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Pesticide risk assessment for the active substance pymetrozine in light of negligible exposure data submitted

European Food Safety Authority (EFSA)

Abstract

EFSA was requested to provide a scientific assessment of additional information submitted to demonstrate whether the active substance pymetrozine can be used such that exposure to humans may be considered negligible. The context of the assessment was that requested by the European Commission following the submission of negligible exposure data. EFSA prepared a statement where the assessment of the information is presented according to the draft technical guidance on assessment of negligible exposure of an active substance in a plant protection product under realistic conditions of use. The outcome was reached on the basis of the evaluation of the representative uses of pymetrozine as an insecticide on potato and oilseed rape as proposed by the applicant to be considered for negligible exposure.

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Summary

Pymetrozine is listed in Annex I of Commission Regulation (EU) No 1141/2010 as amended by Commission Implementing Regulation (EU) No 380/2013. As part of the preceding peer review for renewal of approval of pymetrozine, the European Food Safety Authority (EFSA) proposed in its conclusion to classify pymetrozine as toxic for reproduction category 2 in addition to the harmonised classification as carcinogen category 2. These two classifications trigger the lack of compliance with the approval criteria set out in Annex II of Regulation (EU) No 1107/2009 (in specific with point 3.6.5 of Annex II, as it meets the criteria established in the third paragraph concerning endocrine disrupting properties). By means of a mandate received on 20 September 2016, EFSA was requested to carry out an assessment of the information submitted by the applicant to demonstrate whether the active substance pymetrozine can be used such that exposure to humans may be considered negligible by 15 December 2016.

The applicant, Syngenta Crop Protection AG submitted information to demonstrate negligible exposure in May 2016. EFSA distributed the applicant's submission to the Member States for comments on 22 September 2016 and provided comments as well. EFSA collated all comments and provided its scientific view on the comments received. A final consultation on the conclusions arising from the peer review took place with the Member States via a written procedure in November 2016.

Regarding the dietary exposure assessment, it was argued that based on the available data and information concerning the requested uses in potato and oilseed rape individual residues of pymetrozine and its metabolites in consumable crop parts are unlikely to exceed 0.01 mg/kg though residue trials on the full residue definition for risk assessment are not available. In the absence of toxicological data on the pertinent plant metabolites, it remains unclear whether these residue levels will fully meet the draft technical guidance definition of 'negligible' (draft technical guidance on negligible exposure of an active substance in a plant protection product under realistic conditions of use (European Commission, 2015)), i.e. 'a level so small that it does not appreciably add to the risk and can safely be ignored', given a risk assessment requires not only exposure but also hazard considerations. The potential for groundwater exposure above the parametric drinking water limit by the relevant metabolite CGA371075 in all the pertinent groundwater scenarios for all four representative uses assessed has been identified as a critical area of concern (EFSA 2014b). Again, the residue level cannot be safely ignored as 'negligible' in view of the draft technical guidance.

Regarding the non-dietary exposure assessment, the operator exposure estimates were up to 11.15% of the acute acceptable operator exposure level (AAOEL) without risk mitigation measures in potatoes, and down to 0.07% of the acceptable operator exposure level (AOEL) with risk mitigation measures in oilseed rape. The estimates for workers were up to 2.33% of the AOEL. The estimates for bystanders and residents were up to 7.42% of the AOEL in residential children. All the exposure estimates showed a margin of exposure higher than 2,000 except for the acute exposure of operators (892 without risk mitigation measures and 1,613 with use of gloves when handling granules).

The draft technical guidance on assessment of negligible exposure of an active substance in a plant protection product under realistic conditions of use (European Commission, 2015) does not give any guidance for consideration of negligible exposure for the environment. Also, indirect dietary exposure of humans due to environmental releases and processes (e.g. drinking water or eating wildlife that can be exposed, such as rabbit and fish) is not covered by the draft guidance. Therefore, the assessment of potential negligible exposure of humans via the environment, and to non-target organisms is not assessed in this conclusion.

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1. Introduction

1.1. Background

Pymetrozine is listed in Annex I of Commission Regulation (EU) No 1141/2010¹ as amended by Commission Implementing Regulation (EU) No 380/2013². In accordance with Article 16 of the Regulation, the European Food Safety Authority (EFSA) finalised a conclusion on the peer review of the pesticide risk assessment of the active substance pymetrozine on 22 August 2014 (EFSA, 2014b) and provided its conclusion to the European Commission.

Annex II of Regulation (EU) No 1107/2009³ provides in its points 3.6.3, 3.6.4 and 3.6.5 that active substances classified on the basis of Regulation (EC) No 1272/2008⁴ as carcinogen category 1A or 1B or toxic for reproduction category 1A or 1B, or having endocrine disrupting properties which may cause adverse effects on humans cannot be approved unless the exposure of humans to that active substance in a plant protection product, under realistic proposed conditions of use, is negligible. These conditions under which negligible exposure is assumed is precondition for approval of substances in accordance with Article 4 of the Regulation (EU) No 1107/2009 read in combination with these points.

The European Commission shall propose a decision on renewal/non-renewal of approval for active substances considered under Regulation (EU) No 1107/2009 taking into account the approval criteria of Annex II, points 3.6.3, 3.6.4 and 3.6.5 of that Regulation. As part of the preceding peer review for renewal of approval of pymetrozine, EFSA proposed classification of pymetrozine as toxic for reproduction category 2⁵ in addition to the harmonised classification of pymetrozine as carcinogen category 2. Considering these two classifications and the fact that pymetrozine produced adverse effects on the endocrine organs across different species and timelines, a critical area of concern was identified with regard to Annex II, Point 3.6.5 of Regulation (EC) No 1107/2009 interim provisions for active substances that shall be considered to have endocrine disrupting properties. The proposed classification triggers the lack of compliance with the approval criteria set out in Annex II of Regulation (EU) No 1107/2009 (in specific with point 3.6.5 of Annex II) but this was not known by the applicant at the time of the dossier submission. As a consequence, the applicant did not submit information in its dossier to demonstrate that exposure of humans to the substance, under realistic conditions of use, can be considered negligible. Therefore, in order to inform the decision-making process, the European Commission invited the applicant Syngenta Crop Protection AG to provide further information to demonstrate that the exposure of humans to pymetrozine is negligible under realistic conditions of use. The European Commission then requested the rapporteur Member State (RMS), Germany, to carry out an evaluation of this information and to submit its assessment in the format of an addendum to EFSA for peer review. However, the RMS informed the European Commission that they would not carry out such an assessment as they consider that there is currently no agreed guidance available to determine endocrine disrupting properties of the active substance nor to consider if the exposure of humans to the active substance in a plant protection product, under realistic conditions of use, is negligible.

By means of a general mandate received on 13 January 2016, the European Commission requested EFSA to conduct a peer review and provide its conclusions on particular active substances, to be communicated on an ad-hoc basis, on whether exposure of humans to an active substance, under realistic conditions of use, can be considered negligible, taking into account the draft 'Technical guidance on points 3.6.3 to 3.6.5 of Annex II to Regulation (EC) No 1107/2009, in particular regarding the demonstration of negligible exposure to an active substance in a plant protection product under realistic conditions of use'. With a clarification to the general mandate received on 17 May 2016, the European Commission clarified that taking into account the absence of a final guidance document and ongoing

¹ Commission Regulation (EU) No 1141/2010 of 7 December 2010 laying down the procedure for the renewal of the inclusion of a second group of active substances in Annex I to Council Directive 91/414/EEC and establishing the list of those substances. OJ L 322, 8.12.2011, p. 10–19.

² Commission Implementing Regulation (EU) No 380/2013 of 25 April 2013 amending Regulation (EU) No 1141/2010 as regards the submission of the supplementary complete dossier to the Authority, the other Member States and the Commission. OJ L 116, 26.4.2013, p. 4.

³ 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.

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

discussions in the Standing Committee on Plants, Animals, Food and Feed (PAFF Committee), the draft guidance document made available for stakeholder consultation and published on Commissions' website on 25 June 2015 should be considered (draft dated May 2015; SANCO/2014/12096 (European Commission, 2015)). In the absence of agreed threshold values for assessing negligible exposure, a conclusion regarding such agreed threshold is not possible. However, in order to provide risk managers with the relevant information for decision-making, EFSA was requested to (a) calculate the actual expected exposure values in absolute values and percentage of the established toxicological reference values (e.g. acceptable operator exposure level (AOEL)); (b) consider potential technical mitigation measures to reduce exposure as those mentioned in the draft guidance, that have been proposed by the applicant and/or by the RMS, or by EFSA, if and when appropriate.

By means of a mandate received on 20 September 2016, EFSA was requested to carry out an assessment of the information submitted by the applicant to demonstrate whether the active substance pymetrozine can be used such that exposure to humans may be considered negligible. EFSA was requested to provide this assessment by 15 December 2016.

The applicant, Syngenta Crop Protection AG, submitted an assessment on negligible exposure for the representative uses on potato and oilseed rape in May 2016. EFSA distributed the applicant's submission to the Member States for comments on 22 September 2016 and provided comments as well. EFSA collated all comments and provided its scientific view on the comments received.

A final consultation on the conclusions arising from the peer review of the applicant's submission took place with the Member States via a written procedure in November 2016.

The conclusions laid down in this report were reached on the basis of the risk managers' decisions proposed in the draft European Commission technical guidance and the peer review of the negligible exposure data submitted by the applicant. A key supporting document to this statement is the peer review report, which is a compilation of the documentation developed to evaluate and address all issues raised in the peer review, from the compilation of comments to the statement. The peer review report (EFSA, 2016) comprises the following documents:

- the compiled comments received on the applicant's assessment;
- the comments received on the draft EFSA statement.

Given the importance of the applicant's submission and the peer review report, these documents are considered as background documents to this statement.

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

1.2. The active substance and its use pattern

Pymetrozine is the ISO common name for 6-methyl-4-{{(E)-pyridin-3-ylmethylidene}amino}-4,5-dihydro-1,2,4-triazin-3(2H)-one (IUPAC).

The representative formulated product for the evaluation was 'A9364J', a water-dispersible granule (WG) containing 500 g/kg pymetrozine.

The representative uses evaluated in the peer review for renewal of approval of pymetrozine comprised applications by foliar spraying to control whiteflies, aphids and *Meligethes* spp. in ware potato, oilseed rape, field and greenhouse tomato and aubergine. The full details of the good agricultural practice (GAP) and a list of all relevant end points can be found in Appendix A of the previous EFSA conclusion (EFSA, 2014b).

In the applicant submission for the negligible exposure assessment, the applicant has proposed only potato and oilseed rape to be considered for negligible exposure. The applicant has also proposed application every third year as GAP for oilseed rape. The details of the GAP submitted by the applicant to be considered for the negligible exposure assessment are presented in the Appendix A of this statement.

2. Assessment

The applicant has submitted to the European Commission information to demonstrate that the exposure of humans to pymetrozine can be considered negligible under the proposed conditions of use. The applicant's assessment was subject to a peer review in September–October 2016.

EFSA prepared a statement where the assessment of the information is presented according to the draft technical guidance on assessment of negligible exposure of an active substance in a plant

protection product under realistic conditions of use (points 3.6.3–3.6.5, and 3.8.2 of Annex II of Regulation (EC) No 1107/2009) (European Commission, 2015) and the EFSA guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products (EFSA, 2014a).

2.1. Negligible exposure to humans

2.1.1. Dietary exposure

The negligible exposure estimates have only been assessed for the representative uses in oilseed rape and potatoes as supported by the applicant (Appendix A to this statement). Not other uses previously supported for the EFSA conclusion (EFSA, 2014b) were considered. The residue field data for potato and oilseed were not analysed for the full residue definition for dietary risk assessment proposed as outcome of the peer review of pymetrozine. Given the evidence from the metabolism data and the available field trials, it is expected that for pymetrozine and for the majority of its metabolites individual residues > 0.01 mg/kg are unlikely to occur in these crops or in relevant rotational crops. However, as for the interpretation of the terminology 'negligible', the draft technical guidance (European Commission, 2015) further refers for risk assessment purposes to 'a level so small that it does not appreciably add to the risk and can safely be ignored'. The levels of residues have always to be seen in context with the toxicological/hazardous properties of these residues to appropriately evaluate their relevance for dietary safety. It is noted that in the conclusion on the peer review (EFSA, 2014b), a data gap was set for an assessment of the toxicological profile of several plant metabolites and therefore a scientific assessment of the extent of risk related to dietary exposure to these metabolites is currently not possible.

The potential for groundwater exposure above the parametric drinking water limit of 0.1 µg/L has been identified as a critical area of concern (EFSA, 2014b) for the relevant metabolite CGA371075 in all the pertinent groundwater scenarios for all four representative uses assessed. The metabolite was assessed as relevant from the toxicological point of view according to the guidance document on the assessment of the relevance of metabolites in groundwater (European Commission, 2003), consequent to the harmonised classification of pymetrozine as carcinogen category 2. EFSA peer review of pymetrozine also proposed classification of the active substance as reproductive toxicant category 2 (see Sections 2 and 4 in EFSA 2014b). Therefore, the exposure of groundwater to this metabolite is not expected to meet the approval criteria provided for in Article 4 of Regulation (EC) No 1107/2009, and consequently, it cannot be considered negligible from the point of view of the draft technical guidance (European Commission, 2015). Since in this case, the trigger for groundwater exposure is exceeded by the relevant metabolite CGA371075 in all the pertinent scenarios, the residue level cannot be safely ignored in view of the interpretation of the term 'negligible' in the draft technical guidance (European Commission, 2015) as to 'a level so small that it does not appreciably add to the risk and can safely be ignored'. It is noted that in the applicant submission for the negligible exposure assessment, the applicant has proposed application every third year as GAP for oilseed rape. EFSA does not agree that rotation every third year of oilseed rape is a forced rotation by agronomic reasons. However, it could eventually be proposed as a restriction to manage the risk of contamination of groundwater by CGA371075. In such a case, calculations provided by the RMS in the renewal assessment report (RAR), show that the level of 0.1 µg/L will be still exceeded in three of the six scenarios when applied to winter oilseed rape. The draft technical guidance (European Commission, 2015) does not provide criteria on how many scenarios (if any) the limit of 0.1 µg/L can be exceeded by a substance or relevant metabolite in a representative use to be still considered for negligible exposure.

2.1.2. Non-dietary exposure

The AOEL for pymetrozine is 0.03 mg/kg body weight (bw) per day on the basis of the 90-day and 1-year dog studies, applying an uncertainty factor of 100 (EFSA, 2014b). The acute acceptable operator exposure level (AAOEL) was not discussed during the peer review but the applicant's proposal to use the acute reference dose (ARfD) of 0.1 mg/kg bw can be agreed upon, on the basis of the rabbit developmental toxicity study, supported by the 28-day rat study and applying an uncertainty factor of 100. The dermal absorption values for Plenum 50WG (A9364J) are 0.05% for the concentrate, 2% for the 1/500 dilution and 5% for the 1/2000 dilution. The reference values for pymetrozine are presented in Table 1.

Table 1: Reference values for pymetrozine

	Value (mg/kg bw per day)	Study	Uncertainty factor
ADI ^(a)	0.03	Overall 90-day and 1-year, dog	100
ARfD ^(a)	0.1	Developmental toxicity, rabbit and 28-day gavage, rat	100
AOEL ^(a)	0.03	Overall 90-day and 1-year, dog	100
AAOEL ^(a)	0.1	Developmental toxicity, rabbit and 28-day gavage, rat	100

bw: body weight.

(a): ADI: acceptable daily intake; ARfD: acute reference dose; AOEL: acceptable operator exposure level (short- to long-term exposure); AAOEL: acute AOEL (acute exposure), reference value used with the EFSA calculator for acute exposure.

It is noted that the negligible exposure estimates have only been assessed for the representative uses in oilseed rape and potatoes (as supported by the applicant and presented in Appendix A), and not for other uses previously supported for the EFSA conclusion (EFSA, 2014b).

First tier assessment:

With the EFSA calculator (EFSA, 2014a), exposure estimates have been provided for operators, workers, residents and bystanders, for the representative uses of pymetrozine on oilseed rape and potatoes. The resident exposure assessment also covers longer term exposure for the bystander, and the acute exposure assessment for the bystander also covers acute exposure scenarios for the resident. The results are presented in Tables 2, 3 and 4, including possible risk mitigation measures. As a conservative approach, the bystander exposure assessment has taken into account all possible exposure pathways (including spray drift, vapour, surface deposits and entry into treated crops).

Second tier assessment:

Considerations are also given to the margin of exposure (MoE) between non-dietary exposure and the no observed adverse effect levels (NOAELs) for the critical effects triggering the proposed classifications as carcinogen category 2⁵ (NOAEL 11 mg/kg bw per day in the mouse long-term study) and toxic for reproduction category 2 (NOAEL 10 mg/kg bw per day in the rabbit developmental study). These results are also included in the Tables 2, 3 and 4.

Table 2: Non-dietary exposure scenarios and margin of exposure (MoE) – Operators

EFSA Model	Risk mitigation measures	% AOEL or AAOEL ^(a)	MoE ^(c) Repr	MoE ^(c) Carc
Operator – Use in oilseed rape (75 g a.s./ha, 200 L/ha)				
Short- to long-term exposure	Work wear – arms, body and legs covered	4.90	6,667	7,333
	Work wear – arms, body and legs covered + gloves when handling granules	3.85	8,333	9,166
	Water-soluble bag + full PPE/RPE ^(b) (gloves, work wear and FFP2/P2)	0.07	476,190	523,810
Acute exposure	Work wear – arms, body and legs covered	9.85	1,020	1,122
	Work wear – arms, body and legs covered + gloves when handling granules	5.80	1,724	1,897
	Water-soluble bag + full PPE/RPE (gloves, work wear and FFP2/P2)	0.11	90,909	100,000
Operator – Use in potatoes (100 g a.s./ha, 200 L/ha)				
Short- to long-term exposure	Work wear – arms, body and legs covered	5.75	5,882	6,470
	Work wear – arms, body and legs covered + gloves when handling granules	4.37	7,692	8,462
	Water-soluble bag + full PPE/RPE ^(b) (gloves, work wear and FFP2/P2)	0.08	413,223	454,545

EFSA Model	Risk mitigation measures	% AOEL or AAOEL ^(a)	MoE ^(c) Repr	MoE ^(c) Carc
Acute exposure	Work wear – arms, body and legs covered	11.15	892	982
	Work wear - arms, body and legs covered + gloves when handling granules	6.15	1,613	1,774
	Water-soluble bag + full PPE/RPE ^(b) (gloves, work wear and FFP2/P2)	0.12	90,090	99,099

a.s.: active substance.

(a): AOEL: acceptable operator exposure level (short- to long-term exposure); AAOEL: acute AOEL (acute exposure), reference value used with the EFSA calculator for acute exposure.

(b): PPE: personal protective equipment; RPE: respiratory protective equipment.

(c): MoE: margin of exposure for carcinogenicity or reproductive toxicity (exposure vs NOAEL for critical effect).

Table 3: Non-dietary exposure scenarios and margin of exposure (MoE) – Workers

EFSA Model	Risk mitigation measures	% AOEL ^(a)	MoE ^(a) Repr	MoE ^(a) Carc
Worker – Use in oilseed rape (75 g a.s./ha, 200 L/ha)				
Short- to long-term exposure	Working clothing	1.75	20,000	22,000
Worker-Use in potatoes (100 g a.i./ha, 200 L/ha)				
Short- to long-term exposure	Working clothing	2.33	14,285	15,714

a.s.: active substance; a.i.: active ingredient.

(a): AOEL: acceptable operator exposure level (short- to long-term exposure); MoE: margin of exposure for carcinogenicity or reproductive toxicity (exposure vs NOAEL for critical effect).

Table 4: Non-dietary exposure scenarios and margin of exposure (MoE) – Residents/bystanders

EFSA Model	Risk mitigation measures	% AOEL ^(a)	% AAOEL ^(a)	MoE ^(a) Repr	MoE ^(a) Carc
Resident/Bystander – Use in oilseed rape (75 g a.s./ha, 200 L/ha)					
Resident – child	Buffer zone 2–3 m	6.76	–	5,000	5,500
Resident – adult		2.02	–	16,667	18,333
Resident – child	Drift reduction nozzles 50% + buffer zone 10 m	5.62	–	5,882	6,471
Resident – adult		1.77	–	20,000	22,000
Bystander – child	Buffer zone 2–3 m	–	3.6	2,778	3,056
Bystander – adult		–	1.08	9,090	10,000
Bystander – child	Drift reduction nozzles 50% + buffer zone 10 m	–	2.16	4,762	5,238
Bystander – adult		–	0.67	14,286	15,714
Residents/Bystanders – Use in potatoes (100 g a.s./ha, 200 L/ha)					
Resident – child	Buffer zone 2–3 m	7.42	–	4,545	5,000
Resident – adult		2.35	–	14,285	15,714
Resident – child	Drift reduction nozzles 50% + increased buffer zone 10 m	6.20	–	5,263	5,789
Resident – adult		2.09	–	16,667	18,333
Bystander – child	Buffer zone 2–3 m	–	3.91	2,564	2,820
Bystander – adult		–	1.22	8,333	9,166
Bystander – child	Drift reduction nozzles 50% + increased buffer zone 10 m	–	2.38	4,348	4,783
Bystander – adult		–	0.79	12,500	13,750

a.s.: active substance.

(a): AOEL: acceptable operator exposure level (short- to long-term exposure); AAOEL: acute AOEL (acute exposure), reference value used with the EFSA calculator for acute exposure; MoE: margin of exposure for carcinogenicity or reproductive toxicity (exposure vs NOAEL for critical effect).

2.2. Negligible exposure to non-target organisms

The draft technical guidance on assessment of negligible exposure of an active substance in a plant protection product under realistic conditions of use (European Commission, 2015) does not give any guidance for consideration of negligible exposure for non-target organisms. Therefore, the assessment of potential negligible exposure to non-target organisms is not assessed in this conclusion. Nevertheless, EFSA notes that data gaps were identified in EFSA (2014b) for endpoints to assess risk

for aquatic organisms other than aquatic invertebrates, and that with these outstanding data gaps it would not be possible to assess which level can be considered to be a level so small that it does not appreciably add to the risk and can thus be safely ignored ('negligible' according to the draft technical guidance on assessment of negligible exposure of an active substance in a plant protection product under realistic conditions of use (European Commission, 2015).

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Abbreviations

a.s.	active substance
AAOEL	acute acceptable operator exposure level
ADI	acceptable daily intake
AOEL	acceptable operator exposure level
ARfD	acute reference dose
bw	body weight
CIPAC	Collaborative International Pesticides Analytical Council Limited
ECHA	European Chemicals Agency
EUROPOEM	European Predictive Operator Exposure Model
GAP	Good Agricultural Practice
MoE	margin of exposure
NOAEL	no observed adverse effect level
PAFF	Standing Committee on Plants, Animals, Food and Feed
PHI	preharvest interval
PPE	personal protective equipment
RPE	respiratory protective equipment
SMILES	Simplified Molecular-Input Line-Entry System
WG	water-dispersible granule

Appendix A – List of representative uses evaluated for negligible exposure

Crop and/or situation ^(a)	Member State or Country	Product name	F G or I ^(b)	Pests or Group of pests controlled ^(c)	Formulation		Application				Application rate per treatment			PHI ^(l) (days)	Remarks: ^(m)
					Type ^(d-f)	Conc. of as ⁽ⁱ⁾	Method kind ^(f-h)	Growth stage & season ^(j)	Number min-max ^(k)	Interval between applications (min)	g a.s./hL min-max	Water L/ha min-max	g a.s./ha min-max		
Potato (ware)	EU	A9364J	F	Aphids	WG	500	Foliar spray	BBCH 20-89	1	n/a	–	150-600	100	7	Every second year only (crop rotation, good agricultural practice)
Oilseed rape	EU	A9364J	F	<i>Meligethes</i> spp.	WG	500	Foliar spray	BBCH 51-59	1	n/a	–	150-400	75	n/a	Every third year only (crop rotation, good agricultural practice)

a.s.: active substance.

(a): For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (e.g. fumigation of a structure).

(b): Outdoor or field use (F), glasshouse application (G) or indoor application (I).

(c): e.g. biting and sucking insects, soil born insects, foliar fungi, weeds.

(d): e.g. wettable powder (WP), water-soluble granule (WG).

(e): GCPF Codes – GIFAP Technical Monograph No 2, 1989.

(f): All abbreviations used must be explained.

(g): Method, e.g. high-volume spraying, low-volume spraying, spreading, dusting, drench.

(h): Kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plants – type of equipment used must be indicated.

(i): g/kg or g/L.

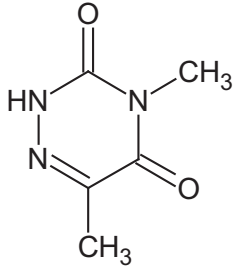
(j): Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application.

(k): The minimum and maximum number of application possible under practical conditions of use must be provided.

(l): PHI: minimum preharvest interval.

(m): Remarks may include: Extent of use/economic importance/restrictions.

Appendix B – Used compound codes

Code/trivial name ^(a)	Chemical name/SMILES notation	Structural formula
CGA371075	4,6-Dimethyl-1,2,4-triazine-3,5(2 <i>H</i> ,4 <i>H</i>)-dione <chem>CN1C(=O)NN=C(C)C1=O</chem>	

SMILES: Simplified Molecular-Input Line-Entry System.

(a): The metabolite name in bold is the name used in the conclusion.