CONCLUSION ON PESTICIDES PEER REVIEW

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

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, the Netherlands, and co-rapporteur Member State, Spain, for the pesticide active substance acetamiprid 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 acetamiprid as an insecticide for the control of aphids in pome fruit and protected tomatoes, and against aphids and Colorado beetle in potatoes. 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.

Keywords: acetamiprid, peer review, risk assessment, pesticide, insecticide

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Erratum: The residue section of this EFSA conclusion wrongly stated that potato crops are not attractive to bees and this argument was the basis for waiving the data requirement for residue data in pollen and bee products on potato crops. This is however not in line with the EFSA guidance on the risk assessment of plant protection products on bees (EFSA, 2013). Therefore, corrections have been made on p. 3, 10 and 19. To avoid confusion, the older version has been removed from the EFSA Journal, but is available on request, as is a version showing all the changes made.

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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. Acetamiprid 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), the Netherlands, and co-rapporteur Member State (co-RMS), Spain, received an application from Nisso Chemical Europe GmbH for the renewal of approval of the active substance acetamiprid. Complying with Article 8 of the Regulation, the RMS checked the completeness of the dossier and informed the applicant, the co-RMS (Spain), the European Commission and the European Food Safety Authority (EFSA) about the admissibility.

The RMS provided its initial evaluation of the dossier on acetamiprid in the renewal assessment report (RAR), which was received by EFSA on 27 November 2015. In accordance with Article 12 of the Regulation, EFSA distributed the RAR to the Member States and the applicant, Nisso Chemical Europe GmbH, for comments on 17 December 2015. 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 17 February 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 and ecotoxicology.

In accordance with Article 13(1) of the Regulation, EFSA should adopt a conclusion on whether acetamiprid 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 acetamiprid as an insecticide on tomato, potato and pome fruit, as proposed by the applicant. Full details of the representative uses can be found in Appendix A of this report.

Data were submitted to conclude that the uses of acetamiprid according to the representative uses proposed result in a sufficient insecticidal efficacy against the target organisms.

A data gap was identified to revise the literature search for the effect of acetamiprid and its metabolites on non-target organisms by better defining the reliability criteria for inclusion or exclusion of the retrieved papers.

No data gaps were identified in the area of identity, physical and chemical properties and analytical methods.

In the area of mammalian toxicology, one data gap was identified for comparative *in vitro* metabolism data between animal species used in pivotal studies and human material (microsomes or intact cell systems).

Sufficient data were provided to propose monitoring and risk assessment residue definitions for plant commodities. For animal products, EFSA proposes to limit the enforcement residue definition to the N-desmethyl metabolite (IM-2-1), expressed as acetamiprid since acetamiprid is extensively metabolised by animals and not detected in any animal matrices, except in milk. A maximum residue limit (MRL) was proposed for potato only and data gaps were identified for the submission of residue trials on pome fruits and tomato conducted according to the supported Good Agricultural Practice (GAPs). In addition, a data gap has been identified for the submission of processing studies on tomato. Information on residues in pollen and bee products is requested for potato since this crop shows attractiveness to bees for pollen collection. A risk for the consumers was not identified considering the supported use on potato only. In contrast, considering the acute reference dose (ARfD) value of 0.025 mg/kg body weight (bw) and the highest residue levels related to the uses evaluated under the Article 12 MRL review, an exceedance of the ARfD is identified for several food commodities. Therefore, the MRLs listed in the European Union (EU) legislation for these food commodities need to be reconsidered.

The data available on environmental fate and behaviour are sufficient to carry out the required environmental exposure assessments at the EU level, with the notable exception that a data gap was identified for information on the effect of water treatment processes on the nature of residues of both the active substance and its identified metabolites potentially present in surface water, when surface water is abstracted for drinking water. This gap leads to the consumer risk assessment from the consumption of drinking water being not finalised for all the representative uses. For the representative

use on protected tomatoes, groundwater exposure by the toxicologically relevant metabolite IM-1-5 has been indicated for soil conditions represented by the Forum for the Co-ordination of Pesticide Fate Models and their Use (FOCUS) Hamburg and Kremsmunster groundwater scenarios.

Several data gaps were identified in the area of ecotoxicology, i.e. to further address the risk assessment for birds, mammals, aquatic organisms, bees and non-target arthropods.

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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 Member States, the applicant(s) 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 3 months where additional information is required to be submitted by the applicant(s) in accordance with Article 13(3).

In accordance with Article 1 of the Regulation, the RMS, the Netherlands, and co-RMS, Spain, received an application from Nisso Chemical Europe GmbH for the renewal of approval of the active substance acetamiprid. Complying with Article 8 of the Regulation, the RMS checked the completeness of the dossier and informed the applicant, the co-RMS (Spain), the European Commission and EFSA about the admissibility.

The RMS provided its initial evaluation of the dossier on acetamiprid in the RAR, which was received by EFSA on 27 November 2015 (Netherlands, 2015).

In accordance with Article 12 of the Regulation, EFSA distributed the RAR to the Member States and the applicant, Nisso Chemical Europe GmbH, for consultation and comments on 17 December 2015. 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 17 February 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 and the RMS on 25 March 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 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 Member States via a written procedure in September 2016.

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 acetamiprid as an insecticide for the control of aphids in pome fruit and protected tomatoes, and against aphids and Colorado beetle in potatoes, 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, 2016b), 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 (25 March 2016);
- the evaluation table (12 October 2016);
- the report(s) of the scientific consultation with the Member State experts (where relevant);
- the comments received on the assessment of the additional information (where relevant);
- the comments received on the draft EFSA conclusion.

Given the importance of the RAR, including its revisions (Netherlands, 2016), 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 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

Acetamiprid is the ISO common name for (*E*)-N^1-[(6-chloro-3-pyridyl)methyl]-N^2-cyano-N^1-methylacetamidine (IUPAC).

The representative formulated product for the evaluation was 'Acetamiprid 20 SG' a water-soluble granule (SG) containing 200 g/kg acetamiprid.

The representative uses evaluated were foliar spray applications for the control of aphids in pome fruit and protected tomato, and against aphids and Colorado beetle in potato. 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 uses of acetamiprid according to the representative uses proposed at the European Union (EU) level result in a sufficient insecticidal efficacy against the target organisms, following the guidance document SANCO/10054/2013-rev. 3 (European Commission, 2013).

A search of the scientific peer-reviewed open literature was provided and it was conducted in accordance with the 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, 2011a). However, the reliability criteria for inclusion and exclusion of the retrieved ecotoxicology papers were not transparently reported, making the complete analysis of the search not reproducible and a data gap was identified.

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/10597/2003-rev. 10.1 (European Commission, 2012) and SANCO/825/00-rev. 8.1 (European Commission, 2010).

The reference specification for first approval was updated. The proposed specification is based on batch data from industrial scale production. The minimum purity of the active substance as manufactured is 990 g/kg. There is no FAO specification available. The RMS/co-RMS and DE disagreed with updating the reference specification; however, there were no data supporting the original specification that was based on pilot plant production.

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 acetamiprid or the representative formulation. It should be noted, however, that label instructions are needed because of the excessive foaming of the formulation. The main data regarding the identity of acetamiprid and its physical and chemical properties are given in Appendix A.

Adequate methods are available for the generation of data required for the risk assessment. High-performance liquid chromatography with ultraviolet detector (HPLC-UV) methods are available for the determination of acetamiprid in the technical material and in the representative formulation.

Acetamiprid residues can be monitored in food and feed of plant origin with the quick, easy, cheap, effective and safe (QuEChERS) multiresidue method by high-performance liquid chromatography with tandem mass spectrometry (HPLC–MS/MS) with a limit of quantification (LOQ) of 0.01 mg/kg in all plant commodity groups. The QuEChERS multiresidue method with HPLC–MS/MS can also be used for the determination of the compound of the residue definition for monitoring in products of animal origin (*N*-desmethyl-acetamiprid (IM-2-1)) with an LOQ of 0.01 mg/kg in all animal matrices. Adequate HPLC–MS/MS methods are available for the determination of the residues of acetamiprid in soil and air with LOQs of 0.002 mg/kg and of 0.002 μg/m^3, respectively. Residues of acetamiprid in drinking water and surface water can be determined by HPLC–MS/MS with a LOQ of 0.1 μg/L, while monitoring metabolite IM-1-5 in drinking water and surface water can be done by HPLC–MS/MS with a LOQ of 0.05 μg/L. Acetamiprid residues in blood can be determined by HPLC–MS/MS with a LOQ of 0.05 mg/L.

2. Mammalian toxicity

The following guidance documents were followed in the production of this conclusion: SANCO/221/2000-rev. 10-final (European Commission, 2003), SANCO/10597/2003-rev. 10.1 (European Commission, 2012) and Guidance on dermal absorption (EFSA PPR Panel, 2012).

Acetamiprid has been discussed by the experts in mammalian toxicology during the peer review meeting PRAS 146. Considering the updated technical specification for the renewal, toxicologically relevant impurities were not identified, and the batches used for the toxicity studies can be considered as representative of the technical material.

In toxicokinetic studies, acetamiprid was rapidly and extensively absorbed after oral administration, showing the highest concentrations in the adrenals, thyroid, liver and kidney, with no potential for accumulation and main excretion via urine. A data gap has been identified for comparative *in vitro* metabolism data between animal species used in pivotal studies and human material (microsomes or intact cell systems) in order to determine the relevance of the toxicological animal data, and to identify potentially unique human metabolites. This data gap was not supported by the RMS.

In three studies for acute oral toxicity, two have shown results triggering a more severe classification (Acute Tox 3 H301 Toxic if swallowed) than the one reported in Annex VI of Regulation (EC) No 1272/2008 (CLP Regulation), therefore the experts agreed on Acute Tox 3.

In short-term studies, the liver was the main target organ. For the 90-day rat study, the no observed adverse effect level (NOAEL) is 12.4 mg/kg body weight (bw) per day, based on bodyweight decrease and liver effects (increased weight and centrilobular hepatocyte hypertrophy). For the 90-day mouse study, the NOAEL is 106.1 mg/kg bw per day, based on body and liver weight changes. For the 90-day dog study, the NOAEL is 13 mg/kg bw per day, based on growth retardation in males. For the 1-year dog study, the NOAEL is 20 mg/kg bw per day, based on growth retardation. The agreed short-term NOAEL in dogs is 13 mg/kg bw per day.

In the available *in vitro* genotoxicity studies, acetamiprid showed negative results except for the chromosome aberration study where clastogenicity was observed in the absence and presence of metabolic activation. Negative results were also obtained *in vivo* (micronucleus, chromosome aberration and unscheduled DNA synthesis (UDS)), and the exposure of the target organ was sufficiently demonstrated in the chromosome aberration test. Acetamiprid was concluded as unlikely to be genotoxic *in vivo*.

Long-term studies for acetamiprid were performed with rats and with mice. In the 2-year rat study, the systemic NOAEL is 7.1 mg/kg bw per day, based on body weight reductions in females and histopathological changes in the liver in males. The NOAEL for carcinogenic effects is 7.1 mg/kg bw per day, based on an increased incidence of adenocarcinoma in the mammary gland. Considering that there was a continuum between hyperplasia (significant at high dose) and increased incidence of adenocarcinoma, the majority of the experts agreed on a proposal for classification as Carc. Cat 2,[3] on which the RMS expressed disagreement. In the 18-month mouse study, the systemic NOAEL is 20.3 mg/kg bw per day, based on the increased hypertrophy in the liver, amyloidosis in the adrenal

[3] It should be noted that harmonised classification and labelling is formally proposed and decided in accordance with Regulation (EC) No 1272/2008.

cortex and increased spleen weight. The NOAEL for carcinogenic effects is 186.3 mg/kg bw per day in the absence of tumorigenic effect.

In the reproductive toxicity studies, no specific adverse effect on the fertility parameters and on the fetal development was observed. In the multigeneration study, the parental NOAEL is 17.9 mg/kg bw per day, based on decreased body weight gain and food consumption; the offspring NOAEL is 17.9 mg/kg bw per day, based on a decreased number of live pups; and the reproductive NOAEL is 51 mg/kg bw per day (high dose tested). In the developmental rat study, the maternal NOAEL is 16 mg/kg bw per day based on decreased body weight gain and food consumption, and increased liver weight; and the developmental NOAEL is 16 mg/kg bw per day based on an increased incidence of shortened 13th rib. In the developmental rabbit study, the maternal NOAEL is 15 mg/kg bw per day based on decreased bodyweight gain and food consumption; and the developmental NOAEL is 30 mg/kg bw per day (high dose tested).

Acetamiprid is proposed to be classified as carcinogenic category 2 but not as toxic for reproduction category 2, in accordance with the provisions of Regulation (EC) No 1272/2008, and therefore the conditions of the 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 are not met. On the basis of the available data and current knowledge (OECD Conceptual Framework, as analysed in EFSA Scientific Committee (2013)), it is concluded that acetamiprid is unlikely to be an endocrine disruptor.

In an acute neurotoxicity study, acetamiprid induced behavioural changes and reduced locomotor activity, resulting in a NOAEL of 10 mg/kg bw. In a subchronic neurotoxicity study, no neurotoxic effect was observed and the systemic NOAEL was 14.8 mg/kg bw per day. No delayed neurotoxic potential was shown in a study with hens. For the rat developmental neurotoxicity study (already evaluated by the PPR Panel (EFSA PPR Panel, 2013b)), the experts agreed that the data do not allow any firm conclusion since important endpoints such as motor activity, learning and memory evaluation could not be properly assessed. Moreover, it could not be concluded that reduced auditory startle responses in offspring at 10 mg/kg bw were not related to treatment, resulting in a NOAEL of 2.5 mg/kg bw per day. No immunotoxic potential was demonstrated in rats and mice.

Several toxicity tests were provided for different metabolites of acetamiprid. The metabolite IM-1-5 is a relevant groundwater metabolite based on its acute oral toxicity (triggering the proposal for classification Acute Tox. 3, H301 Toxic if swallowed). The metabolites IM-2-1 (found in livestock) and IC-O (found in plants), being identified as major metabolites of acetamiprid in rats, are considered as covered by the parent.

The acceptable daily intake (ADI), the acute reference dose (ARfD), the acceptable operator exposure level (AOEL) and the acute acceptable operator exposure level (AAOEL[4]) are 0.025 mg/kg bw per day on the basis of the rat developmental neurotoxicity study (uncertainty factor (UF) 100). During the first review, the ADI and AOEL values were 0.07 mg/kg bw per day based on the 2-year and multigeneration rat studies (UF 100), and the ARfD was 0.1 mg/kg bw based on the rat acute neurotoxicity study (UF 100) (European Commission, 2004).

For the treatment of potatoes, the operator exposure estimates were below the AOEL without the use of personal protective equipment (PPE) (UK and German models). For the treatment of pome fruits, the use of PPE was not required with the German model and the agricultural operator exposure model (AOEM). For the indoor treatment of tomatoes, the use of PPE was necessary with the European Crop Protection Association (ECPA) Southern glasshouse model but not with the Dutch model. For both indoor and outdoor crops, the exposure estimates for re-entry workers are below the AOEL without use of PPE (European Predictive Operator Exposure Model (EUROPOEM) II and AOEM); and also below the AOEL for the bystanders and residents.

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 on MRL setting (European Commission, 2015) and the Joint Meeting on Pesticide Residues (JMPR) recommendations on livestock burden calculations (JMPR, 2004, 2007).

Metabolism is primary crops was investigated in the fruit, leafy, root and oilseeds/pulses crop groups, using ^{14}C-acetamiprid applied by dotting to the surface of the leaves and fruits (aubergine, apple), by spraying (cabbage, carrot, cotton) or using soil application (cabbage). In all plant parts,

[4] It is noted that the AAOEL value, agreed by the experts, has not been used for the non-dietary risk assessment.

acetamiprid was identified as the major component of the radioactive residues (total radioactive residue (TRR)) accounting for ca. 30–90% TRR 14–90 days after the last application, except in head cabbage where the 6-chloronicotinic acid metabolite (IC-0) was the sole component identified, representing 46% TRR (0.023 mg eq/kg) and in cotton seeds (24% TRR at harvest, 0.27 mg/kg). IC-0 was also detected in carrot roots (26% TRR, 0.02 mg/kg). Other identified metabolites were observed at low levels, accounting mostly for less than 5% TRR, except metabolites IM-1-4 in immature carrot leaves (43% TRR). Having regard to the low persistence of acetamiprid in soil (highest field period required for 90% dissipation (DT_{90}) 43 days and 20°C lab DT_{90} 54 days), confined rotational crop studies were not conducted with the active substance and the metabolism in rotational crops was investigated using the more persistent soil metabolite IM-1-5 (period required for 50% dissipation (DT_{50}) 319–663 days) at a single plant back interval of 0 days. In the different rotational crops investigated (wheat, turnip, spinach), IM-1-5 was shown to remain the main component of the radioactive residues accounting in mature plant at harvest for 77–94% TRR. Additional field rotational crop studies conducted in northern and southern EU with acetamiprid applied onto the bare soil at ca. 300 g/ha, confirmed that acetamiprid, IM-1-4 and IM-1-5 residues are not expected to be present in rotational crops.

Since acetamiprid was identified by far, as the major component of the residues in almost all plant matrices and since the toxicity of the IC-0 metabolite was concluded to be covered by the toxicity of the parent acetamiprid, the plant residue definitions for monitoring and risk assessment were limited to acetamiprid. These residue definitions are identical to the definitions proposed in the framework of the review of the existing maximum residue levels (MRLs) under Article 12 of Regulation (EU) No 396/2005 (EFSA, 2011b) and implemented in the EU legislation.

Sufficient residue trials were submitted to derive an MRL proposal of 0.01 mg/kg (LOQ) on potato. In contrast, no MRLs were proposed for apple and tomato and residue trials conducted according to the proposed GAP were requested (data gap). Residue data are supported by storage stability studies where acetamiprid residues were concluded to be stable up to 1 year in high water-, high oil- and high acid-content commodities and up to 8 months in high starch-content matrices (potato tuber). Acetamiprid was stable under standard hydrolysis conditions. Processing studies on apple were submitted and processing factors were derived for juice and wet pomace. Studies were not submitted on tomato. However, since the supported uses of acetamiprid are expected to result in residue levels leading to an acute consumer exposure above 10% of the ARfD, a data gap was identified for the submission of processing studies on tomato.

Metabolism studies on livestock conducted on animals dosed with ^{14}C-acetamiprid at 10 mg/kg dry matter (DM) over 7 (goat) or 17 (poultry) consecutive days were submitted. Most of the radioactivity was excreted in urine and faeces and only 2% of the administrated radioactivity was recovered in organs, tissues, blood and milk or eggs. Acetamiprid was extensively metabolised and not detected in any animal matrices except in milk. The major component was identified as the N-desmethyl metabolite (IM-2-1) representing 50–89% TRR in all animal matrices, except goat muscle (10% TRR) where residues were mainly composed of the metabolite IM-2-2 accounting for 50% TRR (0.03 mg eq/kg). The metabolic profile was confirmed by the feeding studies on cow and poultry where IM-2-1 was detected as the most abundant component in all animal matrices. Acetamiprid was not present in poultry and only detected in significant levels in milk at all feeding levels and at the highest feeding level in the other matrices. Based on these studies, the residue definition was proposed as 'IM-2-1 expressed as acetamiprid' for monitoring and as 'the sum of acetamiprid and IM-2-1, expressed as acetamiprid' for risk assessment. Conversion factors (CF) of 1.3 and 1.1 were derived for milk and other mammalian products, respectively. CF values were concluded to be unnecessary for poultry products. It is highlighted that RMS expressed its disagreement on the livestock residue definition for risk assessment and proposes to include IM-2-1 compound only. Having regard to the estimated animal dietary burden considering the representative use on potato only, MRLs were not required for animal products.

Fish studies were not provided and are not requested, as pome fruit and tomato are not listed as feed items for fish and residues were below the LOQ in potato tubers. Information on residues in pollen and bee products was not provided and is not requested for tomato since the supported use on this crop is limited to indoor use (permanent glasshouse) only, and for pome fruit as the treatment takes place after flowering. However, since potato shows attractiveness to bees for pollen collection (EFSA, 2013) residues of acetamiprid in pollen and bee products cannot be excluded and further information is requested (data gap).

The consumer risk assessment was conducted with the EFSA PRIMo rev.2 model. Since MRLs could not be derived for pome fruits and tomato, the consumer risk assessment related to the representative uses was conducted taking into account the use on potato only. No risk was identified for the

consumers; the highest chronic intake was estimated to be less than 1% of the ADI (DE, child) and the highest acute intake 6% of the ARfD (UK infant).

The decrease of the ADI and ARfD to the value of 0.025 mg/kg bw (per day) has already been recommended by the EFSA PPR Panel in 2013 (EFSA PPR Panel, 2013b) and these values have already been considered by EFSA in its previous assessments (EFSA, 2014, 2015a, 2016a). Based on the proposed ADI value of 0.025 mg/kg bw per day, a chronic intake concern has not been identified for the consumers in the preceding risk assessment (EFSA, 2016a) that included all existing uses identified during the Article 12 MRL review (EFSA, 2011b), with the highest calculated intake accounting for 20% of the ADI (DE, child). In contrast, considering the ARfD value of 0.025 mg/kg bw and the highest residue levels related to the uses evaluated under the Article 12 MRL review (EFSA, 2011b), an exceedance of the ARfD is identified for the following food commodities (% of ARfD within brackets): scarole (262%), apple (251%), spinach (233%), pear (233%), lettuce (204%), kale (197%), celery (143%), beet leaves (133%), peach (133%), purslane (115%), Chinese cabbage (108%) and head cabbage (105%). Therefore, for these food commodities, the MRLs listed in the EU legislation need to be reconsidered. It is noted that identical animal and plant residue definitions have been proposed for risk assessment during the peer review and in the framework of the Article 12 MRL review.

For enforcement of animal products, it is proposed to limit the residue definition to metabolite IM-2-1 only, while the residue definition recommended under the Article 12 MRL review and currently implemented in the EU legislation also includes acetamiprid. Since acetamiprid was extensively metabolised and never detected in poultry matrices and almost not detected in cow matrices (except milk) at median feeding level (8N level when referring to the animal burden estimated under the Article 12 MRL review), the inclusion of acetamiprid in the enforcement residue definition is concluded to be unnecessary. Moreover, animal dietary burdens estimated in previous EFSA assessments need to be recalculated, since the uses of acetamiprid on apple and kale and their contribution to the animal intakes needs to be reconsidered as ARfD exceedances have been identified for these crops. Therefore, MRLs for animal products have to be reconsidered.

4. Environmental fate and behaviour

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 acetamiprid (pyridine ring ^{14}C labelled) was investigated in a total of seven soils. An additional study (in one soil) was considered to be of limited value but was used to establish worst case estimates for the maximum value observed for metabolites IM-I-2 and 6-chloronicotinic acid (IC-0). Acetamiprid exhibited very low to moderate persistence in soil degrading to form the major (> 10% applied radioactivity (AR)) metabolites IM-1-2 (max. 55% AR), IM-1-4 (max. 72% AR), (IC-0, max. 11% AR) and IM-1-5 (max. 20% AR). In the available laboratory incubations, metabolites IM-1-2 and IC-0 exhibited low persistence, metabolite IM-1-4 exhibited low to high persistence and IM-1-5 exhibited high to very high persistence in soil. It was noted that low persistence of metabolite IM-1-4 and formation of metabolite IM-1-5 occurred only in the soils stated to be calcareous. Unextractable radioactivity (not extracted by acetone, acetone/water then methanol/ammonium acetate followed by Soxhlet with acetonitrile/water) increased up to 17–32% AR after 112–120 days and mineralisation of the pyridine ring to carbon dioxide accounted for 10–61% AR after 112–120 days. Acetamiprid degradation under anaerobic conditions was investigated in a single soil where acetamiprid exhibited high persistence forming the major metabolite IM-1-4. Photolysis on soil was investigated in a microbially active soil. Irradiation did not enhance the degradation of acetamiprid at the soil surface. Acetamiprid exhibited high mobility in soil with metabolite IM-1-2 exhibiting very high to high mobility, IM-1-4 and IC-0 exhibiting high to medium mobility and IM-1-5 exhibiting medium mobility. It was concluded that the adsorption of all these compounds was not pH dependent. In satisfactory field dissipation studies carried out at a total of eight sites (in Italy, in the UK, France (3), Spain (2) and Hungary (spray application to the soil surface on bare soil plots in late spring/early summer where grass subsequently emerged except at calcareous sites (four) where soil was maintained bare)), acetamiprid exhibited very low to moderate persistence. Sample analyses were also carried out for IM-1-2 and IM-1-4 except at one Spanish, one Hungarian and two French sites that had calcareous soils, where the analysis made was for just acetamiprid and IM-1-5. The pattern of occurrence of the metabolites IM-1-2, IM-1-4 and IM-1-5 (where measured residues in the 0–10 cm soil layer were 50–73%, < 3.9–39% and 24–60% of the maximum parent measured residue, respectively) combined with the study designs, resulted in the RMS concluding reliable kinetic values that represented

degradation or dissipation for the metabolites could not be estimated. The metabolite exposure assessments presented by the RMS in the RAR were completed using kinetic endpoints from just the laboratory incubations.

Acetamiprid was stable under the sterile conditions of aqueous hydrolysis investigations at pH 4, 5, 7 and 9 at 22–25°C. Metabolite IM-1-5 hydrolysed slowly under the sterile conditions of aqueous hydrolysis investigations at pH 4, 7 and 9 at 20°C. Aqueous photolysis was investigated for acetamiprid and metabolites IM-1-4, IC-0 and IM-1-5. Acetamiprid was photolysed slowly, yielding the major photolysis metabolite IB-1-1 (max 35% after 30 days). Metabolite IC-0 was rapidly photolysed in water, metabolite IM-1-4 is stable to photolysis and metabolite IM-1-5 was slightly photolysed. Fate and behaviour of acetamiprid in aquatic environment was investigated in two aerobic water/sediment systems. Acetamiprid only partitioned partially to the sediment (max 39.0% AR after 14 days) with the majority of the acetamiprid present remaining in the water phase. Acetamiprid was moderately persistent in both systems. Three major metabolites were found in the water phase: IM-1-2 (max. 11% AR), IM-1-4 (max. 12% AR) and IC-0 (max. 26% AR). Metabolite IM-1-4 (max. 31% AR) was also a major metabolite in the sediment. Mineralisation of the pyridine ring ^{14}C radiolabel to CO_2 accounted for 10–28.3% AR after 155 days (study end) and the unextractable residue in the sediment (extraction method as described above for soil) accounted for up to 21.12–40.65% AR at the end of the study. The necessary surface water and sediment exposure assessments (predicted environmental concentrations (PEC) calculations) were carried out for the metabolites IM-1-2, IM-1-4, IC-0, IB-1-1 and IM-1-5, using the FOCUS (FOCUS, 2001) step 2 approach (version 2.1 of the steps 1-2 in FOCUS calculator). For the active substance acetamiprid, 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 for pome fruit and 10 m for potatoes being implemented for the drainage scenarios (representing a 71–91% and 64–3% spray drift reduction, respectively), and combined no-spray buffer zones with vegetative buffer strips of up to the same distance for each crop (reducing solute flux in run-off by 80% and erosion run-off of mass adsorbed to soil by 95% for pome fruit and 60% and 85%, respectively, for potatoes) being implemented for the run-off scenarios. The SWAN tool (version 3.2) was appropriately used to implement these mitigation measures in the simulations. However, risk managers and others may wish to note that while run-off mitigation is included in the step 4 calculations available, the FOCUS (FOCUS, 2007) report acknowledges that for substances with a Freundlich organic carbon adsorption coefficient (K_{Foc}) < 2,000 mL/g (i.e. acetamiprid), the general applicability and effectiveness of run-off mitigation measures had been less clearly demonstrated in the available scientific literature, than for more strongly adsorbed compounds.

For the representative protected tomato use, the necessary surface water and sediment exposure assessments (PEC) were appropriately carried out using the FOCUS (2001) step 2 approach (version 2.1 of the steps 1-2 in FOCUS calculator), which was then modified by post processing the spray drift input results (option no run-off or drainage was selected) to obtain a 0.1% emission of acetamiprid from glasshouses being redeposited on adjacent surface water bodies. This approach has been accepted by the Member State experts as an assumption that can be used in the EU level surface water exposure assessments for glasshouse uses and is referred to in FOCUS (2008) guidance as being appropriate, except when applications are made with ultralow volume application techniques when 0.2% emission is prescribed. EFSA notes that the GAP table indicates that water volumes should be 300–1,500 L/ha for application to tomatoes, so the representative use is not for an ultralow volume application technique.

The necessary groundwater exposure assessments were appropriately carried out using FOCUS (FOCUS, 2009) scenarios and the models PEARL 4.4.4 and PELMO 4.4.3[4] for the active substance acetamiprid and its metabolites IM-1-2, IM-1-4, IC-0 and IM-1-5. The potential for groundwater exposure from the representative uses on pome fruit and potatoes by acetamiprid, IM-1-2, IM-1-4, IC-0 and IM-1-5 above the parametric drinking water limit of 0.1 μg/L was concluded to be low in geoclimatic situations that are represented by all nine FOCUS groundwater scenarios. This was also the case for the representative use on protected tomatoes for the five scenarios defined by FOCUS for outdoor tomatoes and winter cereals as a surrogate crop at the Jokionen and Kremsmunster scenarios (where tomato cropping is not defined). However, for just the metabolite IM-1-5, for the Hamburg and Okehampton scenarios, using winter cereals as a surrogate crop for tomatoes, 80th percentile annual average recharge concentrations moving below 1 m were predicted to be above the 0.1 μg/L limit with predicted concentrations being 0.106 and 0.113 μg/L, respectively. Metabolite IM-1-5 is considered a toxicologically relevant groundwater metabolite (see Section 2).

The applicant did not provide satisfactory information to address the effect of water treatments processes on the nature of the residues that might be present in surface water, when surface water is abstracted for drinking water. This has led to the identification of a data gap (see Section 7) and results in the consumer risk assessment not being finalised (see Section 9).

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 (2013a) 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, the EFSA (2013) was used for risk assessment in order to reach a conclusion for the representative uses.

Several aspects of the risk assessment of acetamiprid were discussed at the Pesticides Peer Review Meeting 147.

For the representative use on tomatoes in permanent glasshouse, a specific risk assessment to birds, mammals, bees and non-target-arthropods is not necessary (EFSA, 2015b).

The first tier risk assessment to **birds** indicated a low risk for the representative use on potatoes but a high acute risk and long-term risk to small insectivorous birds for the representative use on pome fruit was concluded. No risk refinement was available for the acute risk. However, the experts at the Pesticides Peer Review Meeting 147 considered as a line of evidence that the geometric mean lethal dose (LD_{50}) used for risk assessment was too conservative and concluded that the acute risk can be considered as low. However, when drafting the conclusion, EFSA identified a data gap for further acute risk assessment refinement, in order to ensure that more sensitive bird species are covered. The long-term risk was refined by assuming the generic focal species blue tit (*Cyanistes caeruleus*) as a specific focal species with a proportion of diet obtained in the treated area (PT) of 0.79, on the basis of the literature data. This refinement was considered by the experts at Pesticides Peer Review Meeting 147 as sufficient worst case to cover the potential uncertainties such as the limited geographical distribution of blue tit and the PT derived from data pooled over a long period. The refined long-term toxicity exposure ratio (TER) was 4.8; therefore, further risk assessment refinement should be considered as a risk could not be excluded (data gap).

At the Pesticides Peer Review Meeting 147 the experts agreed to use the long-term endpoint from the neurodevelopmental toxicity study (no observed effect level (NOEL) 2.5 mg a.s./kg bw per day) for the risk assessment to mammals. A first tier risk assessment indicated a low acute risk to **mammals**, but a high long-term risk to small herbivorous mammals for the representative uses on pome fruit and potatoes was concluded. EFSA noted that also the long-term risk to frugivorous mammals, which should be considered a relevant scenario for the use in pome fruit, was indicated as high. The refined risk assessment, based on measured residue decline, indicated still a high risk for both field representative uses. However, a field study was provided giving information that was taken into account in a weight of evidence approach to conclude a low risk to mammals from the representative use on potatoes. Therefore, a data gap was identified to further address the risk to mammals (e.g. small herbivorous and frugivorous) for the representative use on pome fruit only.

On the basis of a number of toxicity data available for aquatic organisms, aquatic insects were the most sensitive organisms. Since several standard acute toxicity data were available for insects and crustacea, the geometric mean effective concentration (EC_{50}) values were calculated. The risk assessment based on PEC_{sw} FOCUS step 2, indicated a low risk to fish, algae and aquatic plants. A risk assessment to amphibians, based on growth no observed effect concentration (NOEC), was also available and indicated a low risk. However, the risk based on the geometric mean EC_{50}, was indicated as high to aquatic insects for all the representative uses, including tomatoes in glasshouse. A mesocosm study was available to refine the risk assessment. This study was discussed at the Pesticides Peer Review Meeting 147. The endpoint selected was a NOEC of 1.1 μg a.s./L and was considered suitable only for the risk assessment for the representative use on pome fruit. Furthermore, to account for uncertainties related to species belonging to Naididae, which were observed to be

sensitive at the selected endpoint, the highest assessment factor (AF) of 3 was proposed and further data were considered necessary to address the effects on Naididae (data gap). Based on the endpoint from the mesocosm study, the risk was indicated as low for the representative use on pome fruit at FOCUS step 4, with a 20 m no-spray buffer zone and, for all the R scenarios, a 20 m vegetated buffer strip. The risk assessment for the representative use on potatoes was updated based on standard toxicity endpoints as agreed at the experts' meeting. The TERs calculated with PEC_{sw} FOCUS step 3 indicated a high risk for all the scenarios. Further refinements were not available. It is, however, noted that TERs calculated by EFSA with the PEC_{sw} FOCUS step 4 at 10 m as reported in the fate section, also indicated a high risk for all the scenarios. Therefore, for the representative use on potato a data gap was identified to further address the risk to aquatic organisms. A data gap was also identified for the representative use on tomatoes in permanent glasshouse as the refinement presented in the RAR was only based on the mesocosm endpoint that, as explained above, was deemed suitable only for pome fruit.

The risk for the pertinent metabolites is low based on TERs calculated with PEC_{sw} FOCUS step 2.

Acute toxicity (contact and oral) studies for **honeybees** and **bumble bees** (contact), performed with the representative formulation ('EXP 60707A'/'Acetamiprid 20 SG') were available. A honeybee chronic oral toxicity study and a study on larvae with the active substance were also available. An assessment of the hypopharyngeal glands (HPG) was not performed in the chronic test; therefore, a data gap was identified to further assess sublethal effects. It is noted that on the basis of literature data included in the RAR, sublethal effects at 0.1 μg/bee were observed. However, the relevance of these effects for the colony survival and development is not assessable, but likely low. Using the endpoints derived from the studies available in the dossier, a risk assessment for honeybees was performed by EFSA in accordance with EFSA (2013). A low risk to honeybees (acute, chronic and larvae) and to bumble bees (acute) was concluded for all scenarios for the representative uses on pome fruit (post-flowering application) and potatoes.

Several higher tier studies (semifield and field) were available and discussed at the Pesticides Peer Review Meeting 147. Some effects were seen on mortality, flight intensity and brood development, but a clear pattern could not be drawn. Furthermore, several concerns were raised in relation to robustness and reliability of these studies due to severe deficiencies and drawbacks identified such as short study duration, lack of exposure measurement and low number of colonies used. Their representativeness for situations other than those in the experiment was also considered questionable. It was concluded that these studies cannot be used to draw any firm conclusion on the risk to honeybees, particularly to exclude any potential chronic effect or effect on brood development. This outcome should be further considered for the assessment of uses other than the representative uses evaluated in this conclusion, as the exposure of bees through other uses of acetamiprid might be considerably higher.

Insufficient information was available to perform a first tier risk assessment to honeybees for relevant metabolites in pollen and nectar. However, most of the plant metabolites were reported in the RAR as not having an insecticidal activity and the exposure from these metabolites is expected to be very low. Therefore, the experts concluded that the risk from metabolites could be expected as low.

The risk through exposure via residues in guttation fluid could not be excluded on the basis of the screening level assessment (data gap). No specific assessment was performed for the puddle scenario. The risk for exposure via surface water on the basis of the worst case PEC_{sw} FOCUS step 3 was indicated as low.

No data were available to perform a complete risk assessment for bumble bees or solitary bees. Information was available in the RAR from public literature data indicating that bumble bees may be more sensitive than honeybees.

For the representative use on tomatoes in permanent glasshouses, the risk to the introduced pollinators should be further considered within the integrated pest management (IPM) practices.

As regards **non-target arthropods**, the standard tests with the two species *Aphidius rhopalosiphi* and *Typhlodromus pyri*, resulted in 100% mortality. Extended laboratory and aged residue study were available with these species. Aged residue studies were also available with *Chrysoperla carnea* and *Coccinella septempunctata*. The risk assessment based on median lethal rate (LR_{50}), indicated a high in-field risk for both *A. rhopalosiphi* and *T. pyri*; while the off-field risk was low for *T. pyri*. The off-field risk for *A. rhopalosiphi* was demonstrated as low for the representative use on potatoes only when risk mitigation measures comparable to a 10 m no-spray buffer zone were considered. For the representative use on pome fruits, the maximum acceptable risk mitigation measures were not sufficient to demonstrate a low off-field risk. The aged residue studies indicated a potential for

recolonisation or recovery of treated in-field areas by *T. pyri*, *A. rhopalosiphi* and other relatively less sensitive flying and multivoltine species such as *C. carnea* and *C. septempunctata*. However, these data could not be considered sufficient to demonstrate the recovery and recolonisation of in-field areas within a year and off-field areas within an ecologically relevant timeframe for more sensitive species, such as *A. rhopalosiphi*, for the representative uses in pome fruit. Therefore, a data gap has been identified to further address the risk to non-target arthropods for the representative use on pome fruit.

No standard toxicity tests were available on **earthworms** but a field study was provided indicating no adverse effect (> 50%) on earthworm population (i.e. abundance and biomass) when acetamiprid is applied up to 80 g a.s./ha. The experts at the Pesticides Peer Review Meeting 147 expressed concerns regarding the representativeness of this study for areas other than the experimental sites. However, it was noted that the exposure in the study covered the maximum PECs estimated for the representative uses on potatoes and pome fruit. Therefore, the risk to earthworms for these uses could be considered as low. Considering the low soil persistence of acetamiprid, the risk to earthworms for the representative use in tomatoes in permanent glasshouse was deemed as low. The risk to other soil macroorganisms for all the representative uses and the risk to the pertinent soil metabolites were considered as low.

The risk was concluded as low for **terrestrial non-target plants**, **soil microorganisms** and organisms of biological methods for **sewage treatment plants**.

Regarding the endocrine disruptor potential, as reported in Section 2, it is unlikely that acetamiprid is an endocrine disruptor in mammals; however, no firm conclusion can be draw for birds and fish.

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
Acetamiprid	Very low to moderate persistence Single first-order and biphasic kinetics DT_{50} 0.8–7.9 days (DT_{90} 2.8–54.5 days, 20°C pF 2.5% or 45% MWHC soil moisture) European field dissipation studies single first-order and biphasic kinetics DT_{50} 0.4–13 days (DT_{90} 7.4–43.1 days)	Low risk for soil living organisms
IM-1-2	Low persistence Single first-order kinetics DT_{50} 1.6–1.9 days (20°C 45% MWHC soil moisture)	Low risk for soil living organisms
IM-1-4	Low to high persistence Single first-order kinetics DT_{50} 2.3–146 days (20°C 45% MWHC soil moisture)	Low risk for soil living organisms
6-chloronicotinic acid (IC-0)	Low persistence Single first-order kinetics DT_{50} 1.2–5.6 days (20°C 45% MWHC soil moisture)	Low risk for soil living organisms
IM-1-5	High to very high persistence Single first-order kinetics DT_{50} 319–663 days (20°C pF 2 or 45% MWHC soil moisture)	Low risk for soil living 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
Acetamiprid	High mobility K_{Foc} = 71–138 mL/g	No	Yes	Yes
IM-1-2	Very high to high mobility K_{Foc} = 19–95 mL/g	No	Information not available assessment not triggered	Yes based on the proposed classification Acute Tox 3 and Carc cat 2 for acetamiprid
IM-1-4	High to medium mobility K_{Foc} = 132–488 mL/g	No	Information not available assessment not triggered	Yes based on the proposed classification Acute Tox 3 and Carc cat 2 for acetamiprid
6-chloronicotinic acid (IC-0)	High to medium mobility I_{Foc} = 70–258 mL/g	No	Information not available assessment not triggered	Yes based on the proposed classification Acute Tox 3 and Carc cat 2 for acetamiprid
IM-1-5	Medium mobility K_{Foc} = 173–429 mL/g	No for scenarios defined by FOCUS for apples potatoes and outdoor tomatoes Yes using winter cereals as a surrogate scenario at the Hamburg (0.106 µg/L) and Okehampton (0.113 µg/L) outdoor scenario definitions where tomatoes were not defined but where protected cropping of tomatoes can occur	Information not available, not required when IM-1-5 is considered toxicologically relevant as a groundwater metabolite, based on the toxicity to mammals resulting from the classification proposals	Yes based on the proposed classification Acute Tox 3 for IM-1-5; and on the proposed classification Carc cat 2 for acetamiprid

K_{Foc}: Freundlich organic carbon adsorption coefficient; FOCUS: Forum for the Co-ordination of Pesticide Fate Models and their Use.
(a): At least one FOCUS scenario or relevant lysimeter.

Table 3: Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Acetamiprid	Low risk for the use on pome fruit taking into account risk mitigation measures; high risk for the use on potatoes and glasshouse tomatoes
IM-1-2	Low risk
IM-1-4	Low risk
6-Chloronicotinic acid (IC-0)	Low risk
IM-1-5	Low risk
IB-1-1	Low risk

Table 4: Air

Compound (name and/or code)	Toxicology
Acetamiprid	Low acute toxicity by inhalation (rat LC_{50} > 1.15 mg/L air per 4 h)

LC_{50}: lethal concentration, median.

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 search of the scientific peer-reviewed open literature was provided and it was conducted 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, 2011a). However, the reliability criteria for inclusion and exclusion of the retrieved ecotoxicology papers were not transparently reported, making the complete analysis of the search not reproducible and a data gap was identified (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown).
- Comparative *in vitro* metabolism data between animal species used in pivotal studies and human material (microsomes or intact cell systems) in order to determine the relevance of the toxicological animal data, and to identify potentially unique human metabolites (relevant for all representative uses evaluated; not supported by the RMS; submission date proposed by the applicant: unknown; see Section 2).
- Residue trials on pome fruits conducted according to the supported GAP are requested (relevant for the representative use on pome fruits; submission date proposed by the applicant: unknown; see Section 3).
- Residue trials on tomato conducted under indoor conditions according to the supported GAP are requested (relevant for the representative use on tomato; submission date proposed by the applicant: unknown; see Section 3).
- Since the supported use of acetamiprid on tomato is expected to result in residues leading to an acute consumer exposure above 10% of the ARfD, processing studies on tomato are requested (relevant for the representative use on tomato; submission date proposed by the applicant: unknown; see Section 3).
- Residue data in pollen and bee products are requested (relevant for the representative use on potato; submission date proposed by the applicant: unknown; see Section 3).
- The effect of water treatment processes on the nature of residues present in surface, when surface water is abstracted for drinking water (Article 4 (approval criteria for active substances) 3(b) of Regulation (EC) No 1107/2009) has not been assessed. In the first instance, a consideration of the processes of ozonation and chlorination may be considered appropriate. If an argumentation is made that concentrations at the point of abstraction for drinking water purposes will be low, this argumentation should cover metabolites predicted to be in surface water, as well as the active substance (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 4).
- The acute and long-term risk to small insectivorous birds should be further addressed (relevant for the representative use on pome fruits; submission date proposed by the applicant: unknown; see Section 5).
- The long-term risk to mammals (e.g. small herbivorous and frugivorous) should be further addressed (relevant for the representative use on pome fruit; submission date proposed by the applicant: unknown; see Section 5).
- Data on the effects on the aquatic organisms Naididae should be provided (relevant for the representative use on pome fruit; submission date proposed by the applicant: unknown; see Section 5).
- The risk to aquatic organisms should be further considered (relevant for representative uses on potatoes and tomatoes; submission date proposed by the applicant: unknown; see Section 5).
- Data on sublethal effects on bees (i.e. HPG) should be provided (relevant for representative on pome fruit and potatoes; submission date proposed by the applicant: unknown; see Section 5).
- The risk to honeybees via exposure to residue in guttation fluids should be further considered (relevant for representative on pome fruit and potatoes; submission date proposed by the applicant: unknown; see Section 5).
- The risk to non-target arthropods should be further addressed (relevant for representative use on pome fruits; 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

- Mitigation measures comparable to 20 m no-spray buffer zone and 20 m vegetated strip were needed to achieve a low risk to aquatic organisms for the use in pome fruit (see Section 5).
- Mitigation measures comparable to 10 m no-spray buffer zone were needed to achieve a low risk to non-target arthropods for the use in potatoes (see Section 5).

9. Concerns

9.1. 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[5] 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 could not be finalised for the representative uses on pome fruits and tomatoes as data gaps have been identified for residue trials conducted according to the supported GAPs (see Section 3).
2) The consumer risk assessment from the consumption of water could not be finalised, while satisfactory information was not available to address the effect of water treatment processes on the nature of the residues that might be present in surface water, when surface water is abstracted for drinking water (see Section 4).

9.2. 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 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 the 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.

No critical areas of concern have been identified for the representative uses assessed.

9.3. 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.)

[5] 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.

Table 5: Overview of concerns

Representative use		Pome fruit	Potato	Tomato (permanent glasshouse)
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	X[1,2]	X[2]	X[1,2]
Risk to wild non-target terrestrial vertebrates	Risk identified	X		
	Assessment not finalised			
Risk to wild non-target terrestrial organisms other than vertebrates	Risk identified	X		
	Assessment not finalised			
Risk to aquatic organisms	Risk identified		X	X
	Assessment not finalised			
Groundwater exposure to active substance	Legal parametric value breached			
	Assessment not finalised			
Groundwater exposure to metabolites	Legal parametric value breached[(a)]			2/9 FOCUS surrogate scenarios
	Parametric value of 10 µg/L[(b)] breached			
	Assessment not finalised			

FOCUS: Forum for the Co-ordination of Pesticide Fate Models and their Use.
Columns are grey if no safe use can be identified. The superscript numbers relate to the numbered points indicated in Sections 9.1 and 9.2. Where there is no superscript number, see Sections 2–6 for further information.
(a): When the consideration for classification made in the context of this evaluation under Regulation (EC) No 1107/2009 is confirmed under Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008.
(b): Value for non-relevant metabolites prescribed in SANCO/221/2000-rev. 10 final, European Commission (2003).

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Abbreviations

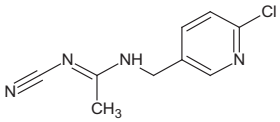
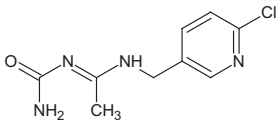
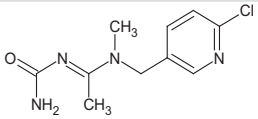
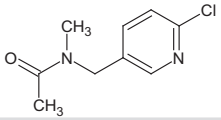
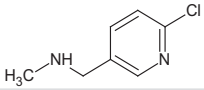
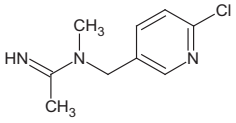
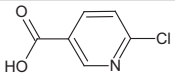
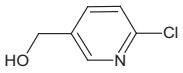
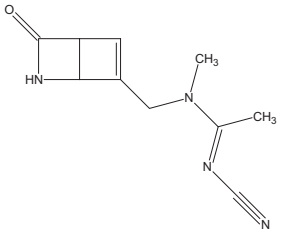
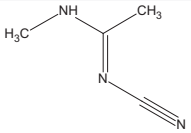
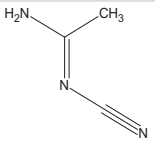
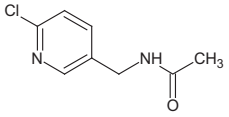
a.s.	active substance
AAOEL	acute acceptable operator exposure level
ADI	acceptable daily intake
AF	assessment factor
AOEL	acceptable operator exposure level
AOEM	agricultural operator exposure model
AR	applied radioactivity
ARfD	acute reference dose
bw	body weight
CF	conversion factor
DM	dry matter
DT_{50}	period required for 50% dissipation (define method of estimation)
DT_{90}	period required for 90% dissipation (define method of estimation)
EC_{50}	effective concentration
ECPA	European Crop Protection Association
EEC	European Economic Community
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
HPLC–MS	high-pressure liquid chromatography–mass spectrometry
HPLC–MS/MS	high-performance liquid chromatography with tandem mass spectrometry
HPLC-UV	high-performance liquid chromatography with ultraviolet detector
HPG	hypopharyngeal glands
IPM	integrated pest management
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_{Foc}	Freundlich organic carbon adsorption coefficient
LC_{50}	lethal concentration, median
LD_{50}	lethal dose, median; dosis letalis media
LR_{50}	lethal rate, median
LOQ	limit of quantification
MRL	maximum residue level
MWHC	maximum water-holding capacity
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration

NOEL	no observed effect level
OECD	Organisation for Economic Co-operation and Development
PEC	predicted environmental concentration
PEC_{air}	predicted environmental concentration in air
PEC_{gw}	predicted environmental concentration in groundwater
PEC_{sed}	predicted environmental concentration in sediment
PEC_{soil}	predicted environmental concentration in soil
PEC_{sw}	predicted environmental concentration in surface water
PPE	personal protective equipment
PT	proportion of diet obtained in the treated area
QuEChERS	quick, easy, cheap, effective and safe method
RAR	renewal assessment report
RMS	rapporteur Member State
SG	water-soluble granule
SFO	single first-order
SMILES	simplified molecular-input line-entry system
TRR	total radioactive residue
UDS	unscheduled DNA synthesis
UF	uncertainty factor
UV	ultraviolet
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): http://dx.doi.org/10.2903/j.efsa.2016.4610

Appendix B – Used compound codes

Code/trivial name[(a)]	Chemical name/SMILES notation	Structural formula
***N*-Desmethyl-acetamiprid** **IM-2-1**	(*E*)-*N*-[(6-Chloro-3-pyridyl)methyl]-*N′*-cyanoacetamidine Clc1ccc(CNC(\C)=N\C#N)cn1	
IM-2-2	(*E*)-*N′*-Carbamoyl-*N*-[(6-chloro-3-pyridyl)methyl] acetamidine Clc1ccc(CNC(\C)=N\C(N)=O)cn1	
IM-1-2	(*E*)-*N′*-Carbamoyl-*N*-[(6-chloro-3-pyridyl)methyl]-*N*-methylacetamidine Clc1ccc(CN(C)C(\C)=N\C(N)=O)cn1	
IM-1-3	*N*-[(6-Chloro-3-pyridyl)methyl]-*N*-methylacetamide Clc1ccc(CN(C)C(C)=O)cn1	
IM-1-4	1-(6-Chloro-3-pyridyl)-*N*-methylmethanamine Clc1ccc(CNC)cn1	
IM-1-5	*N*-[(6-Chloro-3-pyridyl)methyl]-*N*-methylacetamidine Clc1ccc(CN(C)C(C)=N)cn1	
6-Chloronicotinic acid (IC-0) (IV-0)	6-Chloronicotinic acid OC(=O)c1cnc(Cl)cc1	
IM-I-0 (IM-0)	(6-Chloro-3-pyridyl)methanol OCc1cnc(Cl)cc1	
IB-1-1	(*E*)-*N′*-Cyano-*N*-[(3-oxo-2-azabicyclo[2.2.0]hex-5-en-6-yl)methyl]-*N*- methylacetamidine O=C1NC2C(CN(C)C(\C)=N\C#N)=CC12	
IS-1-1	(1*E*)-*N′*-Cyano-*N*-methylethanimidamide C/C(=N\C#N)NC	
IS-2-1	*N*-Cyanoethanimidamide C/C(N)=N\C#N	
IM-2-3	*N*-[(6-Chloropyridin-3-yl)methyl]acetamide Clc1ccc(CNC(C)=O)cn1	

SMILES: simplified molecular-input line-entry system.
(a): The compound name in bold is the name used in the conclusion.