Peer review of the pesticide risk assessment of the active substance imazosulfuron

European Food Safety Authority (EFSA)

Abstract

The conclusions of EFSA following the peer review of the initial risk assessments carried out by the competent authorities of the rapporteur Member State, Slovenia, and co-rapporteur Member State, Finland, for the pesticide active substance imazosulfuron are reported. The context of the peer review was that required by Commission Implementing Regulation (EU) No 844/2012. The conclusions were reached on the basis of the evaluation of the representative uses of imazosulfuron as a herbicide on winter cereals (wheat, barley and rye) and triticale. The reliable end points, appropriate for use in regulatory risk assessment, are presented. Missing information identified as being required by the regulatory framework is listed. Concerns are identified.

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Summary

Commission Implementing Regulation (EU) No 844/2012 (hereinafter referred to as ‘the Regulation’) lays down the procedure for the renewal of the approval of active substances submitted under Article 14 of Regulation (EC) No 1107/2009. The list of those substances is established in Commission Implementing Regulation (EU) No 686/2012. Imazosulfuron is one of the active substances listed in Regulation (EU) No 686/2012.

In accordance with Article 1 of the Regulation, the rapporteur Member State (RMS), Slovenia, and co-rapporteur Member State (co-RMS), Finland, received an application from Sumitomo Chemical Agro Europe S.A.S. for the renewal of approval of the active substance imazosulfuron. Complying with Article 8 of the Regulation, the RMS checked the completeness of the dossier and informed the applicant, the co-RMS (Finland), the European Commission and the European Food Safety Authority (EFSA) about the admissibility.

The RMS provided its initial evaluation of the dossier on imazosulfuron in the renewal assessment report (RAR), which was received by EFSA on 1 February 2016. In accordance with Article 12 of the Regulation, EFSA distributed the RAR to the Member States and the applicant, Sumitomo Chemical Agro Europe S.A.S., for comments on 11 March 2016. EFSA also provided comments. In addition, EFSA conducted a public consultation on the RAR. EFSA collated and forwarded all comments received to the European Commission on 11 May 2016.

Following consideration of the comments received on the RAR, it was concluded that additional information should be requested from the applicant, and that EFSA should conduct an expert consultation in the areas of mammalian toxicology, environmental fate and behaviour, and ecotoxicology.

In accordance with Article 13(1) of the Regulation, EFSA should adopt a conclusion on whether imazosulfuron can be expected to meet the approval criteria provided for in Article 4 of Regulation (EC) No 1107/2009 of the European Parliament and of the Council.

The conclusions laid down in this report were reached on the basis of the evaluation of the representative uses of imazosulfuron as a herbicide on winter cereals (wheat, barley and rye) and triticale as proposed by the applicant. Full details of the representative uses can be found in Appendix A of this report.

The use of imazosulfuron according to the representative uses proposed at the European Union (EU) level results in a sufficient herbicidal efficacy against the target weeds.

A data gap was identified for the relevance criteria used in the search of the scientific peer-reviewed open literature on the active substance and its relevant metabolites.

In the section on identity, physical chemical properties, analytical methods, a data gap was identified for a method of monitoring for residues of metabolite IPSN.

In the area of mammalian toxicology and non-dietary exposure, a data gap was identified to further assess the phototoxicity potential of imazosulfuron at ultraviolet B (UVB) ranges. A data gap concerning an in vitro comparative metabolism study on imazosulfuron lead to an issue that could not be finalised. No conclusion can be drawn on the potential for groundwater exposure to be below the parametric drinking water limit of 0.1 µg/L by metabolite IPSN, which is considered relevant because it cannot be excluded that it shares the developmental toxicity of the parent (issue that could not be finalised). An issue that could not be finalised was set for the identification of imazosulfuron as having endocrine disruption properties considering the interpretation of the second interim provisions of Annex II, Point 3.6.5 of Regulation (EC) No 1107/2009.

In the area of residues, the consumer risk assessment could not be finalised in view of the identified data gaps for rotational crops metabolism data addressing the fate of imazosulfuron in leafy and root and tuber vegetables at the 30 days plant back intervals (PBI) and for the potential for residues of IPSN, HMS, ADPM and UDPM in rotational crops in view of their moderate to high persistence in soil. No risk was identified for the consumers regarding imazosulfuron residues only; the highest chronic intake (TMDI) was estimated to be less than 0.1% of the ADI (Danish child) and the highest acute intake (ESTI) 0.1% of the ARfD (British 4-6 years child).

The data available on environmental fate and behaviour are sufficient to carry out the required environmental exposure assessments at the EU level for the representative uses, with the notable exception that the groundwater exposure assessment for metabolite IPSN cannot be finalised. Additionally, soil persistence endpoints for imazosulfuron metabolites under field conditions are not available.

In the ecotoxicology area, a data gap was identified for addressing the risk to aquatic organisms, particularly macrophytes. Several data gaps were identified for bees.
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Background

Commission Implementing Regulation (EU) No 844/2012\(^1\) (hereinafter referred to as ‘the Regulation’) lays down the provisions for the procedure of the renewal of the approval of active substances, submitted under Article 14 of Regulation (EC) No 1107/2009\(^2\). This regulates for the European Food Safety Authority (EFSA) the procedure for organising the consultation of the Member States, the applicant and the public on the initial evaluation provided by the rapporteur Member State (RMS) and/or co-rapporteur Member State (co-RMS) in the renewal assessment report (RAR), and the organisation of an expert consultation where appropriate.

In accordance with Article 13 of the Regulation, unless formally informed by the European Commission that a conclusion is not necessary, EFSA is required to adopt a conclusion on whether the active substance can be expected to meet the approval criteria provided for in Article 4 of Regulation (EC) No 1107/2009 within 5 months from the end of the period provided for the submission of written comments, subject to an extension of up to 8 months where additional information is required to be submitted by the applicant in accordance with Article 13(3).

In accordance with Article 1 of the Regulation, the RMS Slovenia and co-RMS Finland received an application from Sumitomo Chemical Agro Europe S.A.S. for the renewal of approval of the active substance imazosulfuron. Complying with Article 8 of the Regulation, the RMS checked the completeness of the dossier and informed the applicant, the co-RMS (Finland), the European Commission and EFSA about the admissibility.

The RMS provided its initial evaluation of the dossier on imazosulfuron in the RAR, which was received by EFSA on 1 February 2016 (Slovenia, 2016a).

In accordance with Article 12 of the Regulation, EFSA distributed the RAR to the Member States and the applicant, Sumitomo Chemical Agro Europe S.A.S., for consultation and comments on 11 March 2016. EFSA also provided comments. In addition, EFSA conducted a public consultation on the RAR. EFSA collated and forwarded all comments received to the European Commission on 11 May 2016. At the same time, the collated comments were forwarded to the RMS for compilation and evaluation in the format of a reporting table. The applicant was invited to respond to the comments in column 3 of the reporting table. The comments and the applicant’s response were evaluated by the RMS in column 3.

The need for expert consultation and the necessity for additional information to be submitted by the applicant in accordance with Article 13(3) of the Regulation were considered in a telephone conference between EFSA, the RMS on 17 June 2016. On the basis of the comments received, the applicant’s response to the comments and the RMS’s evaluation thereof, it was concluded that additional information should be requested from the applicant, and that EFSA should conduct an expert consultation in the areas of mammalian toxicology, environmental fate and behaviour, and ecotoxicology.

The outcome of the telephone conference, together with EFSA’s further consideration of the comments, is reflected in the conclusions set out in column 4 of the reporting table. All points that were identified as unresolved at the end of the comment evaluation phase and which required further consideration, including those issues to be considered in an expert consultation, were compiled by EFSA in the format of an evaluation table.

The conclusions arising from the consideration by EFSA, and as appropriate by the RMS, of the points identified in the evaluation table, together with the outcome of the expert consultation and the written consultation on the assessment of additional information, where these took place, were reported in the final column of the evaluation table.

A final consultation on the conclusions arising from the peer review of the risk assessment took place with the Member States via a written procedure in December-January 2017.

This conclusion report summarises the outcome of the peer review of the risk assessment of the active substance and the representative formulation, evaluated on the basis of the representative uses of imazosulfuron as a herbicide on triticale and winter cereals as wheat, barley and rye, as proposed by the applicant. A list of the relevant end points for the active substance and the formulation is provided in Appendix A.

\(^1\) Commission Implementing Regulation (EU) No 844/2012 of 18 September 2012 setting out the provisions necessary for the implementation of the renewal procedure for active substances, as provided for in Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market. OJ L 252, 19.9.2012, p. 26–32.

\(^2\) Regulation (EC) No 1107/2009 of 21 October 2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. OJ L 309, 24.11.2009, p. 1–50.
In addition, a key supporting document to this conclusion is the peer review report (EFSA, 2017), which is a compilation of the documentation developed to evaluate and address all issues raised in the peer review, from the initial commenting phase to the conclusion. The peer review report comprises the following documents, in which all views expressed during the course of the peer review, including minority views, where applicable, can be found:

- the comments received on the RAR;
- the reporting table (22 June 2016);
- the evaluation table (16 December 2016);
- the reports of the scientific consultation with Member State experts;
- the comments received on the assessment of the additional information;
- the comments received on the draft EFSA conclusion.

Given the importance of the RAR, including its revisions (Slovenia, 2016a,b), and the peer review report, both documents are considered as background documents to this conclusion and thus are made publicly available.

It is recommended that this conclusion report and its background documents would not be accepted to support any registration outside the European Union (EU) for which the applicant has not demonstrated that it has regulatory access to the information on which this conclusion report is based.

**The active substance and the formulated product**

Imazosulfuron is the ISO common name for 1-(2-chloroimidazo[1,2-a]pyridin-3-ylsulfonyl)-3-(4,6-dimethoxypyrimidin-2-yl)urea (IUPAC).

The representative formulated product for the evaluation was ‘Imazosulfuron 50 WG’, a water-dispersible granule (WG) containing 500 g/kg imazosulfuron.

The representative uses evaluated were spray applications in winter wheat, winter barley, winter rye and triticale to control dicotyledonous weeds. Full details of the Good Agricultural Practices (GAPs) can be found in the list of end points in Appendix A.

Data were submitted to conclude that the use of imazosulfuron according to the representative uses proposed at the EU level results in a sufficient herbicidal efficacy against the target weeds following the guidance document SANCO/10054/2013-rev. 3 (European Commission, 2013).

A data gap has been identified for the relevance criteria used in the search of the scientific peer-reviewed open literature on the active substance and its relevant metabolites, dealing with side effects on health, the environment and non-target species and published within the 10 years before the date of submission of the dossier, to be conducted and reported in accordance with EFSA guidance on the submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (EFSA, 2011).

**Conclusions of the evaluation**

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

The following guidance documents were followed in the production of this conclusion: SANCO/3029/99-rev. 4 (European Commission, 2000a), SANCO/3030/99-rev. 4 (European Commission, 2000b), SANCO/825/00-rev. 8.1 (European Commission, 2010) and SANCO/10054/2013-rev. 3 (European Commission, 2013).

The reference specification from the first approval was updated. The proposed specification is based on batch data from industrial scale production. The minimum purity of the technical material is 980 g/kg. There is no FAO specification available.

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 imazosulfuron or the representative formulation. The main data regarding the identity of imazosulfuron and its physical and chemical properties are given in Appendix A.

Adequate methods are available for the generation of pre-approval data required for the risk assessment. Methods of analysis are available for the determination of the active substance in the technical material and representative formulation.
Monitoring imazosulfuron residues in food and feed of plant origin can be done by the Quick, Easy, Cheap, Effective, Rugged, and Safe (QuEChERS) method using liquid chromatography with tandem mass spectrometry (LC-MS/MS) with limit of quantifications (LOQs) of 0.01 mg/kg in all commodity groups. An analytical method for monitoring residues in food and feed of animal origin is not needed as no maximum residue levels (MRLs) were proposed for the animal matrices.

LC-MS/MS methods are available enabling the determination of imazosulfuron residues in soil and water with LOQs of 0.1 µg/kg and 0.01 µg/L, respectively. Metabolite IPSN was considered relevant if it occurs in ground water above 0.1 µg/L (see Section 2), as a consequence a data gap was identified for an analytical method for the determination of this metabolite in ground water.

Residues of imazosulfuron in air can be determined by high-performance liquid chromatography-ultraviolet (HPLC-UV) with a LOQ of 11.25 µg/m³. Imazosulfuron residues in body fluids and tissues can be monitored by the QuEChERS method using LC-MS/MS with LOQs of 0.01 mg/L and 0.01 mg/kg, respectively.

2. Mammalian toxicity

The toxicological profile of the active substance imazosulfuron and its metabolites was discussed at the Pesticides Peer Review Experts’ Meeting 148 and assessed based on the following guidance documents: SANCO/221/2000-rev. 10-final (European Commission, 2003), SANCO/10597/2003-rev. 10.1 (European Commission, 2012), Guidance on Dermal Absorption (EFSA PPR Panel, 2012) and Guidance on the Application of the CLP Criteria (ECHA, 2015).

To assess the toxicological profile of the active substance the applicant submitted a set of toxicity studies. The proposed technical specification of the active substance and associated impurities is supported from the toxicological point of view. Impurities are not considered relevant from the toxicological point of view.

In the toxicokinetics studies, imazosulfuron was extensively and rapidly absorbed. Oral absorption was estimated to be approximately 89%. There was no evidence for accumulation. Excretion of substance was predominantly in urine but with appreciable amounts excreted through the bile/faecal route. It is unknown whether a unique human metabolite might be formed since an in vitro comparative metabolism study was not submitted leading to a data gap and issue that could not be finalised. The RMS did not agree.

In the acute toxicity studies, the substance has low acute toxicity when administered orally, dermally or by inhalation to rats. It is not a skin or eye irritant or a skin sensitiser.

Imazosulfuron was not phototoxic in the 3T3 neutral red uptake phototoxicity assay (NRU-PT) test. Since the absorption of imazosulfuron was higher at UVB than at UVA ranges, the 3T3 NRU-PT test might not be an appropriate test for UVB absorbers. It is noted, however, that there is no OECD test for UVB absorber leading to a data gap. A photogenotoxicity test is not required for imazosulfuron.

In short-term oral toxicity studies with rats, mice and dogs, the critical effects were observed in the liver (hepatocellular hypertrophy; rats and mice) and thyroid (increased weight and histopathological findings; dogs). The dog was the most sensitive species. The relevant short-term oral no observed adverse effect level (NOAEL) is 75 mg/kg body weight (bw) per day (1-year dog study).

Based on available genotoxicity studies, the active substance is unlikely to be genotoxic.

In long-term toxicity and carcinogenicity studies with rats and mice, the critical effects included ocular toxicity (retinal atrophy and cataracts) in rats and hepatotoxicity (increased liver weight and hepatocellular hypertrophy) in mice. The mouse was the most sensitive species. The relevant long-term NOAELs are 106 mg/kg bw per day for the rat and 73 mg/kg bw per day for the mouse. No evidence of carcinogenicity was observed in rats and mice.

In reproductive toxicity studies with rats, reproductive and offspring toxicity was observed at the same dose level inducing significant parental toxicity including mortality, reduced body weight and water consumption. The relevant parental, reproductive and offspring NOAELs are 77.8 mg/kg bw per day.

In the developmental toxicity studies, the maternal NOAELs are 1,000 mg/kg bw per day for the rat and 125 mg/kg bw per day for the rabbit (highest dose level tested). No developmental toxicity was observed in rats, whereas increased incidence of fused skull bones and bent hyoid arch was observed in rabbits. The developmental NOAELs are 1,500 mg/kg bw per day for the rat (highest dose level tested) and 50 mg/kg bw per day for the rabbit. Overall, during the experts’ meeting experts agreed that increased incidence of fused skull bones and bent hyoid arch in rabbits suggest that classification regarding developmental toxicity would be required for imazosulfuron as Toxic to reproduction.
Imazosulfuron did not show a neurotoxic potential in acute and short-term neurotoxicity studies in rats. Results from general toxicity studies and immunotoxicity studies suggest that imazosulfuron may have immunotoxic potential but at higher dose levels than dose levels inducing other systemic toxicity effects.

Imazosulfuron is not listed in Annex VI of the CLP Regulation (EC) No 1272/2008. During the peer review, imazosulfuron was not proposed to be classified as carcinogenic category 2 but proposed as toxic for reproduction category 2 (based on increased incidence of fused skull bones and bent hyoid arch in rabbits) in accordance with the provisions of Regulation (EC) No 1272/2008. The only evidence of toxic effects on endocrine organs was thyroid toxicity in dogs (no mechanistic data are available); in other toxicity studies including reproduction toxicity studies and tested species (rats, mice, rabbits), there was no evidence of toxic effects on endocrine organs. Therefore, the conditions of the second interim provisions of Annex II, Point 3.6.5 of Regulation (EC) No 1107/2009 concerning human health for the consideration of endocrine disrupting properties may be met leading to a data gap and an issue that could not be finalised. The RMS did not consider that interim criteria were met. Regarding the scientific risk assessment, the only evidence of potential endocrine activity of imazosulfuron was thyroid toxicity in dogs. No mechanistic data are available. However, in other toxicity studies including reproduction toxicity studies, there was no evidence of endocrine disruption.

The acceptable daily intake (ADI) and acceptable operator exposure level (AOEL) set during the first review was 0.75 and 0.53 mg/kg bw per day, respectively. An acute reference dose (ARfD) was considered not applicable (European Commission, 2004). The experts derived new human health-based reference values on the basis of re-assessment of the developmental toxicity study in rabbits. The point of departure was then the developmental NOAEL of 50 mg/kg bw per day based on fused skull bones in rabbit at 125 mg/kg bw per day. An uncertainty factor (UF) of 2 in addition to the standard UF of 100 was applied. The use of an additional UF of 2 provides a margin of safety of at least 300 relative to the lowest observable adverse effect level (LOAEL) for malformation in rabbits. No correction for oral absorption was needed to apply to the AOEL and AAOEL. The agreed ADI, ARfD, AOEL and AAOEL are 0.25 mg/kg bw per day.

The RMS estimated non-dietary exposure (i.e. operator, worker, bystander and resident) considering default dermal absorption values of imazosulfuron in ‘Imazosulfuron 50 WG’ of 25% for the concentrate and of 75% for the dilution as input values. Considering the representative uses with ‘Imazosulfuron 50 WG’ as a herbicide in cereals, the estimated operator exposure was below the AOEL (5% of the AOEL) without the use of personal protective equipment (PPE) during mixing and loading and application according to the German Model. Worker exposure was below the AOEL without the use of PPE (0.3% of the AOEL). Bystander and resident exposure was below the AOEL (maximum 0.11% of the AOEL; adult resident).

Toxicity studies with the metabolite IPSN indicated that the metabolite is unlikely to be genotoxic based on standard in vitro test battery and of moderate acute oral toxicity to rats. No conclusion can be drawn on the potential for groundwater exposure to be below the parametric drinking water limit of 0.1 µg/L by metabolite IPSN (see data gap in Section 4), although it is very unlikely that the predicted environmental concentrations (PECs) of this metabolite in groundwater will be above 0.75 µg/L. Since it cannot be excluded that metabolite IPSN share the developmental toxicity of the parent, the metabolite should be considered relevant if it occurs in groundwater above 0.1 µg/L leading to an issue that could not be finalised.

Toxicity studies with the metabolite IPSA found as a residue (see Section 3) indicated that this metabolite is negative in the Ames test and of low acute oral toxicity to rats. Based on the results of

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3 Imazosulfuron is not listed in Annex VI to the CLP Regulation (there is no harmonised classification and labelling). It should be noted that harmonised classification and labelling is formally proposed and decided in accordance with Regulation (EC) No 1272/2008.

4 Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006. OJ L 353, 31.12.2008, p. 1-1355.

5 The data gap and issue that could not be finalised were identified by EFSA during the finalisation of the conclusion considering the interpretation of the second interim provisions of Annex II, Point 3.6.5 of Regulation (EC) No 1107/2009.
the Ames test, structurally similarities with IPSN and the results from quantitative structure-activity relationship (QSAR) analysis the metabolite is considered unlikely to be genotoxic.

Metabolite ADPM is negative in the Ames test and common metabolite to other sulfonyl urea herbicides (amido-, azim-, bens-, flaza- and nicosulfuron; See Section 3). Data available from other sulfonyl urea herbicides indicated that it is of moderate acute oral toxicity study in rats (amidosulfuron, azimsulfuron and bensulfuron) and mouse (flzasulfuron, nicosulfuron).

3. Residues

The assessment in the residue section is based on the OECD guidance document on overview of residue chemistry studies (OECD, 2009), the OECD publication on MRL calculations (OECD, 2011), the European Commission guideline document on MRL setting (European Commission, 2016) and the Joint Meeting on Pesticide Residues (JMPR) recommendations on livestock burden calculations (JMPR, 2004, 2007).

Metabolism was investigated in wheat (cereal crop group) following foliar application using 14C-imidazole- and 14C-pyrimidine-labelled imazosulfuron. The experimental design was representative of the supported use on cereals. A single application was carried out at rates of 50 g a.s./ha (4 N) and 250 g a.s./ha (20 N), respectively, at growth stage BBCH 25. Metabolites identification was not made in wheat grain for both labels that is justified by the low recovered total residues in grain (0.001–0.0026 mg eq/kg) while the total residues in straw at harvest were only 0.019–0.022 mg eq/kg at the 4 N rate dosed study. The parent compound was never detected neither in immature plant nor in straw at harvest. At the exaggerated dose rate (20 N) and in mature wheat straw, HMS metabolite was recovered at a negligible proportion < 3.6% total radioactive residue (TRR) (< 0.0051 mg eq/kg) while the presence of label specific metabolites IPSA (< 11.6% TRR; < 0.0178 mg eq/kg) and ADNG (glucose conjugate of ADPM) (< 6% TRR; < 0.0089 mg eq/kg) bearing either the imidazole ring or the pyrimidine amine structure indicated that cleavage of the sulfonyleurea bridge occurred. Despite the low rate of identification, a significant part of the radioactivity in immature plants and straw at harvest was characterised as polar compounds. In the low total residues recovered in these commodities, it can be concluded that no individual component is expected to be present at a level > 0.01 mg eq/kg in wheat commodities at maturity. Considering the representative uses on wheat, barley, rye and triticale (cereals), the relevant residue for both enforcement and risk assessment on this crop group was proposed as parent imazosulfuron by default. These residue definitions are identical to the definitions proposed in the framework of the review of the existing MRLs under Article 12 of Regulation (EU) No 396/2005 (EFSA, 2012) and implemented in the EU legislation.

A confined rotational crop metabolism study was conducted with bare soil application of imazosulfuron 14C-labelled on the imidazolyl and pyrimidinyl rings, respectively, at a dose rate of 1 kg a.s./ha (80 N rate). The potential incorporation of soil residues into succeeding crops was investigated in sorghum and wheat crop parts at 30, 120 and 365 days plant back intervals (PBIs). Parent imazosulfuron was never detected while HMS was recovered in significant proportions in sorghum forage and stover (up to 33% TRR) at 30 days PBI, UDPM was the major residue in wheat hay and sorghum forage/stover (23% TRR and 15% TRR, respectively) at 120/365 days PBI and amino acids conjugates of IPSA were predominant in sorghum/wheat forage and in wheat straw (67% and 51% TRR, respectively) at all PBIs but the actual concentration of these compounds accounted for less than 0.01 mg eq/kg considering the exaggerated dosed study. The major part of the radioactive residues in grain was shown to be incorporated into natural plant constituents. However, no metabolites identification was attempted in kale and radish at 30 days PBI considering a crop failure and at 144 days PBI as the TRRs were very low in all crop parts (< 0.01 mg eq/kg). Additional metabolism data addressing the fate of imazosulfuron in leafy and root and tuber vegetables grown in rotation at the shortest PBI (30 days) are therefore requested. Furthermore and having regard to the high persistence of IPSN metabolite in soil (DT50 > 1,000 days) and to the medium persistence of HMS (DT50: 92.9 days), ADPM (DT90: 9.6–231 days) and UDPM (DT90: 12.2–66 days), the potential for residues of these metabolites in rotational crops should be further investigated.

Sufficient residue trials on wheat and barley were submitted to derive an MRL of 0.01 mg/kg (LOQ) on cereal grain. Although the longest storage period of samples in the residue trials is 262 and 287 days, respectively, for cereal grain and straw, residue data can be considered as sufficiently supported by storage stability studies where imazosulfuron residues were concluded to be stable for 224 days in high starch content matrices and 231 days in cereal straw in view of the constant and high storage stability recoveries observed throughout the storage time intervals. These storage stability
data address the data gap identified in the framework of the review of the existing MRLs for the submission of a storage stability study in high starch content commodities to cover the maximum storage period (210 days) of residue trials on cereals and rice (EFSA, 2012).

Investigations of the effect of industrial and/or household processing are not triggered in view of the very low residues in cereal grains (< 0.01 mg/kg).

Livestock metabolism studies were not submitted and not triggered considering the representative uses on cereals.

From the metabolic pattern depicted in primary and rotational crops, the identified metabolites ADPM (ADNG, its glucoside conjugate is actually formed) and UDPM are common metabolites to other pyrimidinylsulfonylurea herbicides and therefore imazosulfuron may be an additional contributor to the overall exposure of consumers to these metabolites, of which an assessment has not yet been concluded.

The consumer dietary risk assessment was conducted with the EFSA PRIMo rev.2 model. No risk was identified for the consumers regarding imazosulfuron residues only; the highest chronic intake (TMDI) was estimated to be less than 0.1% of the ADI (Danish child) and the highest acute intake (IESTI) 0.1% of the ARfD (British 4-6 years child). Considering the agreed toxicological reference values (Section 2), chronic and acute intake concerns have not been identified for the consumers when all the existing uses evaluated under the Article 12 MRL review have been included in the consumer dietary intake calculation. It is, however, highlighted that the overall consumer exposure assessment related to the representative uses and the existing uses assessed under Article 12 will have to be reconsidered pending upon the outcome of identified data gaps.

The available metabolism data and residue field trials demonstrated a no residue situation in all cereal crop parts. Therefore, it can reasonably be assumed that the residues of imazosulfuron and its metabolites in pollen and bee products are expected to be negligible. This assumption should be reconsidered in view of the outstanding data on rotational crops.

MRL applications were not included in the RAR.

4. Environmental fate and behaviour

Imazosulfuron was discussed at the Pesticides Peer Review TC 140 in October 2016.

The rates of dissipation and degradation in the environmental matrices investigated were estimated using FOCUS (2006) kinetics guidance. In soil laboratory incubations under aerobic conditions in the dark, imazosulfuron exhibited moderate to medium persistence, forming the major (> 10% applied radioactivity (AR)) metabolites IPSN (max. 25.8% AR) and HMS (max. 12.7% AR), which exhibited low to very high and low to medium persistence, respectively. Mineralisation of the imidazolyl and pyrimidinyl ring 14C radiolabel to carbon dioxide accounted for 3.2% AR and 8% AR, respectively, after 120 days. The formation of unextractable residues for this radiolabel accounted for about 50% AR and 67% AR for the two labels after 120 days. The slower degradation of imazosulfuron in anaerobic soil incubations resulted in the formation of a novel metabolite, ADPM (max 9.2% AR), which exhibited low persistence in aerobic conditions. A data gap was identified for a kinetic evaluation of the soil degradation data under anaerobic conditions taking into consideration also the formation of metabolite IPSN from metabolite HMS. Imazosulfuron degraded slowly in soil under illuminated conditions, forming metabolite UDPM (> 5% AR in two consecutive sampling times), which exhibited moderate to medium persistence. Imazosulfuron and metabolite IPSN exhibited high to medium mobility in soil, HMS exhibited high soil mobility, UDPM exhibited high to slight soil mobility and ADPM exhibited the whole range of mobility from very high mobility to immobile. It was concluded that the adsorption of imazosulfuron and its metabolites was not pH dependent. In field dissipation studies carried out at four sites in Europe (Germany, the Netherlands, Austria and Hungary; spray application to the soil surface on bare soil plots in autumn), imazosulfuron exhibited moderate to high persistence. Field study DT50 values were accepted as being reasonable estimates of degradation only for the German field trial. Field study DT50 values were derived following normalisation to FOCUS reference conditions (20°C and pF2 soil moisture) following the EFSA (2014a) DT50 guidance. The field data endpoints for the active substance were combined with laboratory soil DT50 values to derive modelling endpoints. A data gap was identified for soil dissipation rates under field conditions not normalised to 20°C and pF2 for metabolites IPSN, HMS, ADPM and UDPM. In a lysimeter study of 3 years duration, all chromatographically resolved components in leachate accounted for < 0.08 µg/L, as annual average concentrations.
In laboratory incubations in dark aerobic natural sediment water systems, imazosulfuron exhibited moderate to high persistence. The unextractable sediment fraction was the major sink for the imidazolyl and pyrimidinyl ring 14C radiolabel, accounting for about 80% AR at study end (120 days), except for one system, where the non-extractable residues in the sediment accounted for only 6% AR after 120 days. Mineralisation of these radiolabels accounted for < 5% AR at the end of the study. The rate of decline of imazosulfuron in a laboratory sterile aqueous photolysis experiment was fast relative to that occurred in the aerobic sediment water incubations. Chromatographically resolved component accounting for > 10% AR at pH 7 were: ADPM (max 35.3% AR), UDPM (max 11.1% AR), SDPM (max 13.8% AR) and IHOA (max 20.4% AR). The necessary surface water and sediment exposure assessments (PEC calculations) were carried out for the metabolites IPSN, HMS, ADPM, UDPM, IHOA and SDPM, using the FOCUS (FOCUS, 2001) step 1 and step 2 approach (version 2.1) of the steps 1–2 in FOCUS calculator. The available PECsw and PECsed for metabolites IPSN, HMS, ADPM and UDPM are based on soil DT50 values derived from the geometric mean DT50 laboratory and field data from the German and Austrian trials and therefore should not be considered acceptable. However, taking into consideration the large margin of safety of the available risk assessment to aquatic organisms for these metabolites, it is unlikely that this shortcoming has an impact on the final risk assessment. For the active substance imazosulfuron, appropriate step 3 (FOCUS, 2001) and step 4 calculations were available. The step 4 calculations appropriately followed the FOCUS (FOCUS, 2007) guidance, with no-spray drift buffer zones of up to 20 m being implemented (representing a 91–93% spray drift reduction). The SWAN tool (version 3.1) was appropriately used to implement these mitigation measures in the simulations.

The necessary groundwater exposure assessments were carried out using FOCUS (FOCUS, 2009) scenarios and the models PEARL 4.4.4 and PELMO 5.5.3. However, the available PECgw are based on some incorrect input parameters (in particular formation fraction (f.f.) for IPSN, HMS and UDPM, and soil DT50 for IPSN, HMS and ADPM) and therefore cannot be considered acceptable. Nevertheless, it is the EFSA opinion that this data gap is considered not to have an impact on the final conclusion of the available PECgw values, which indicated that the potential for groundwater exposure from the representative uses by imazosulfuron, HMS, UDPM and ADPM above the parametric drinking water limit of 0.1 µg/L is low in geoclimatic situations that are represented by all nine FOCUS groundwater scenarios. For metabolite IPSN, this deduction is less certain. When the correct soil laboratory DT50 value is pooled together with the available field DT50 value, the resulting geometric mean DT50 (in case the null hypothesis H0 is rejected) is longer (= 71.1 days) than the soil DT50 used in the available modelling (= 51.2 days). Therefore, EFSA cannot confirm that for metabolite IPSN the 80th percentile annual average recharge concentrations moving below 1 m are below 0.1 µg/L, but it is unlikely that they will be > 0.75 µg/L. Based on the information available in the mammalian toxicology section, metabolite IPSN is considered relevant because it cannot be excluded that it shares the developmental toxicity of the parent (see Section 2).

The applicant provided appropriate information to address the effect of water treatment processes on the nature of the residues that might be present in surface water and groundwater, when surface water or groundwater are abstracted for drinking water. The conclusion of this consideration was that neither imazosulfuron nor any of its degradation products that trigger assessment would be expected to undergo any substantial transformation due to oxidation at the disinfection stage of usual water treatment processes.

The PEC in soil, surface water, sediment and groundwater covering the representative uses assessed can be found in Appendix A of this conclusion.

5. Ecotoxicology

The risk assessment was based on the following documents: European Commission (2002a,b), SETAC (2001), EFSA (2009), EFSA PPR Panel (2013) and EFSA (2013). According to Regulation (EU) No 283/2013, data should be provided regarding the acute and chronic toxicity to honeybees and data to address the development of honeybee brood and larvae. As the European Commission (2002a) does not provide a risk assessment scheme which is able to use the chronic toxicity data for adult honeybees and the honeybee brood, when performing the risk assessment according to European Commission (2002a), the risk to adult honeybees from chronic toxicity and the risk to bee brood, could not be finalised due to the lack of a risk assessment scheme. Therefore, EFSA (2013) was used for risk assessment in order to reach a conclusion for the representative uses.

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6 Simulations utilised the agreed Q10 of 2.58 (following EFSA, 2008) and Walker equation coefficient of 0.7.
The reproductive endpoints for both birds and mammals were discussed and agreed during the Pesticide Peer Review Meeting 149. A low acute and reproductive risk via dietary exposure to birds and wild mammals was concluded for all representative uses of imazosulfuron.

A low risk to both birds and wild mammals was concluded for exposure to imazosulfuron via secondary poisoning and via consumption of contaminated water.

The available data were sufficient to conclude a low acute and chronic risk to fish, aquatic invertebrates, sediment-dwelling invertebrates and algae exposed to imazosulfuron, using PECsw calculated with FOCUS step 1. Several studies were available to address the toxicity of imazosulfuron and the representative formulation to aquatic macrophytes. Based on the lower available Tier I ErC50 (Lemna gibba) and on step 3 FOCUS PECsw, a high risk was identified in all scenarios for both spring and autumn application on cereals. A multispecies laboratory study was available to refine the risk assessment. Such study was discussed during the Pesticide Peer Review Meeting 149. As several major issues were pointed out, it was agreed that no reliable endpoint could be derived from this study; therefore, no refined endpoint was available for the risk assessment. Nevertheless, the multispecies test could be used as an evidence that the tier 1 endpoint for Lemna seems to be sufficiently protective for the other species. Step 4 FOCUS PECsw were calculated by considering 20 m no-spray buffer zones. Using this mitigation measure, a high risk was still identified in 3/9 and 7/9 FOCUS scenarios for spring and autumn application, respectively (data gap). A low risk to aquatic organisms was concluded for all imazosulfuron metabolites.

A low acute (contact and oral) and chronic (adult and larvae) risk to honeybees due to consumption of contaminated pollen and nectar was concluded based on the screening step in accordance with the risk assessment performed by EFSA following the scheme presented in EFSA (2013). A low acute and chronic risk (adult and larvae) honeybees was concluded on the basis of the screening assessment for exposure via residues in surface water. No data were submitted to estimating imazosulfuron concentration in puddle water. However, a low risk was also concluded for exposure via residues in puddle water, as the concentration needed to trigger a high risk would have to be several orders of magnitude higher than PECsw calculated with FOCUS step 1. The screening risk assessment for exposure via residues in guttation fluids showed that the chronic ETR was above the trigger for honeybee larvae and adult (data gap). Other assessments that were not available included sublethal effects (i.e. HPG, data gap), accumulative effects, and metabolites occurring in pollen and nectar (data gap). Data to perform a risk assessment for bumble bees and solitary bees were not available.

A low risk to non-target arthropods, earthworms, and other soil macro and microorganisms was concluded for all representative uses of imazosulfuron. A low risk to soil organisms was also concluded for all pertinent soil metabolites of imazosulfuron.

A high risk to non-target terrestrial plants was identified for all representative uses of imazosulfuron, unless mitigation measures are applied. Drift-reducing measures at least equivalent to 15 m no-spray buffer strips are necessary to achieve a low risk for all representative uses of imazosulfuron.

A low risk is concluded for biological methods of sewage treatment.

With regard to the endocrine disruption potential, the assessment for mammals is presented in Section 2, and no firm conclusion can be drawn regarding fish and birds.
6. **Overview of the risk assessment of compounds listed in residue definitions triggering assessment of effects data for the environmental compartments (Tables 1–4)**

**Table 1: Soil**

| Compound (name and/or code) | Persistence                                                                 | Ecotoxicology                  |
|-----------------------------|-----------------------------------------------------------------------------|--------------------------------|
| Imazosulfuron               | Moderate to medium persistence  
  Single first-order and biphasic DT_{50} 26.3–82.5 days (DT_{90} 266 – > 1,000 days; 20°C, pF 2 and 45% MWHC soil moisture)  
  Moderate to high persistence under field conditions  
  European field dissipation studies single first-order and biphasic DT_{50} 11.4–162.6 days (DT_{90} 292–540 days) | Low risk to soil organisms    |
| IPSN                        | Low to very high persistence  
  Single first-order DT_{50} 8.8 – > 1,000 days (20°C, pF 2 and 45% MWHC soil moisture) | Low risk to soil organisms    |
| HMS                         | Low to medium persistence  
  Single first-order DT_{50} 8.2–92.9 days (20°C, pF 2 and 45% MWHC soil moisture) | Low risk to soil organisms    |
| ADPM                        | Low persistence  
  Single first-order and biphasic DT_{50} 2.5–9.7 days (DT_{90} 9.6–231 days; 20°C, pF 2 and 40–53% MWHC soil moisture) | Low risk to soil organisms    |
| UDPM                        | Moderate to medium persistence  
  Single first-order DT_{50} 12.2–66 days (20°C, pF 2 soil moisture) | Low risk to soil organisms    |

DT_{50}: period required for 50% dissipation; DT_{90}: period required for 90% dissipation; MWHC: maximum water-holding capacity.
### Table 2: Groundwater

| Compound (name and/or code) | Mobility in soil | > 0.1 µg/L at 1 m depth for the representative uses(a) | Pesticidal activity | Toxicological relevance |
|-----------------------------|------------------|-----------------------------------------------------|---------------------|------------------------|
| Imazosulfuron               | High to medium mobility $K_{OC}$ 135-428 mL/g | No | Yes | Yes |
| IPSN                        | High to medium mobility $K_{OC}$ 59-201 mL/g | Data gap | Open | Yes (it cannot be excluded that it shares the developmental toxicity potential of imazosulfuron; unlikely to be genotoxic; moderate acute oral toxicity to rats) |
| HMS                        | High mobility $K_{OC}$ 58-82 mL/g | No (to be confirmed by revised PEC$_{gw}$ based on the agreed endpoints) | Assessment not triggered (no data) | Assessment not triggered (no data) |
| ADPM                       | Very high mobility to immobile $K_{OC}$ 42-11,289 mL/g | No (to be confirmed by revised PEC$_{gw}$ based on the agreed endpoints) | Assessment not triggered (no data) | Assessment not triggered (Ames test negative, moderated acute oral toxicity to rats and mice) |
| UDPM                       | High to slight mobility $K_{OC}$ 112-3,708 mL/g | No (to be confirmed by revised PEC$_{gw}$ based on the agreed endpoints) | Assessment not triggered (no data) | Assessment not triggered (no data) |

$K_{OC}$: Freundlich organic carbon adsorption coefficient; PEC$_{gw}$: predicted environmental concentration in groundwater.

(a): At least one FOCUS scenario or a relevant lysimeter.

### Table 3: Surface water and sediment

| Compound (name and/or code) | Ecotoxicology |
|-----------------------------|--------------|
| Imazosulfuron               | High risk to aquatic organisms |
| IPSN                        | Low risk to aquatic organisms |
| HMS                        | Low risk to aquatic organisms |
| ADPM                       | Low risk to aquatic organisms |
| UDPM                       | Low risk to aquatic organisms |
| IHOA                       | Low risk to aquatic organisms |
| SDPM                       | Low risk to aquatic organisms |

### Table 4: Air

| Compound (name and/or code) | Toxicology |
|-----------------------------|------------|
| Imazosulfuron               | Low acute inhalation toxicity to rats |
7. **Data gaps**

This is a list of data gaps identified during the peer review process, including those areas in which a study may have been made available during the peer review process but not considered for procedural reasons (without prejudice to the provisions of Article 56 of Regulation (EC) No 1107/2009 concerning information on potentially harmful effects).

- A data gap has been identified for the relevance criteria used in the search of the scientific peer-reviewed open literature on the active substance and its relevant metabolites, dealing with side effects on health, the environment and non-target species and published within the 10 years before the date of submission of the dossier, to be conducted and reported in accordance with EFSA guidance on the submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (EFSA, 2011).
  - Monitoring method for residues of metabolite IPSN in ground water with a LOQ of 0.1 µg/L (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Sections 1 and 2).
  - Comparative *in vitro* metabolism study on imazosulfuron (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 2).
  - Further phototoxicity assessment on imazosulfuron at UVB ranges (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 2).
  - Mechanistic data investigating whether thyroid toxicity in dogs is endocrine-mediated. This data gap is relevant for the interpretation of the second interim provisions of Annex II, Point 3.6.5 of Regulation (EC) No 1107/2009 (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 2).
  - Rotational crops metabolism data addressing the fate of imazosulfuron in leafy and root and tuber vegetables grown in rotation at the shortest PBI (30 days) (relevant for all representative uses evaluated in wheat, barley, rye and triticale; submission date proposed by the applicant: unknown; see Section 3).
  - The potential for residues of IPSN, HMS, ADPM and UDPM in rotational crops (relevant for all representative uses evaluated in wheat, barley, rye and triticale; submission date proposed by the applicant: unknown; see Section 3).
  - A kinetic evaluation of the soil degradation data under anaerobic conditions from the study (CA 7.1.2.1.1/01 in Slovenia a,b) taking into consideration also the formation of metabolite IPSN from metabolite HMS is not available (relevant for all representative uses evaluated; data already submitted by the applicant but not properly reported and evaluated by the RMS; see Section 4).
  - Soil dissipation rates under field conditions not normalised to reference conditions for metabolites IPSN, HMS, ADPM and UDPM (relevant for all representative uses evaluated; data already submitted by the applicant but not admissible by the peer review; see Section 4).
  - A revised groundwater exposure assessment for metabolite IPSN based on the new agreed endpoints (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 4).
  - Further data to address the chronic risk to macrophytes due to exposure to imazosulfuron (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 5).
  - Based on EFSA (2013), further data to address the chronic risk to honeybees (larvae and adults) due to exposure via consumption of contaminated guttation water (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 5).
  - Based on EFSA (2013), suitable data to address the risk of sublethal effects (e.g. HPG development effects) to honeybees due to exposure to imazosulfuron (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 5).
  - Information to assess the risk to honeybees due to plant metabolites occurring in pollen and nectar (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 5).
8. **Particular conditions proposed to be taken into account to manage the risk(s) identified**

- No spray buffer zones up to 20 m wide are necessary to protect aquatic organisms for all representative uses of imazosulfuron (see Section 5).
- Drift-reducing measures at least equivalent to 15 m no-spray buffer strips are necessary to reduce the exposure of non-target terrestrial plants to imazosulfuron for all representative uses (see Section 5).

9. **Concerns**

9.1. **Concerns for the representative uses evaluated**

9.1.1. **Issues that could not be finalised**

An issue is listed as ‘could not be finalised’ if there is not enough information available to perform an assessment, even at the lowest tier level, for the representative uses in line with the uniform principles in accordance with Article 29(6) of Regulation (EC) No 1107/2009 and as set out in Commission Regulation (EU) No 546/2011 and if the issue is of such importance that it could, when finalised, become a concern (which would also be listed as a critical area of concern if it is of relevance to all representative uses).

An issue is also listed as ‘could not be finalised’ if the available information is considered insufficient to conclude on whether the active substance can be expected to meet the approval criteria provided for in Article 4 of Regulation (EC) No 1107/2009.

1) The consumer risk assessment cannot be finalised in view of the identified data gaps for rotational crops metabolism data addressing the fate of imazosulfuron in leafy and root and tuber vegetables at the 30 days PBI and for the potential for residues of soil persistent metabolites in rotational crops (see Section 3).

2) The need for further tests and risk assessment to unique human metabolites could not be finalised while an in vitro comparative metabolism study on imazosulfuron was not submitted (see Section 2).

3) The groundwater exposure assessment for metabolite IPSN could not be finalised. Based on the information available, this metabolite is considered relevant because it cannot be excluded that it shares the developmental toxicity of the parent. However, it is very unlikely that with the revised satisfactory FOCUS groundwater modelling, the PEC\textsubscript{gw} values for this metabolite will be above 0.75 \( \mu \text{g}/\text{L} \) (see Sections 2 and 4).

4) The identification of imazosulfuron as having endocrine disruption properties considering the interpretation of the second interim provisions of Annex II, Point 3.6.5 of Regulation (EC) No 1107/2009 could not be finalised. During the peer review, imazosulfuron was not proposed to be classified as carcinogenic category 2 but proposed as toxic for reproduction category 2 (based on increased incidence of fused skull bones and bent hyoid arch in rabbits) in accordance with the provisions of Regulation (EC) No 1272/2008. The only evidence of toxic effects on endocrine organs was thyroid toxicity in dogs (no mechanistic data are available); in other toxicity studies including reproduction toxicity studies and tested species (rats, mice, rabbits) there was no evidence of toxic effects on endocrine organs.

9.1.2. **Critical areas of concern**

An issue is listed as a critical area of concern if there is enough information available to perform an assessment for the representative uses in line with the uniform principles in accordance with Article 29 (6) of Regulation (EC) No 1107/2009 and as set out in Commission Regulation (EU) No 546/2011, and if this assessment does not permit the conclusion that, for at least one of the representative uses, it may be expected that a plant protection product containing the active substance will not have any

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7 Commission Regulation (EU) No 546/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards uniform principles for evaluation and authorisation of plant protection products. OJ L 155, 11.6.2011, p. 127–175.
harmful effect on human or animal health or on groundwater, or any unacceptable influence on the environment.

An issue is also listed as a critical area of concern if the assessment at a higher tier level could not be finalised due to lack of information, and if the assessment performed at a lower tier level does not permit the conclusion that, for at least one of the representative uses, it may be expected that a plant protection product containing the active substance will not have any harmful effect on human or animal health or on groundwater, or any unacceptable influence on the environment.

An issue is also listed as a critical area of concern if, in the light of current scientific and technical knowledge using guidance documents available at the time of application, the active substance is not expected to meet the approval criteria provided for in Article 4 of Regulation (EC) No 1107/2009.

None.

9.1.3. Overview of the concerns identified for each representative use considered

(If a particular condition proposed to be taken into account to manage an identified risk, as listed in Section 8, has been evaluated as being effective, then ‘risk identified’ is not indicated in Table 5.)

Table 5: Overview of concerns

| Representative use | Winter cereals (wheat, barley and rye) and triticale Spring application | Winter cereals (wheat, barley and rye) and triticale Autumn application |
|--------------------|-------------------------------------------------------------------------|---------------------------------------------------------------------|
| Operator risk      | Risk identified                                                         | Assessment not finalised                                              |
| Worker risk        | Risk identified                                                         | Assessment not finalised                                              |
| Resident/ bystander risk | Risk identified                                                      | Assessment not finalised                                              |
| Consumer risk      | Risk identified                                                         | Assessment not finalised                                              |
| Risk to wild non-target terrestrial vertebrates | Risk identified | Assessment not finalised |
| Risk to wild non-target terrestrial organisms other than vertebrates | Risk identified | Assessment not finalised |
| Risk to aquatic organisms | Risk identified | 3 out of 9 FOCUS scenarios | 7 out of 9 FOCUS scenarios |
| Groundwater exposure to active substance | Legal parametric value breached | Assessment not finalised |
| Groundwater exposure to metabolites | Legal parametric value breached | Parametric value of 10 μg/L breached |
|                     | Assessment not finalised                    | X³                                   |

The superscript numbers relate to the numbered points indicated in Sections 9.1.1. Where there is no superscript number, see Sections 2–6 for further information.
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Abbreviations

a.s. active substance
AAOEL acute acceptable operator exposure level
AchE acetylcholinesterase
AOEL acceptable operator exposure level
AR applied radioactivity
ArfD acute reference dose
bw body weight
CLP classification, labelling and packaging
DAR draft assessment report
DT_{50} period required for 50% dissipation (define method of estimation)
DT_{90} period required for 90% dissipation (define method of estimation)
ECHA European Chemicals Agency
EEC European Economic Community
ErC_{50} effective concentration (growth rate)
ETR exposure toxicity ratio
ETR_{acute} exposure toxicity ratio for acute exposure
ETR_{chronic} exposure toxicity ratio for chronic exposure
ETR_{larvae} exposure toxicity ratio for larvae
ETR_{HPG} exposure toxicity ratio for effects on honeybee hypopharyngeal glands
EUROPOEM European Predictive Operator Exposure Model
FAO Food and Agriculture Organization of the United Nations
FOCUS Forum for the Co-ordination of Pesticide Fate Models and their Use
GAP Good Agricultural Practice
HPLC high-pressure liquid chromatography or high-performance liquid chromatography
HPG hypopharyngeal glands
IESTI international estimated short-term intake
ISO International Organization for Standardization
IUPAC International Union of Pure and Applied Chemistry
JMPR Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues (Joint Meeting on Pesticide Residues)

$K_{\text{doc}}$ organic carbon linear adsorption coefficient

$K_{\text{Foc}}$ Freundlich organic carbon adsorption coefficient

LC–MS/MS liquid chromatography with tandem mass spectrometry

LOAEL lowest observable adverse effect level

LOQ limit of quantification

MRL maximum residue level

MS mass spectrometry

MWHC maximum water-holding capacity

NOAEL no observed adverse effect level

NRU-PT Neutral Red Uptake Phototoxicity Assay

OECD Organisation for Economic Co-operation and Development

PBI plant back intervals

PEC predicted environmental concentration

PEC$_{\text{air}}$ predicted environmental concentration in air

PEC$_{\text{gw}}$ predicted environmental concentration in groundwater

PEC$_{\text{sed}}$ predicted environmental concentration in sediment

PEC$_{\text{soil}}$ predicted environmental concentration in soil

PEC$_{\text{sw}}$ predicted environmental concentration in surface water

PPE personal protective equipment

RAR renewal assessment report

RMS rapporteur Member State

QSAR quantitative structure–activity relationship

SMILES simplified molecular-input line-entry system

STMR supervised trials median residue

TMDI theoretical maximum daily intake

TRR total radioactive residue

UF uncertainty factor

UV ultraviolet

W/S water/sediment

WG water-dispersible granule

WHO World Health Organization
Appendix A – List of end points for the active substance and the representative formulation

Appendix A can be found in the online version of this output (‘Supporting information’ section): https://doi.org/10.2903/j.efsa.2017.4695
## Appendix B – Used compound codes

| Code/trivial name<sup>a)</sup> | Chemical name/SMILES notation | Structural formula |
|-------------------------------|--------------------------------|--------------------|
| ACIS | N-(Carbamimidoylcarbamoyl)-2-chloroimidazo[1,2-a]pyridine-3-sulfonamide N=C(N)NC(=O)NS(-O)(=-O)c1c(Cl)nc2ccccn12 | ![Structural formula for ACIS](image) |
| ADNG | 4,6-Dimethoxypyrimidin-2-yl α-D-glucopyranoside COc1nc(nc(OC)c1)O[C@H]2O[C@H][CO][C@H]1O[C@H]1O[C@H]2O | ![Structural formula for ADNG](image) |
| ADPM | 4,6-Dimethoxypyrimidin-2-amine COc1cc(OC)nc(N)n1 | ![Structural formula for ADPM](image) |
| AHMP | 2-Amino-6-methoxypyrimidin-4-ol Oc1cc(OC)nc(N)n1 | ![Structural formula for AHMP](image) |
| HDS | 2-Chloro-4-{[4,5-dimethoxy-6-oxo-1,6-dihydropyrimidin-2-yl]carbamoyl}imidazo[1,2-a]pyridine-3-sulfonamide Oc1nc(nc(OC)c1OC)NC(=O)NS(-O)(=-O)c2c(Cl)nc3ccccn23 | ![Structural formula for HDS](image) |
| HMS | 2-Chloro-4-{[4-methoxy-6-oxo-1,6-dihydropyrimidin-2-yl]carbamoyl}imidazo[1,2-a]pyridine-3-sulfonamide Oc1nc(nc(OC)c1)NC(=O)NS(-O)(=-O)c2c(Cl)nc3ccccn23 | ![Structural formula for HMS](image) |
| IHOA | (2-Iminopyridin-1(2H)-yl)(oxo)acetic acid N=C1C=CC-CN1C(-O)C(=O)O | ![Structural formula for IHOA](image) |
| IHDU | 2-Chloro-4-{[5-hydroxy-4,6-dimethoxypyrimidin-2-yl]carbamoyl}imidazo[1,2-a]pyridine-3-sulfonamide COc1nc(nc(OC)c1O)NC(=O)NS(-O)(=-O)c2c(Cl)nc3ccccn23 | ![Structural formula for IHDU](image) |
| IHDU-glu | 2-Chloro-4-{[5-(α-D-glucopyranosylxy)-4,6-dimethoxypyrimidin-2-yl]carbamoyl}imidazo[1,2-a]pyridine-3-sulfonamide Clc2nc1ccccn1c2S(-O)(=-O)NC(-O)Nc4nc(OC)c(O[C@H]3O[C@H][CO][C@H]1O[C@H][O][C@H]3O)c(OC)n4 | ![Structural formula for IHDU-glu](image) |
| Code/trivial name<sup>(a)</sup> | Chemical name/SMILES notation | Structural formula |
|-------------------------------|--------------------------------|--------------------|
| IPSA                          | 2-Chlorimidazo[1,2-\textbf{a}]pyridine-3-sulfonic acid O=S(=O)(O)c1c(Cl)nc2ccccn12 | ![Structural formula for IPSA](image1) |
| IPSN                          | 2-Chlorimidazo[1,2-\textbf{a}]pyridine-3-sulfonamide NS(=O)(=O)c1c(Cl)nc2ccccn12 | ![Structural formula for IPSN](image2) |
| SDPM                          | [(4,6-Dimethoxypyrimidin-2-yl)carbamoyl]sulfamic acid O=\textbf{C}(Nc1nc(cc(OC)n1)OC)NS(=O)(=O)O | ![Structural formula for SDPM](image3) |
| UDPM                          | 1-(4,6-Dimethoxypyrimidin-2-yl)urea O=\textbf{C}(N)Nc1nc(cc(OC)n1)OC | ![Structural formula for UDPM](image4) |

SMILES: simplified molecular-input line-entry system.

<sup>(a)</sup>: The compound name in bold is the name used in the conclusion.