kg dry soil
	IN-JJ998		<25% at 0.028 mg IN-JJ998/kg dry soil and at 0.139 mg IN-JJ998/kg dry soil
Carbon mineralisation	Chlorsulfuron 75WG		<25% at 0.025 mg chlorsulfuron/kg dry soil and 0.125 mg chlorsulfuron/kg dry soil
	IN-A4098		<25% at 0.041 mg IN-A4098/kg dry soil and at 0.204 mg IN-A4098/kg dry soil

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

Test organism	Test substance	Time scale	End point[1]
	IN-A4097		<25% at 0.025 mg IN-A4097/kg dry soil and at 0.125 mg IN-A4097/kg dry soil
	IN-JJ998		<25% at 0.028 mg IN-JJ998/kg dry soil and at 0.139 mg IN-JJ998/kg dry soil
Field studies[2]: litter bag test (Southern EU) Chlorsulfuron 75WG: 18.75 g/ha chlorsulfuron/ha onto litter bags; 28.82 g chlorsulfuron/ha onto the bare soil in which the litter bags were buried. There was no significant impact on straw degradation of greater than 4.4%. IN-A4097: 6.13 µg/kg soil (18.4 g/ha) incorporated into the soil; 21.47 µg/kg soil(64.41 g/ha) incorporated into the soil. Both treatments were then oversprayed with Chlorsulfuron 75WG at 18.75 g a.s./ha. There was no significant impact on straw degradation relative to the control of greater than 10% after 12 months			
Indicate if not required			

[1] indicate where end point has been corrected due to log Pow >2.0 (e.g. LC_{50corr})
[2] litter bag, field arthropod studies not included at 8.3.2/10.5 above, and earthworm field studies

Toxicity/exposure ratios for soil organisms

Cereals (early and late), 18.75 g a.s./ha

Test organism	Test substance	Time scale	Soil PEC	TER	Trigger
Earthworms					
	Chlorsulfuron 75WG	Acute	0.0371	>20216	10
	Chlorsulfuron 75WG	Chronic	0.0246	7622	5
	IN-A4097	Acute	0.0213	>46948	10
	IN-A4097	Chronic	0.0213	1174	5
	IN-A4098	Acute	0.0044	>227273	10
	IN-A4098	Chronic	0.0044	45	5
	IN-JJ998	Acute	0.0073	>136986	10
	IN-JJ998	Chronic	0.0073	68493	5

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

Test organism	Test substance	Time scale	Soil PEC	TER	Trigger
Other soil macro-organisms					
Collembola	IN-A4097	Chronic	0.0213*	42	5
	IN-A4098	Chronic	0.0044*	51	5
	IN-JJ998	Chronic	0.0073*	38	5

* Plateau PEC(10 years, 0-10cm depth). Application rate of 18.75 ga.s./ha for chlorsulfuron with 25% interception = 14.1 g/ha

Effects on non target plants (Annex IIA, point 8.6, Annex IIIA, point 10.8)

Most sensitive species	Test substance	ER_{50} (g/ha) vegetative vigour	ER_{50} (g/ha) emergence	Exposure (g/ha)[2]	TER	Trigger
Sugar beet	Chlorsulfuron 75WG	0.09	5.08	0.519 0.036	**0.2** (1 m) **2.5** (15m) / 5 (15 m + 50% drift reduction	5
Pea	Chlorsulfuron 75WG	5.30	1.09	0.519 0.107	**2.1** (1 m) 10.2 (5m)	5

[1] explanation of how exposure has been estimated should be provided (e.g. based on Ganzelmeier drift data)
[2] for preparations indicate whether dose is expressed in units of a.s. or preparation

Effects on biological methods for sewage treatment (Annex IIA 8.7)

Test type/organism	Endpoint
Activated sludge	Chlorsulfuron (as): EC_{50} > 100 mg as/L

Ecotoxicologically relevant compounds (consider parent and all relevant metabolites requiring further assessment from the fate section)

Compartment	
soil	chlorsulfuron, IN-A4097 and IN-A4098, IN-JJ998 and IN-V7160 (photolysis metabolite) and IN-D5293 (for anaerobic conditions)
water	chlorsulfuron, IN-A4097, IN-A4098, IN-JJ998, IN-M6957 and IN-V7160 (photolysis metabolite) and IN-D5293 (for anaerobic conditions)

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1 – list of endpoints

sediment	
groundwater	chlorsulfuron, IN-A4097, IN-JJ998

Classification and proposed labelling with regard to ecotoxicological data (Annex IIA, point 10 and Annex IIIA, point 12.3)

	RMS/peer review proposal
Active substance	N, R50/R53

	RMS/peer review proposal
Preparation	N, R50/R53

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

APPENDIX 2 – ABBREVIATIONS USED IN THE LIST OF ENDPOINTS

ADI	acceptable daily intake
AOEL	acceptable operator exposure level
ARfD	acute reference dose
a.s.	active substance
bw	body weight
CA	Chemical Abstract
CAS	Chemical Abstract Service
CIPAC	Collaborative International Pesticide Analytical Council Limited
d	day
DAR	draft assessment report
DM	dry matter
DT_{50}	period required for 50 percent dissipation (define method of estimation)
DT_{90}	period required for 90 percent dissipation (define method of estimation)
ε	decadic molar extinction coefficient
EC_{50}	effective concentration
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINKS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
ER50	emergence rate, median
EU	European Union
FAO	Food and Agriculture Organisation of the United Nations
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
g	gram
GAP	good agricultural practice
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GLP	good laboratory practice
GS	growth stage
h	hour(s)
H	Henry's Law constant (calculated as a unitless value) (see also K)
ha	hectare
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
ISO	International Organisation for Standardisation

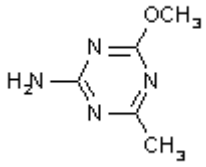
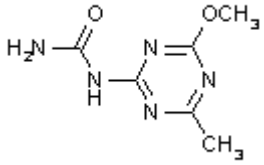
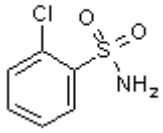
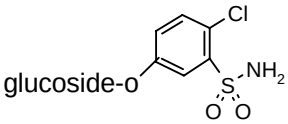
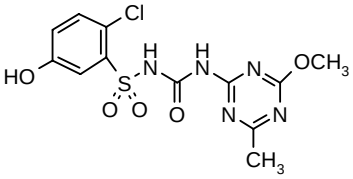
Appendix 2 – abbreviations used in the list of endpoints

IUPAC	International Union of Pure and Applied Chemistry
K_{oc}	organic carbon adsorption coefficient
kg	kilogram
L	litre
LC	liquid chromatography
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LC_{50}	lethal concentration, median
LD_{50}	lethal dose, median; dosis letalis media
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification (determination)
µg	microgram
mN	milli-Newton
MRL	maximum residue limit or level
MS	mass spectrometry
NESTI	national estimated short term intake
NIR	near-infrared-(spectroscopy)
nm	nanometer
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
PEC	predicted environmental concentration
PEC_A	predicted environmental concentration in air
PEC_S	predicted environmental concentration in soil
PEC_{SW}	predicted environmental concentration in surface water
PEC_{GW}	predicted environmental concentration in ground water
pH	pH-value
PHI	pre-harvest interval
pK_a	negative logarithm (to the base 10) of the dissociation constant
P_{ow}	partition coefficient between n-octanol and water
PPE	personal protective equipment
ppm	parts per million (10^{-6})
ppp	plant protection product
r^2	coefficient of determination
RPE	respiratory protective equipment
STMR	supervised trials median residue
TER	toxicity exposure ratio

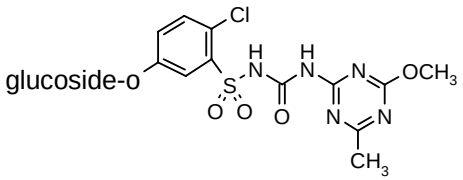
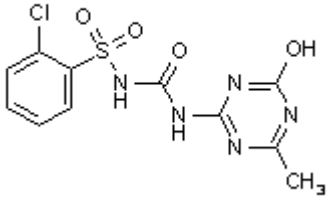
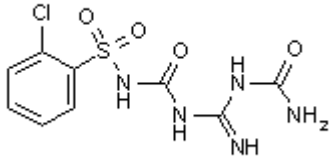
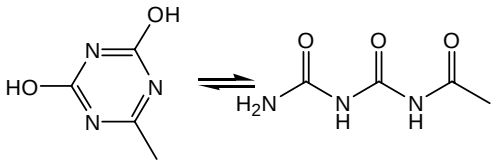
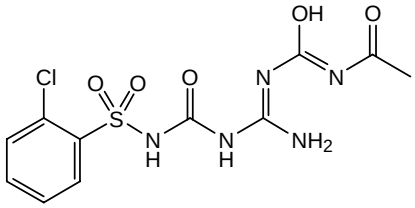
Appendix 2 – abbreviations used in the list of endpoints

TMDI	theoretical maximum daily intake
UV	ultraviolet
WHO	World Health Organisation
WG	water dispersible granule
wk	week
yr	year

APPENDIX 3 – USED COMPOUND CODE(S)

Code/Trivial name	Chemical name	Structural formula
IN-A4098 triazine amine	4-methoxy-6-methyl-1,3,5-triazine-2-amine	
IN-V7160 triazine urea	1-(4-methoxy-6-methyl-1,3,5-triazine-2-yl)urea	
IN-A4097 chlorosulfonamide	2-chlorobenzenesulfonamide	
IN-A5760 5-hydroxychlorosulfonamide	2-chloro-5-hydroxybenzenesulfonamide	
Metabolite B glucose conjugate 5-hydroxychlorsulfuron	2-chloro-5-(β-D-glucopyranosyloxy)-benzenesulfonamide	
IN-N5754 5-hydroxychlorsulfuron	2-chloro-5-hydroxy-N-[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino]carbonyl]benzenesulfonamide	

Appendix 3 – used compound code(s)

IN-69182 glucose conjugate of 5-hydroxychlorsulfuron	2-chloro-5-(β-D-glucopyranosyloxy)-N-[[(4-methoxy-6-methyl-1,3,5-trazi-2yl)amino]-carbonyl]benzenesulfonamide	
IN-M6957 O-desmethylchlorsulfuron	2-chloro-N-[(4-hydroxy-6-methyl-1,3,5-triazin-2-yl)carbamoyl]benzenesulfonamide	
IN-JJ998	N-[(N-carbamoylcarbamimidoyl)carbamoyl]-2-chlorobenzenesulfonamide	
IN-F5475	6-methyl-1,3,5-triazine-2,4-diol N-(carbamoylcarbamoyl)acetamide	
triazine ring-opened acetyltriuret chlorsulfuron	N'-acetyl-N-[(E)-amino({[(2-chlorophenyl)sulfonyl]carbamoyl}amino)methylidene]carbamimidic acid	
IN-B5528	4-amino-6-methyl-1,3,5-triazin-2-ol