European Food Safety Authority

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CONCLUSION ON PESTICIDE PEER REVIEW

Conclusion on the peer review of the pesticide risk assessment of confirmatory data submitted for the active substance dimethoate[1]

European Food Safety Authority[2]

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ABSTRACT

The conclusions of the European Food Safety Authority (EFSA) following the peer review of the initial risk assessment carried out by the competent authority of the rapporteur Member State the United Kingdom, for the pesticide active substance dimethoate are reported. The context of the peer review was that requested by the European Commission following the submission and evaluation of confirmatory mammalian toxicology, residues and ecotoxicology data. The conclusions were reached on the basis of the evaluation of the representative uses of dimethoate as an insecticide on sugar beet and protected lettuce. Concerns are identified.

KEY WORDS

dimethoate, peer review, risk assessment, pesticide, insecticide

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SUMMARY

Dimethoate was included in Annex I to Directive 91/414/EEC on 23 April 2007 by Commission Directive 2007/25/EC, and has been deemed to be approved under Regulation (EC) No 1107/2009, in accordance with Commission Implementing Regulation (EU) No 540/2011, as amended by Commission Implementing Regulation (EU) No 541/2011. It was a specific provision of the approval that the notifier was required to submit to the European Commission further studies to confirm the risk assessment for birds, mammals and non-target arthropods, as well as to confirm the toxicological assessment on metabolites potentially present in crops by 1 October 2009.

In accordance with the specific provision, the notifier, the Dimethoate Task Force, submitted an updated dossier in September 2009, which was evaluated by the designated RMS, the United Kingdom, in the form of an Addendum to the Draft Assessment Report. In compliance with Guidance Document SANCO 5634/2009 rev.4.5, the RMS distributed the Addendum to Member States, the notifier and the EFSA for comments on 11 August 2011. The RMS collated all comments in the format of a Reporting Table, which was submitted to the European Commission in October 2011.

Following consideration of the comments received, the Commission requested EFSA to provide scientific and technical assistance and to deliver its conclusions on those issues where different views had been expressed in the commenting.

A data gap was identified in the toxicology section for toxicological information on metabolites XI, XII, XX and XXIII. Reference values of dimethoate are applicable to metabolite III.

An acute dietary intake concern was identified for lettuce ((IESTI = 107% of the ARfD of dimethoate) (DE, Child)). The consumer risk assessment has to be regarded as provisional in view of the lack of information on the contribution of the metabolites XI, XII, XX and XXIII to the overall toxicological burden.

A high acute and long-term risk to birds and a high long-term risk to mammals was concluded for the representative use on sugar beet. The risk to non-target arthropods was considered as low with an in-field buffer zone of 5 m.

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BACKGROUND

Dimethoate was included in Annex I to Directive 91/414/EEC on 23 April 2007 by Commission Directive 2007/25/EC[3], and has been deemed to be approved under Regulation (EC) No 1107/2009[4], in accordance with Commission Implementing Regulation (EU) No 540/2011[5], as amended by Commission Implementing Regulation (EU) No 541/2011[6]. EFSA previously finalised a Conclusion on this active substance on 23 June 2006 in the EFSA Scientific Report (2006) 84 (EFSA, 2006).

It was a specific provision of the approval that the notifier was required to submit to the European Commission further studies to confirm the risk assessment for birds, mammals and non-target arthropods, as well as to confirm the toxicological assessment on metabolites potentially present in crops by 1 October 2009.

In accordance with the specific provision, the notifier, the Dimethoate Task Force, submitted an updated dossier in September 2009, which was evaluated by the designated rapporteur Member State (RMS), the United Kingdom, in the form of an Addendum to the Draft Assessment Report (United Kingdom, 2011). In compliance with Guidance Document SANCO 5634/2009 rev.4.5 (European Commission, 2011), the RMS distributed the Addendum to Member States, the notifier and the EFSA for comments on 11 August 2011. The RMS collated all comments in the format of a Reporting Table, which was submitted to the European Commission in October 2011.

Following consideration of the comments received, the Commission requested EFSA to provide scientific and technical assistance and to deliver its conclusions on those issues where different views had been expressed in the commenting.

A final consultation on the conclusions arising from the peer review took place with Member States via a written procedure in April 2013.

The conclusions laid down in this report were reached on the basis of the peer review of the RMS's evaluation of the confirmatory data submitted in relation to dimethoate. A key supporting document to this conclusion 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 in the Reporting Table to the conclusion. The Peer Review Report (EFSA, 2013) comprises the following documents:

- the Reporting Table,
- the comments received on the draft EFSA conclusion.

Given the importance of the Final Addendum to the Addendum to the DAR (United Kingdom, 2013) and the Peer Review Report, these documents are considered respectively as background documents A and B to this conclusion.

[3] Commission Directive 2007/25/EC of 23 April 2007 amending Council Directive 91/414/EEC to include dimethoate, dimethomorph, glufosinate, metribuzin, phosmet and propamocarb as active substances. OJ No L 106, 24.4.2007, p. 34–42.
[4] Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. OJ No L 309, 24.11.2009, p. 1-50.
[5] Commission Implementing Regulation (EU) No 540/2011 of 25 May 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the list of approved active substances. OJ L 153, 11.6.2011, p.1-186.
[6] Commission Implementing Regulation (EU) No 541/2011 of 1 June 2011 amending Implementing Regulation (EU) No 540/2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the list of approved active substances. OJ L 153, 11.6.2011, p.187-188.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Dimethoate is the ISO common name for *O,O*-dimethyl *S*-methylcarbamoylmethyl phosphorodithioate or 2-dimethoxyphosphinothioylthio-*N*-methylacetamide (IUPAC).

Dimethoate belongs to the class of aliphatic amide organothiophosphate insecticides such as omethoate and mecarbam. It belongs also to the classes of organothiophosphate acaricides. Dimethoate acts by contact and systemic action by inhibiting the enzyme acetylcholinesterase.

The representative formulated product for the evaluation was "Danadim Dimethoate 40" ("400 g/L EC"), an emulsifiable concentrate (EC), registered under different trade names in Europe.

The evaluated representative uses as insecticide comprise spraying to control biting and sucking insects in sugar beet and protected lettuce. The GAP for dimethoate and the associated application rates have been revised by the notifier under the confirmatory data procedure. As the application rate has been lowered for the sugar beet use, the risk assessment presented in the EFSA Scientific Report (2006) 84 is also covering the GAP presented under this procedure.

CONCLUSIONS OF THE EVALUATION

1. Mammalian toxicity

Further to dimethoate and omethoate, that were assessed in the previous EFSA conclusion (EFSA, 2006), metabolites III, X, XI, XII, XX and XXIII were found to be potentially present in residues at significant levels during the assessment of confirmatory data by the residue section and a toxicological assessment was considered necessary.

Some toxicological information has been submitted on **metabolite III** (*dimethoate carboxylic acid*) to show that the metabolite has lower toxicity than the parent dimethoate; however the reliability of these data is rather limited. Metabolite III is a major metabolite in the rat and in humans, based on its chemical structure and *in vivo* metabolism data, it is unlikely that the metabolite would present higher toxicity than dimethoate, and it may be concluded that the reference values of dimethoate are applicable to this metabolite.

Metabolite XII (*des-O-methyl isodimethoate*) was not found in rat metabolism studies. It has been shown to be less acutely toxic than dimethoate, at least 200 times less, based on acute toxicity studies measuring acetyl cholinesterase inhibition. Regarding chronic toxicity, no repeated dose investigations of acetylcholinesterase inhibition or other endpoints have been undertaken, therefore it is not possible to conclude whether the metabolite has a higher, similar or lower toxicity than dimethoate. In addition, it is noted that metabolite XII shows some structural similarity to omethoate, which was found to be chronically more toxic than dimethoate and presenting other critical effects than acetylcholinesterase inhibition, namely on reproduction and development. A data gap has been identified for toxicological information to address the chronic toxicity profile of metabolite XII that should include genotoxicity, reproductive and developmental toxicity.

Metabolite XX (*O-desmethyl omethoate carboxylic acid*) has been shown to be less acutely toxic than dimethoate, at least 200 times less, based on acute toxicity studies measuring acetylcholinesterase inhibition. The metabolite was not found in metabolism studies in the rat performed with dimethoate and was found as a minor metabolite of omethoate. Therefore its toxicity cannot be considered as being covered by the toxicity data package provided for either dimethoate or omethoate. Regarding chronic toxicity, no repeated dose investigations of acetylcholinesterase inhibition or on other endpoints have been undertaken; therefore it is not possible to conclude whether the metabolite has a higher, similar or lower toxicity than dimethoate. In addition, it is noted that metabolite XX shows

some structural similarity to omethoate, which was found to be chronically more toxic than dimethoate. A data gap has been identified for toxicological information to address the chronic toxicity profile of metabolite XX, which should include genotoxicity, reproductive and developmental toxicity.

According to the residue section, **metabolites XXIII (***O-desmethyl-N-desmethyl omethoate*) and **XI** (*O-desmethyl omethoate*) need a toxicological assessment. No toxicological information has been provided and a data gap was identified on this issue.

Regarding **metabolite X** (*desmethyl dimethoate*)**,** it has been highlighted as needing a toxicological assessment in the residue section for a non-representative GAP. As no toxicological information is available on this metabolite, this potential data gap is noted for crops that may undergo sterilisation.

2. Residues

The assessment in the residue section below is based on the guidance documents listed in the document 1607/VI/97 rev.2 (European Commission, 1999), and the JMPR recommendations on livestock burden calculations stated in the 2004 and 2007 JMPR reports (JMPR, 2004 and 2007).

The metabolism in plants was investigated after spray applications in potatoes (root and tuber crops), wheat (cereals) and olives (fruiting crops) using ^{14}C-dimethoate labelled on both methoxy groups. No dimethoate or omethoate was detected in mature potato tubers and wheat grain at harvest whilst they were recovered but at a very low proportion in wheat straw and olive fruits (<10% of TRR). In mature crops, the metabolic pattern of dimethoate consisted of an extensive degradation of the parent molecule into a wide range of metabolites. The predominant compound of the total residues in all the matrices was the **metabolite XXIII** (*O-desmethyl-N-desmethyl omethoate*) accounting for 43% TRR in potato tuber, 26% TRR in wheat whole plant, up to 40% TRR in wheat straw and grain and up to 60% TRR in olive fruit (green, black). The following **metabolites XX** (*O-desmethyl omethoate carboxylic acid*)**, XII** (*des-O-methyl isodimethoate*) and **XI** (*O-desmethyl omethoate)* represented also a significant proportion of the total residues (>10% TRR) either in potato tuber or in the different wheat plant parts. Although not detected in potatoes and cereal plant parts, the **metabolite III** (*dimethoate carboxylic acid*) was identified in amounts higher than dimethoate and omethoate in the olive fruits but its toxicological properties are covered by the toxicity studies of the parent dimethoate (section 1).

Dimethoate exhibits a low persistence in soil and a potential transfer of residues to edible crops in rotation can be excluded. This was observed in the confined rotational crop study with lettuce, turnip and wheat planted 30 and 120 days after a bare soil application of 0.56 kg a.s./ha (1.1 N dose rate). Given the low levels of total radioactive residues in the edible parts of the crops, no further metabolites' identification was requested (EFSA, 2006).

Under simulated processing conditions of sterilisation and baking, brewing and boiling, both dimethoate and omethoate ^{14}C-labelled on the methoxy groups were degraded to a significant extent into the **metabolites X** (*desmethyl dimethoate***)** and **XI (***O-desmethyl omethoate),* respectively. No significant degradation of dimethoate and omethoate was observed during pasteurisation. Studies investigating the effect of processing on the residue levels under practical conditions are not triggered for the representative uses. It is however highlighted that the toxicological properties of the **metabolite X** should be addressed for crops that may undergo sterilisation under normal processing conditions (canned olives, sterilised – EFSA, 2012).

Since similar routes of dimethoate degradation were depicted in potatoes, wheat and olives, a general residue definition for monitoring is set as dimethoate and omethoate, to be determined separately.

The agreed provisional residue definitions for risk assessment were the "sum of dimethoate and 6 x omethoate expressed as dimethoate" for acute risk assessment and the "sum of dimethoate and 3 x omethoate expressed as dimethoate" for chronic risk assessment. EFSA is of the opinion that based on its significant occurrence in all the edible parts of the crops, the metabolite **XXIII** should definitively be included in the residue definition either combined with the parent compound or considered separately based on the requested toxicological assessment of this metabolite. Furthermore, pending on their toxicological properties, metabolites **XII**, **XX** and **XI** may also be included in the residue definition for risk assessment (section 1).

Sufficient GAP compliant residue trials were available for sugar beet and lettuce analysing dimethoate and omethoate residues. These trials were supported by acceptable storage stability data. Pending the outcome of the required information on the toxicological profile of the metabolites identified as relevant in primary crops, a data gap may be identified to provide residue trials analysing these metabolites.

Metabolism studies were submitted in lactating goats and laying hens although no intake is expected for poultry when considering the uses on sugar beet and lettuce. No significant exposure (>0.01 mg/kg) was observed in any matrix except in ruminant liver and milk. Dimethoate was not detected in any matrix. Omethoate was detected in liver and egg white (11% and 3% of TRR, respectively) as well as the metabolite **III** in liver (2.5-18% TRR), milk (8% TRR) and egg white (4% TRR). The major part of the radioactivity was characterised as phosphorylated natural products (62%-87% TRR).

For monitoring, dimethoate and omethoate have to be determined separately whilst the "sum of dimethoate and 6 x omethoate expressed as dimethoate" was set for the acute risk assessment and the "sum of dimethoate and 3 x omethoate expressed as dimethoate" for the chronic risk assessment for animal matrices. These residue definitions should be regarded as provisional as it was agreed that a feeding study in ruminants should be carried out at normal rate with simultaneous administration of dimethoate and omethoate at a ratio representative of the practical conditions (EFSA, 2006). Particular attention should also be given to the potential transfer through the feed items of the metabolites **XXIII, XI** and **XX** in animal matrices if these metabolites are shown to be toxicologically pertinent.

Using the EFSA PRIMo rev.2A and the STMR value for lettuce derived from the sum of dimethoate and 3 x omethoate expressed as dimethoate, a low chronic intake was observed (IEDI = 2.7% of the ADI of dimethoate (ES, Adult)). An acute intake concern was identified when using the HR value (0.4 mg/kg) derived from the sum of dimethoate and 6 x omethoate expressed as dimethoate (IESTI = 107% of the ARfD of dimethoate (DE, Child)). No dietary intake calculation was performed for the representative use on sugar beet since no consumption data for refined sugar are available in the EFSA PRIMo Model. It is however highlighted that in view of the no-residue situation for dimethoate and omethoate observed in the sugar beet root and due to the harsh alkaline conditions in sugar beet processing and the crystallisation steps, no residues are expected to occur in refined sugar. The consumer risk assessment has however to be regarded as provisional in view of the lack of information on the contribution of the metabolites **XXIII, XII**, **XX and XI** to the overall toxicological burden.

3. Ecotoxicology

For the environmental risk assessments the following documents were considered: EFSA, 2009; European Commission 2002a, 2002b and SETAC, 2001.

The confirmatory data in the ecotoxicology section are relevant for the representative uses in sugar beet. No further evaluations were provided for the representative use in lettuce (glasshouse) as these were considered as not necessary.

A high acute, short-term and long-term risk via dietary exposure to **birds** was identified at first tier level. A refined risk assessment was submitted with the confirmatory data. Options for refinements have been proposed for toxicity endpoints, focal species and related PD values, measured residue levels in plants (sugar beet) and insects and residue decline to refine the f(twa). Several options for refinement were questioned during the peer review as reported below. For refinement of the toxicity endpoints, the geometric mean approach was agreed for the acute endpoint, but not for the short-term and the long-term endpoints. Two focal species were proposed for the representative uses on the basis of studies conducted in sugar beet fields in Greece and Germany: the skylark (*Alauda arvensis*), as a small omnivorous species for northern Europe and yellow wagtail (*Motacilla flava*), as a small insectivorous species for both northern and southern Europe. These focal species were considered appropriate; related refined PD values were proposed on the basis of literature data. EFSA considered that more data on the feeding behaviour in the field would be necessary to support the proposed PD values, particularly for acute risk assessment. New residues studies on sugar beet were provided to refine the RUD values. However, the whole residue data set available was not considered to provide appropriate residues on sugar beet plants for use in a refined risk assessment for the representative uses because the GAPs are not covered. The residue study on insects conducted in Spain on citrus was proposed to refine the RUD values for insects. In this study, residue data were produced for canopy-dwelling arthropods but not for ground-dwelling arthropods, which would be more representative of the type found in sugar beet fields. Extrapolating the data from canopy to ground-dwelling arthropods and from arthropods found in citrus orchards to arthropods in sugar beet fields was also considered not appropriate. On the basis of the residue decline observed in residue trials on sugar beet and on the above mentioned residue study on insects, DT_{50} values of 2 days and 1.25 days were proposed for sugar beet foliage and insects respectively to refine the f(twa) for long-term risk assessment. However, these DT_{50} values were not sufficiently supported by data i.e. sugar beet residue data were available for only two time points and the residue trial in insects in citrus was not considered appropriate for sugar beet. To take into account all these concerns, refined TERs were provided in the Addendum 1 (United Kingdom, 2013). The refined risk assessment still indicated a high acute short-term and long-term risk to birds. As a further refinement of the acute risk a body burden modelling according to the pirimicarb opinion (EFSA PPR, 2005) was proposed for the two focal species: skylark and yellow wagtail. General concerns were raised during the peer review as regards the uncertainties related to the input parameters. However, the outcome of this modelling still indicated a high risk in the worst-case scenarios while the outcome of the best-case scenarios cannot be considered reliable as the modelling still included the proposed refined RUD value for insects which was not deemed to be acceptable (discussed above). Overall, it is considered that the confirmatory data do not address the concern raised in the previous peer review of dimethoate and a high risk to birds via dietary exposure is still concluded. The risk from consumption of contaminated water was assessed as low.

A high long-term risk via dietary exposure to **mammals** was identified at first tier level, while the acute risk was assessed as low for the representative uses. Since in the previous peer review of dimethoate it was concluded that the plant metabolite omethoate is chronically more toxic for mammals than the parent a separate risk assessment for this metabolite was carried out. The first tier TERs calculated by assuming that the initial residues of dimethoate are 100% converted to omethoate, indicated a high acute and long-term risk. To refine the risk assessment, the ratios between omethoate and dimethoate residue were calculated on the basis of the available residues trials. The 90^{th} percentile ratio was then used to derive a refined combined dimethoate/omethoate RUD value. The difference in toxicity was reflected in the adjusted RUD value. It is noted that, on the basis of the residue data, mammals in-field might be exposed mainly to dimethoate rather than the metabolite omethoate. Therefore the acute risk for omethoate can be considered as addressed. Overall, the long-term risk via dietary exposure for dimethoate was assessed as high and a high long-term risk for omethoate cannot be excluded. The risk from consumption of contaminated water was assessed as low.

The risk for **non-target arthropods** was assessed as high for the representative uses at the first tier. However, in the previous peer review of dimethoate, it was concluded that there is a potential for in-field recovery, provided that the off-field risk is low. The off-field drift rates calculated with an in-field buffer zone of 5 m were below the NOER derived from field studies. Overall, the risk to non-target arthropods can be concluded as low for the representative uses, if an in-field buffer zone of 5 m is applied to protect the off-field population and to ensure the in-field recovery.

4. List of studies to be generated

This is a list of the data gaps identified during the focussed peer review process of confirmatory data. Data gaps identified in the previously finalised EFSA Conclusion on this active substance (EFSA, 2006) that were not part of the focussed peer review process of confirmatory data remain as unchanged.

- Toxicological information to address the chronic toxicity profile of metabolites XII and XX that should include genotoxicity, reproductive and developmental toxicity, and toxicological information on metabolites XXIII and XI to address their acute and chronic toxicological profiles (relevant for all representative uses; submission date unknown; refer to section 1).

- Pending the outcome of the required information on the toxicological profile of the metabolites identified as relevant in primary crops (XXIII, XII, XX and XI**)**, a data gap may be identified to provide residue trials analysing these metabolites (relevant for all representative uses; submission date unknown; refer to section 2).

- A ruminant feeding study carried out at normal rate with simultaneous administration of dimethoate and omethoate at a ratio representative of the practical conditions and with a particular attention to metabolites XXIII, XX and XI (relevant for the use in sugar beet; submission date unknown; refer to section 2).

- The acute and long-term risk assessment for birds and the long-term risk assessment for mammals need to be further refined (relevant for the use in sugar beet; submission date unknown; refer to section 3).

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

- For lettuce, it is recommended to use dimethoate at the latest until growth stage 19 (9th true leave unfold). Application after the starting of the head formation, even with a PHI of 28 days, may result in much higher residue levels, with a higher exceedence of the ARfD.

- An in-field buffer zone of 5 m should be applied to protect the off-field population and to ensure the in-field recovery of non-target arthropods populations.

6. Concerns

6.1 Issues that could not be finalised

An issue is listed as an issue that could not be finalised where 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 of Annex VI to Directive 91/414/EEC and where 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).

1. The consumer risk assessment could not be finalised in view of the lack of information on the toxicity of the dimethoate metabolites **XXIII, XII**, **XX, XI** and their contribution to the overall toxicological burden.

6.2 Critical areas of concern

An issue is listed as a critical area of concern where there is enough information available to perform an assessment for the representative uses in line with the Uniform Principles of Annex VI to Directive 91/414/EEC, and where this assessment does not permit to conclude 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 where the assessment at a higher tier level could not be finalised due to a lack of information, and where the assessment performed at the lower tier level does not permit to conclude 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.

- None identified

7. 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 5, has been evaluated as being effective, then 'risk identified' is not indicated in this table.)

Representative use		**Sugar beet** **(N-EU, S-EU)**	**Lettuce** **(glasshouse)**
Consumer risk	Risk identified		X
	Assessment not finalised	X[1]	X[1]
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		
	Assessment not finalised		
Comments/Remarks			

The superscript numbers in this table relate to the numbered points above. Where there is no superscript number see main text for further information.

REFERENCES

ACD/ChemSketch, Advanced Chemistry Development, Inc., ACD/Labs Release: 12.00 Product version: 12.00 (Build 29305, 25 Nov 2008).

EFSA (European Food Safety Authority), 2006. Conclusion regarding the peer review of the pesticide risk assessment of the active substance dimethoate. EFSA Scientific Report (2006) 84, finalised on 23 June 2006 .

EFSA (European Food Safety Authority), 2009. Guidance Document on Risk Assessment for Birds and Mammals on request of EFSA. EFSA Journal 2009; 7(12):1438.

EFSA (European Food Safety Authority), 2012. Dimethoate - Application to modify the existing MRLs in olives. EFSA Journal 2012; 10(5):2709.

EFSA (European Food Safety Authority), 2013. Peer Review Report to the conclusion regarding the peer review of the pesticide risk assessment of confirmatory data submitted for the active substance dimethoate.

EFSA PPR (EFSA Scientific Panel on Plant health, Plant protection products and their Residues), 2005. Opinion of the Scientific Panel on Plant health, Plant protection products and their Residues on a request from EFSA related to the evaluation of pirimicarb. EFSA Journal (2005) 240, 21pp.

European Commission, 1999. Guidelines for the generation of data concerning residues as provided in Annex II part A, section 6 and Annex III, part A, section 8 of Directive 91/414/EEC concerning the placing of plant protection products on the market, 1607/VI/97 rev.2, 10 June 1999.

European Commission, 2002a. Guidance Document on Terrestrial Ecotoxicology Under Council Directive 91/414/EEC. SANCO/10329/2002 rev.2 final, 17 October 2002.

European Commission, 2002b. Guidance Document on Risk Assessment for Birds and Mammals Under Council Directive 91/414/EEC. SANCO/4145/2000.

European Commission, 2011. Guidance document on the procedures for submission and assessment of confirmatory data following inclusion of an active substance in Annex I of Council Directive 91/414/EEC. SANCO 5634/2009 rev.4.5.

JMPR (Joint Meeting on Pesticide Residues), 2004. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues Rome, Italy, 20–29 September 2004, Report 2004, 383 pp.

JMPR (Joint Meeting on Pesticide Residues), 2007. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues Geneva, Switzerland, 18–27 September 2007, Report 2007, 164 pp.

SETAC (Society of Environmental Toxicology and Chemistry), 2001. Guidance Document on Regulatory Testing and Risk Assessment procedures for Plant Protection Products with Non-Target Arthropods. ESCORT 2.

United Kingdom, 2011. Addendum to the Draft Assessment Report on dimethoate, confirmatory data, August 2011.

United Kingdom, 2013. Final Addendum to the Addendum to the Draft Assessment Report on dimethoate, compiled by EFSA, April 2013.

APPENDICES

APPENDIX A – LIST OF END POINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

List of representative uses evaluated (dimethoate)*

Crop and/or situation	Member State or Country	Product name	F G or I	Pests or Group of pests controlled	Formulation		Application				Application rate per treatment			PHI (days)	Remarks:
(a)			(b)	(c)	Type (d-f)	Conc. of a.s. (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	kg as/hl min max	water l/ha min max	kg as/ha min max	(l)	(m)
Sugar beet	South	Danadim Dimethoate 40	F	Biting and sucking insects	EC	400 g/L	Spraying	1. 16 – 18 2. 35 – 43	2	21 d	0.12-0.024	200-1000	0.24	30	Initially, two applications at BBCH 1. 16-18 and 2. 35-43 were considered.
Sugar beet	North	Danadim Dimethoate 40	F	Biting and sucking insects	EC	400 g/L	Spraying	1. 16 – 18 2. 35 – 43	2	21 d	0.12-0.024	200-1000	0.24	35	Initially, two applications at BBCH 1. 16-18 and 2. 35-43 were considered.
Lettuce	North	Danadim Dimethoate 40	G	Biting and sucking insects	EC	400 g/L	Gantry Spraying	GS19	1	nr	0.17	200	0.34	28	

Remarks:	*	Uses for which risk assessment could not been concluded due to lack of essential data are marked grey	(h)	Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated
	(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)	(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
	(b)	Outdoor or field use (F), glasshouse application (G) or indoor application (I)		
	(c)	*e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds		
	(d)	*e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)	(k)	The minimum and maximum number of application possible under practical conditions of use must be provided
	(e)	GCPF Codes - GIFAP Technical Monograph No 2, 1989		
	(f)	Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench	(l)	PHI - minimum pre-harvest interval
	(g)	All abbreviations used must be explained	(m)	Remarks may include: Extent of use/economic importance/restrictions

Impact on Human and Animal Health

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

Rate and extent of oral absorption ‡	Rapidly and extensively absorbed, > 90% within 24 hours (rat urine, 10 mg/kg bw)
Distribution ‡	Widely and evenly distributed, highest concentration in liver
Potential for accumulation ‡	No evidence for accumulation
Rate and extent of excretion ‡	Rapidly excreted (90% in urine within 24h)
Metabolism in animals ‡	Cleavage to dimethoate carboxylic acid; oxidation to omethoate (~5%)
Toxicologically relevant compounds ‡ (animals and plants)	Parent, omethoate
Toxicologically relevant compounds ‡ (environment)	Parent, omethoate

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	245 mg/kg bw	R22
Rat LD_{50} dermal ‡	>2000 mg/kg bw	
Rat LC_{50} inhalation ‡	1.68 mg/L air /4 hours (whole body); study with a manufacturing concentrate	R20
Skin irritation ‡	Minimal irritant	
Eye irritation ‡	Mild irritant	
Skin sensitisation ‡	No evidence (3-induction Buehler), study insufficient	Provisio-nal R43

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Inhibition of erythrocyte and brain cholinesterase activity	
Relevant oral NOAEL ‡	0.18 mg/kg bw per day (1 year dog study)	
Relevant dermal NOAEL ‡	5 mg/kg bw per day (5-day rat study with a formulation)	
Relevant inhalation NOAEL ‡	No data	

Genotoxicity ‡ (Annex IIA, point 5.4)

Positives *in vitro*, negative *in vivo*. Weight of evidence indicates no significant genotoxic potential	

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

Target/critical effect ‡	Inhibition of erythrocyte and brain cholinesterase activity.	
Relevant NOAEL ‡	0.04 mg/kg bw per day (rat chronic), LOAEL = 0.2 mg/kg bw per day	
Carcinogenicity ‡	No evidence of carcinogenicity.	

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	Parent: Brain and RBC ChE inhibition Reproduction: Reduced pregnancy rate and reduced litter size at birth Offspring: Reduced survival, reduced pup weights	
Relevant parental NOAEL ‡	0.2 mg/kg bw per day	
Relevant reproductive NOAEL ‡	1.2 mg/kg bw per day	
Relevant offspring NOAEL ‡	1.2 mg/kg bw per day	

Developmental toxicity

Developmental target / critical effect ‡	Maternal: Clinical signs, reduced bodyweight Developmental: No evidence of fetotoxicity	
Relevant maternal NOAEL ‡	Rat: 6 mg/kg bw per day	
Relevant developmental NOAEL ‡	Rat: 18 mg/kg bw per day (highest dose tested)	

Neurotoxicity / Delayed neurotoxicity ‡ (Annex IIA, point 5.7)

Acute neurotoxicity ‡	Acute neurotoxicity gavage (rats): NOAEL = 2 mg/kg bw, reduced pupil response (ChE not measured) Acute neurotoxicity diet (rats): NOAEL = 1 mg/kg bw, RBC ChE No evidence of neurotoxicity	
Repeated neurotoxicity ‡	13 week dietary neurotoxicity: NOAEL = 0.06 mg/kg bw per day, RBC ChE Developmental neurotoxicity: NOAEL = 0.1 mg/kg bw per day, reduced pup survival No evidence for neurotoxicity	
Delayed neurotoxicity ‡	No evidence for delayed neurotoxicity in the hen, although NTE inhibition was seen.	

Other toxicological studies ‡ (Annex IIA, point 5.8)

Mechanism studies ‡	No data
Studies performed on metabolites or impurities ‡	Studies were provided on omethoate and a number of metabolites of dimethoate; metabolite XII (*des-O-methyl isodimethoate*) and XX (*O-desmethyl-omethoate-carboxylic acid*) were less potent ChE inhibitors than dimethoate upon acute administration

Studies on omethoate

Acute toxicity	
Oral (rat)	LD_{50} =22 mg/kg bw, LD_{50} =28 mg/kg bw (2 studies)
Dermal (rat)	LD_{50} =232 mg/kg bw, LD_{50} =145 mg/kg bw (2 studies)
Inhalation (rat)	LC_{50} =0.287 mg/L
Short term toxicity	
Rat 90-day	Overall NOAEL approximately 0.1 mg/kg bw per day, based on RBC cholinesterase and brain cholinesterase inhibition
Dog 12-month (gavage)	NOAEL: 0.025 mg/kg bw per day, LOAEL 0.125 mg/kg bw per day, based on decreased RBC & brain cholinesterase (cholinesterase data may be unreliable)
Rabbit 21-day dermal	NOAEL: 2.5 mg/kg bw per day, LOAEL: 20 mg/kg bw per day, based on clinical signs and decreased RBC & brain cholinesterase (cholinesterase data may be unreliable)
Genotoxicity	Weight of evidence indicates that omethoate is mutagenic *in vitro* but not *in vivo*
Carcinogenicity	
Rat	LOAEL: 0.04 mg/kg bw per day, based on a borderline effect on RBC ChE in males No evidence of carcinogenicity
Reproductive toxicity	
Multigeneration study (rats)	Parental NOAEL: 0.03 mg/kg bw per day, based on ChE inhibition Developmental NOAEL: 0.2 mg/kg bw per day, based on increased post-natal loss and decreased pup weight Reproductive NOAEL: 0.2 mg/kg bw per day, based on adverse effects on mating and fertility parameters
Developmental toxicity (rabbits)	Maternal NOAEL: 0.2 mg/kg bw per day, based on clinical signs and cholinesterase inhibition Developmental NOAEL: 0.2 mg/kg bw per day, based on increased post-implantation loss Malformations recorded at 1.0 and 5.0 mg/kg bw per day (primarily arthrogyrposis) are of questionable

	significance

Neurotoxicity

Acute neurotoxicity (rat)	NOAEL: 0.2 mg/kg bw, based on effects in the pupil consistent with ChE inhibition, 0.25 mg/kg bw based on ChE inhibition No evidence of neuropathology or neurotoxicity
Delayed neurotoxicity (hen)	No evidence of delayed neurotoxicity No measurement of ChE activity or NTE inhibition

Summary	Value	Study	Safety factor
ADI for omethoate	0.0003 mg/kg bw per day	Rat multigeneration study and 2 year rat study	100
AOEL for omethoate	0.0003 mg/kg bw per day	12 month dog study	100
ARfD for omethoate	0.002 mg/kg bw	Acute neurotoxicity	100

EFSA note: In the toxicology section, an estimate of the threshold for the toxicologically relevant inhibition of erythrocyte and/or brain cholinesterase activity was made by comparison of NOAELs and LOAELs for cholinesterase inhibition as well as the cholinesterase activity recovery in repeat-dose studies. Omethoate is more toxic than dimethoate and the relative toxicity of omethoate compared to dimethoate following chronic and acute were found to be about ~3:1 and ~6:1, respectively.
In the residue section the above mentioned values were used for the consumers' risk assessment.
In the ecotoxicology section, with regard to the acute mammalian risk assessment, the acute oral LD_{50} in rats for omethoate was compared to the acute oral LD_{50} for dimethoate in the mouse resulting in TEF of 7. With regard to the long-term mammalian risk assessment conducted by the RMS, the TEF is based upon the NOAELs derived from multi-generation studies with dimethoate and omethoate, respectively, resulting in a TEF of 3.

Medical data ‡ (Annex IIA, point 5.9)

	No indications of adverse effects in manufacturing plant personnel. Some reports of intermediate syndrome following dimethoate poisoning.

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	0.001 mg/kg bw per day	Overall NOAEL from rat chronic, reproduction, neurotoxicity and developmental neurotoxicity*	100

AOEL ‡	0.001 mg/kg bw per day	Developmental neurotoxicity and interim values in 2 year rat	100
ARfD ‡	0.01 mg/kg bw	Acute dietary neurotoxicity	100

* Derived from these studies taking account of the NOAELs and LOAELs

Dermal absorption (Annex IIIA, point 7.3)

Dimethoate 400 EC	Concentrate: 0.15% Spray dilution: 2.0% Based on rat *in vivo* and rat/human *in vitro*

Exposure scenarios (Annex IIIA, point 7.2)

Danadim Dimethoate 40 is applied on wheat, olive, sugar beet, tomatoes and lettuce with tractor-mounted spraying devices, knapsack-sprayers and airblast assisted sprayer in orchards.
Recommended application rate of dimethoate from 0.084 to 0.72 kg a.s./ha

Operator	Exposure below the AOEL in protected lettuce only by automatic gantry sprayer application (German and UK models, work rate of 1 ha/day and 0.67 ha/day, respectively, without PPE) and for application on wheat with boom sprayers (German model, PPE worn).
Workers	Exposure for re-entry workers hand harvesting tomato and lettuce is estimated to be below the AOEL.
Bystanders	Estimated exposure below the AOEL

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

	RMS/peer review proposal [7]	
Dimethoate	Xn;	Harmful
	R22	Harmful if swallowed
	R20	Harmful by inhalation
	R43	May cause sensitisation by skin contact (provisional)
Dimethoate	Harmonised classification - Annex VI of Regulation (EC) No 1272/2008 (CLP Regulation)[8]:	

[7] It should be noted that proposals for classification made in the context of the evaluation procedure under Regulation (EC) No 1107/2009 are not formal proposals. Classification is formally proposed and decided in accordance with Regulation (EC) No 1272/2008.
[8] 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, 1-1355.

	Acute Tox. 4*, H302 'harmful if swallowed' Acute Tox. 4*, H312 'harmful in contact with skin'
Omethoate	Harmonised classification - Annex VI of Regulation (EC) No 1272/2008 (CLP Regulation): Acute Tox. 3*, H301 'toxic if swallowed' Acute Tox. 4*, H312 'harmful in contact with skin'

Residues

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

Plant groups covered	Potato (Root & tuber crops), wheat (Cereals) and olives (fruiting crops) - Foliar spray application.
Rotational crops	Wheat (C) , lettuce (L) and turnip (R&T)
Metabolism in rotational crops similar to metabolism in primary crops?	Yes
Processed commodities	Wheat, olives
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Yes, but -extensive degradation of ^{14}C-dimethoate into metabolite *desmethyl dimethoate* (**X)** under sterilisation (60% AR) and to a minor extent under baking/brewing/baking (28% AR) - extensive degradation of ^{14}C-omethoate into metabolite *O-desmethyl omethoate* (**XI)** under sterilisation (62% AR) and to a minor extent under baking/brewing/baking (36% AR) Processing conditions not relevant for the representative uses.
Plant residue definition for monitoring	Dimethoate and omethoate, to be determined separately (all categories of crops).
Plant residue definition for risk assessment	Sum of dimethoate and 6 x omethoate expressed as dimethoate for acute risk assessment Sum of dimethoate and 3 x omethoate expressed as dimethoate for chronic risk assessment (all categories of crops). Residue definitions to be regarded as provisional. Pending on their toxicological properties, metabolites **XXIII**, **XII**, **XX** and **XI** may also be included in the residue definition.
Conversion factor (monitoring to risk assessment)	Open.

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

Animals covered	Goat and hen
Animal residue definition for monitoring	Dimethoate and omethoate, to be determined separately

Animal residue definition for risk assessment	Sum of dimethoate and 6 x omethoate expressed as dimethoate for acute risk assessment Sum of dimethoate and 3 x omethoate expressed as dimethoate for chronic risk assessment Residue definitions to be regarded as provisional. A feeding study is required also considering the potential transfer through the feed items of the metabolites **XXIII, XI** and **XX** in animal matrices if these metabolites are shown to be toxicologically pertinent.
Conversion factor (monitoring to risk assessment)	Open
Metabolism in rat and ruminant similar (yes/no)	Yes
Fat soluble residue: (yes/no)	No (log P_{ow} <4)

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

Confined rotational crop metabolism study with lettuce, turnip and wheat planted 30 and 120 days after a bare soil application of 0.56 kg as/ha (1.1 N dose rate). Given the low levels of total radioactive residues in the edible parts of the crops, no further metabolites' identification was requested.

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

Dimethoate and omethoate residues have been shown to be stable when frozen between -10ºC and -20ºC for up to 27 months in potato, orange fruit, sorghum grain/forage and cotton seed as well as cherries stored for 6 months. These data are sufficient to cover the storage periods for the sample in the residues trials sugar beet roots and tops – 8 months; and protected lettuce – 4.5 months.

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

	Ruminant:	Poultry:	Pig:
	Conditions of requirement of feeding studies		
Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no - If yes, specify the level)	Yes Max dairy = 1.46 mg/kg DM Max beef =1.61 mg/kg DM	No Max = 0.1 mg/kg DM	Yes Max = 1.39 mg/kg DM
Potential for accumulation (yes/no):	No	No	No

Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)	Yes (liver, milk)	No	N/A
	Feeding studies (Specify the feeding rate in cattle and poultry studies considered as relevant) Residue levels in matrices : Mean (max) mg/kg		
Muscle	Feeding study required	Not required	N/A
Liver		Not required	
Kidney		Not required	
Fat		Not required	
Milk			
Eggs		Not required	

N/A: Not applicable

Summary of critical residues data for dimethoate MRL setting (Annex IIA, point 6.3, Annex IIIA, point 8.2)

Crop	Northern or Mediterranean Region	Trials results relevant to the critical GAP **dimethoate (mg/kg)** (a)	Recommendation/comments	MRL	STMR (b)
Sugar beet root	North	3 x <0.02, 2 x <0.01		0.02*	0.02
Sugar beet tops	North	2 x <0.01, , 3 x <0.1	MRLs currently not set for tops		0.1
Sugar beet root	South	8 x <0.01		0.01*	0.01
Sugar beet tops	South	8 x <0.01	MRLs currently not set for tops		0.01
Lettuce (protected)	North	<0.01, 0.01, 2x0.02	application at GS BBCH 12-14	0.4(1)	0.02
		0.01, 0.06, 0.16, 0.17	application at GS BBCH 19 Recommendation is made to use dimethoate at the latest until growth stage 19 (9th true leave unfold) (EFSA, 2006).		

(a) Numbers of trials in which particular residue levels were reported *e.g.* 3 x <0.01, 1 x 0.01, 6 x 0.02, 1 x 0.04, 1 x 0.08, 2 x 0.1, 2 x 0.15, 1 x 0.17
(b) Supervised Trials Median Residue *i.e.* the median residue level estimated on the basis of supervised trials relating to the critical GAP
(1) Rounded OECD-MRL
* indicates that the MRL is set at the level of the LOQ

Summary of critical residues data for omethoate MRL setting (Annex IIA, point 6.3, Annex IIIA, point 8.2)

Crop	Northern or Mediterranean Region	Trials results relevant to the critical GAP **omethoate (mg/kg)** (a)	Recommendation/comments	MRL	STMR (b)
Sugar beet root	North	3 x <0.02, 2 x <0.01		0.02*	0.02
Sugar beet tops	North	0.01, 0.02, 3 x <0.1	MRLs currently not set for tops		0.1
Sugar beet root	South	8 x <0.01		0.01*	0.01
Sugar beet tops	South	4 x <0.01, 2 x 0.02, 0.03, 0.04	MRLs currently not set for tops		0.02

Lettuce (protected)	North	4x<0.01, 0.01	application at GS BBCH 12-14	0.07[(2)]	0.01
		<0.01, 2x0.03, 0.04	application at GS BBCH 19 Recommendation is made to use dimethoate at the latest until growth stage 19 (9th true leave unfold) (EFSA, 2006).		

[(2)] Rounded OECD-MRL
* indicates that the MRL is set at the level of the LOQ

Summary of critical residues data for ACUTE RISK ASSESSMENT (Annex IIA, point 6.3, Annex IIIA, point 8.2)

Crop	Northern or Mediterranean Region	Trials results relevant to the critical GAP **Sum of dimethoate and 6x omethoate expressed as dimethoate[(3)] (mg/kg)** (a)	Recommendation/comments	HR	STMR (b)
Sugar beet root	North		Not relevant for sugar beet root		
Sugar beet root	South				
Lettuce (protected)	North	<0.07, 0.07, 2x0.08	application at GS BBCH 12-14	0.40	0.08
		0.07, 0.24, 0.35, 0.40	application at GS BBCH 19		
[(3)] Omethoate residues were not corrected to be expressed as dimethoate, given that the MW of omethoate is very close (93%) to the MW of dimethoate.					
HRs and STMRs reported in this table do not include the contribution of metabolites* XXIII, XII, XX, XI *and may represent an underestimation of the actual toxicological burden the consumer is exposed to.					

Summary of critical residues data for CHRONIC RISK ASSESSMENT (Annex IIA, point 6.3, Annex IIIA, point 8.2)

Crop	Northern or Mediterranean Region	Trials results relevant to the critical GAP **Sum of dimethoate and 3x omethoate expressed as dimethoate[(4)] (mg/kg)** (a)	Recommendation/comments	HR	STMR (b)
Sugar beet root	North		Not relevant for sugar beet root		
Sugar beet root	South				
Lettuce (protected)	North	<0.04, 0.04, 2x0.05	application at GS BBCH 12-14	0.28	0.05
		0.04, 0.15, 0.26, 0.28	application at GS BBCH 19		
[(4)] Omethoate residues were not corrected to be expressed as dimethoate, given that the MW of omethoate is very close (93%) to the MW of dimethoate.					
HRs and STMRs reported in this table do not include the contribution of metabolites* XXIII, XII, XX, XI *and may represent an underestimation of the actual toxicological burden the consumer is exposed to.					

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

ADI -Dimethoate	0.001 mg/kg bw per day
IEDI (European diet) (% ADI) – EFSA Model rev.2A	2.7% of the ADI (ES, Adult) -STMR on lettuce (0.05 mg/kg)
ARfD-Dimethoate	0.01 mg/kg bw
IESTI (% ARfD) – EFSA Model rev.2A	Lettuce: 107% of ARfD (DE, Child) – HR: 0.4 mg/kg

Note that these chronic and acute exposure assessments must be considered as provisional and may represent underestimations of the actual toxicological burden the consumer is exposed to, as they consider only the combined effect of dimethoate and omethoate. Further data on metabolites XXIII, XII, XX, XI are needed before a robust risk assessment can be carried out.

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

Not required

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

	Dimethoate	Omethoate
Lettuce	0.4	0.07
Sugar beet	0.02*	0.02*

* indicates that the MRL is set at the level of the LOQ

Effects on non-target Species

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

Acute toxicity to mammals ‡	Dimethoate: Mouse LD_{50} (oral) 160 mg a.s./kg bw Omethoate: Rat LD_{50} (oral) 22 mg metabolite/kg bw
Reproductive toxicity to mammals ‡	Dimethoate: Rat NOEC 15 ppm a.s. in diet (1.2 mg a.s./kg bw per day) Omethoate: Rat NOEC 3 ppm metabolite in diet (0.4 mg metabolite/kg bw per day)
Acute toxicity to birds ‡	*Colinus virginianus* (Bobwhite quail). Dimethoate: LD_{50} (oral) 10.5 mg a.s./kg bw, NOEL 5 mg a.s./kg bw Omethoate: LD_{50} (oral) 9.9 mg metabolite/kg bw, NOEL 1.0 mg metabolite/kg bw *Phasianus colchicus* (Ring-necked pheasant). Dimethoate: LD_{50} (oral) 14.1 mg a.s./kg bw, NOEL 10 mg a.s./kg bw Omethoate: LD_{50} (oral) 29 mg a.s./kg bw, NOEL 2.5 mg a.s./kg bw Geometric mean (from studies on ring-necked pheasant, bobwhite quail, wild duck, common quail and white leghorn hen) Dimethoate: LD_{50} (oral) 30.9 mg a.s./kg bw
Dietary toxicity to birds ‡	*Colinus virginianus* (Bobwhite quail): Dimethoate: 5 day LC_{50} (oral) 154 ppm a.s. in diet (14.8 mg a.s. /kg bw per day), NOEC 36 ppm a.s. in diet. *Phasianus colchicus* (Ring-necked pheasant): Dimethoate: 5 day LC_{50} (oral) 396 ppm a.s. in diet (41.9 mg a.s./kg bw per day), NOEC 150 ppm a.s. in diet
Reproductive toxicity to birds ‡	*Colinus virginianus* (Bobwhite quail):: Dimethoate: NOEC 10.1 ppm a.s. in diet (1.0 mg a.s./kg bw per day) *Anas platyrhynchos* (Mallard duck): Dimethoate: NOEC 35.4 ppm a.s. in diet (5.8 mg a.s./kg bw per day)

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

Crop use & vertebrate category	Time scale	TER	Annex VI trigger
Sugar beet: 2 x 0.24 kg a.s./ha, 21 d interval (confirmatory data assessment)			
Small insectivorous bird	Acute	**0.81**	10
	Short-term dietary	**2.04**	10
	Long-term dietary	**0.14**	5

Crop use & vertebrate category	Time scale	TER	Annex VI trigger
Medium herbivorous bird	Acute Short-term dietary Long-term dietary	**0.55** **1.65** **0.21**	10 10 5
Skylark	Acute Short-term dietary Long-term dietary	**7.97** **9.25** **2.54**	10 10 5
Yellow wagtail	Acute Short-term dietary Long-term dietary	**5.26** **6.31** **0.426**	10 10 5
Small granivorous bird (via drinking water)	Acute (leaf scenario) Acute (puddle scenario) Long-term (puddle scenario)	**0.28** 183 5.92	10 10 5
Medium herbivorous mammal (dimethoate)	Acute Long-term dietary	22.8 **0.75**	10 5
Medium herbivorous mammal (omethoate)	Acute Long-term dietary	**3.26** **0.25**	10 5
Medium herbivorous mammal (dimethoate + omethoate)	Acute Long-term dietary	19 **2.85**	10 5
Small granivorous mammal (via drinking water)	Acute (puddle scenario) Long-term (puddle scenario)	1812 13.6	10 5

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

Species	Stage	Test Substance	Dose (kg as/ha)	Endpoint Effect	Annex VI Trigger
Laboratory tests ‡					
Aphidius rhopalo-siphi (aphid parasitoid)	Adult (48 hour exposure to glass plate deposit)	'Dimethoate 400g/L EC' ≡ 'Danidim Dimethoate'	0.01-0.018 g a.s. /ha	**% mortality** g a.s./ha = 40.2%* 0.02 g a.s./ha = 48.4% 0.04 g a.s./ha = 97.3%* 0.08 g a.s./ha =100%* 0.18 g a.s./ha = 100%* Untreated = 8% LR_{50} (95% CL) 0.014 g a.s./ha (0.012 - 0.017) (≡ 0.34 mL form^{n}/ha) **Reproductive capacity** Control = 11.9 mummies/female. No significant effect on reproductive capacity at 0.01 g (0.67 relative to control). Reproductive capacity not	30% effects at proposed maximum individual dose

Species	Stage	Test Substance	Dose (kg as/ha)	Endpoint Effect	Annex VI Trigger
				determined at higher test concns. due to high adult mortality	
Typhlo-dromus pyri (predatory mite)	Adult (48 hour exposure to glass plate deposit)	'Dimethoate 400g/L EC' ≡ 'Danidim Dimethoate'	0.13-13.36 g a.s./ha	**% mortality** 0.13 g a.s./ha = 0% 0.42 g a.s./ha = 6.3% 1.34 g a.s./ha = 28.1%* 4.18 g a.s./ha =76.0%* 13.36 g a.s./ha = 94.8%* Untreated = 4% LR_{50} (95% CL) 2.24 g a.s./ha (1.88 – 2.66) (Equivalent to 5.36 mL form^{n}./ha) **Reproductive capacity** Control 9.1 offspring/female. Reproductive capacity relative to control 0.95, 0.77, 0.69*, at 0.13, 0.42 and 1.34 g a.s./ha. Reproductive capacity not determined at higher test concentrations due to high adult mortality	30% effects at proposed maximum individual dose
Aphidius rhopalo-siphi (aphid parasitoid)	Adult female (48 hour exposure to foliar deposit)	'Dimethoate 400g/L EC' ≡ 'Danidim Dimethoate'	1.5-748 g a.s. /ha	**% mortality** Exposure to 0 day old residues: 3.6 mL product /ha: **78%** 27-1800 mL product /ha: **100%** Water control: 0% Exposure to 7 day old residues: 3.6 mL product /ha: **52%** 27 mL product /ha: **80%** 900-1800 mL product /ha: **94-100%** *** Water control: 4% Exposure to 14 day old residues: 3.6 mL product /ha: 2% ns 27 mL product /ha: 4% ns 900 mL product /ha: 6% ns 1500-1800 mL product /ha: **96-100%** *** Water control: 6% Exposure to 21 day old residues: 900 mL product /ha: 12% ns 1500 mL product /ha: 18% ns 1800 mL product /ha: 14% ns Water control: 8% **No. parasitised aphids /female)** Exposure to 14 day old residues: 3.6 mL product /ha: 23 ns 27 mL product /ha: 20 ns 900 mL product /ha: 16 ns Water control: 18	30% effects at proposed maximum individual dose

Species	Stage	Test Substance	Dose (kg as/ha)	Endpoint Effect	Annex VI Trigger
				Exposure to 21 day old residues: 900 mL product /ha: 22 ns 1500 mL product /ha: 23 ns 1800 mL product /ha: 26 ns Water control: 31	
Chryso-perla carnea (lacewing)	Larvae (48 hour exposure to foliar deposit)	'Dimethoate 400g/L EC' ≡ 'Danidim Dimethoate'	1.5-748 g a.s. /ha	**% corrected mortality** Larval exposure to 0 day old residues: 3.6 mL product /ha: 3% ns 900 mL product /ha: **92%** 1800 mL product /ha: **100%** Larval exposure to 7 day old residues: 900 mL product /ha: **39%** 1800 mL product /ha: **67%** Larval exposure to 14 day old residues: 900 mL product /ha: 6% ns 1800 mL product /ha: **39%** Larval exposure to 21 day old residues: 1800 mL product /ha: 0% **Eggs/female/day & % egg viability)** Larval exposure to 0 day old residues: 3.6 mL product /ha: 30 ns; 90%. Control: 31; 91% Larval exposure to 14 day old residues: 900 mL product /ha: 35 ns; 87% Control: 28; 87% Larval exposure to 21 day old residues: 1800 mL product /ha: 36 ns; 89% Control: 35; 89%	30% effects at proposed maximum individual dose
Aphidius rhopalo-siphi (aphid parasitoid)	Adult female (48h exposure to foliar deposit) Ext. lab. study.	'BAS 152 59 I', an EC (404.2 g/L dimethoate)	0.75-12.0 g a.s. /ha	'BAS 152 59 I' LR_{50} = 7.68 mL/ha (= 3.07 g dimethoate/ha) (a <50% effect on mortality and fecundity were apparent ≤ 1.5 g dimethoate/ha).	ESCORT II <50%

* Statistically significant difference from the control

Field or semi-field tests

Details were submitted for a large number of cereal field trials examining the effects on non-target arthropod populations of a single spray of 340-500g dimethoate/ha, made mostly in the spring or early summer, with a few trials including autumn application. Use at these rates resulted in high initial levels of mortality of a broad range of non-target arthropods, with recovery or partial recovery of the vast majority of groups within 4-7 weeks. Lack of prey sometimes accounted for incomplete in-crop recovery of predator numbers. Ground dwelling predators (e.g. carabids) showed a variable recovery rate in the reported trials, with re-establishment times of between 7 days and 6 months.

Details from cereal and apple orchard field trials using low doses of dimethoate indicate no effects on non-target arthropods from respective use rates of 1.44 g and 10.8 g a.s./ha.

Risk to non-target arthropods

Sugar beet 2 x 0.24 kg a.s./ha:

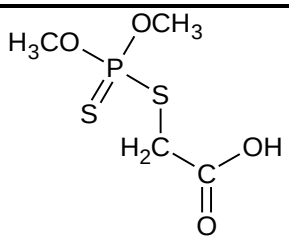
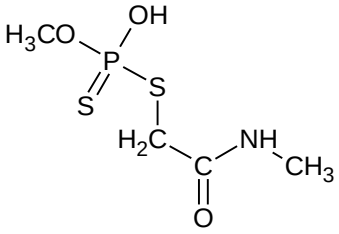
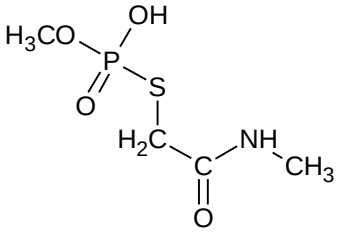
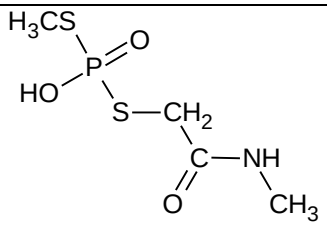
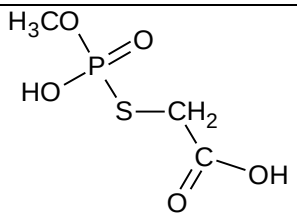
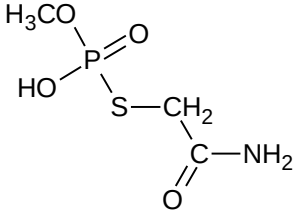
Test substance	Species	Effect (LR_{50} g a.s./ha)	HQ in-field	HQ off-field (1 m)	Trigger
'Dimethoate 400g/L EC'	*Typhlodromus pyri*	2.24	17100	475	2
'Dimethoate 400g/L EC'	*Aphidius rhopalosiphi*	0.014	107	2.97	2

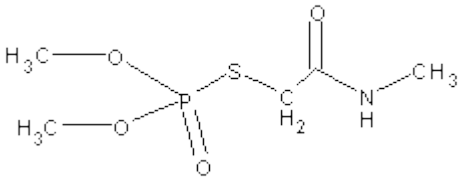
NTA buffer zones

Crop	Application rate (g a.s./ha)	No effect off-field drift (% application rate)	Acceptable drift distance (m) (acceptable drift % application rate) no.applications =1(MAF)	Acceptable drift distance (m) (acceptable drift % application rate) no.applications=GAP
Lettuce (G/NEU)	340	nr	nr	nr
Sugar beet (F/ NEU&SEU)	240	-	5 (Drift = 1.3 g a.s./ha)[1]	5 (Drift = 1.3 g a.s./ha)[1]

[1] based on cereal field study no effect levels

APPENDIX B – USED COMPOUND CODE(S)

Code/Trivial name*	Chemical name**	Structural formula**
Metabolite III *dimethoate carboxylic acid*	[(dimethoxyphosphorothioyl)sulfanyl]acetic acid	
Metabolite X *desmethyl dimethoate*	*O*-methyl *S*-[2-(methylamino)-2-oxoethyl] hydrogen phosphorodithioate	
Metabolite XI *O-desmethyl omethoate*	*O*-methyl *S*-[2-(methylamino)-2-oxoethyl] hydrogen phosphorothioate	
Metabolite XII *des-O-methyl isodimethoate*	*S*-methyl *S*-[2-(methylamino)-2-oxoethyl] hydrogen phosphorodithioate	
Metabolite XX *O-desmethyl-omethoate-carboxylic acid*	{[hydroxy(methoxy)phosphoryl]sulfanyl}acetic acid	
Metabolite XXIII *O-desmethyl-N-desmethyl omethoate*	*S*-(2-amino-2-oxoethyl) *O*-methyl hydrogen phosphorothioate	

Omethoate	2-dimethoxyphosphinoylthio-*N*-methylacetamide	

* The metabolite name in bold is the name used in the conclusion.
** ACD/ChemSketch, Advanced Chemistry Development, Inc., ACD/Labs Release: 12.00 Product version: 12.00 (Build 29305, 25 Nov 2008)

ABBREVIATIONS

a.s.	active substance
ACD	Advanced Chemistry Development
AChE	acetylcholinesterase
ADE	actual dermal exposure
ADI	acceptable daily intake
AOEL	acceptable operator exposure level
AR	applied radioactivity
ARfD	acute reference dose
bw	body weight
ChE	cholinesterase
CL	confidence limits
CLP	classification and labelling proposal
d	day
DAR	draft assessment report
DM	dry matter
DT_{50}	period required for 50 percent disappearance (define method of estimation)
EC	emulsifiable concentrate
ECHA	European Chemical Agency
EFSA	European Food Safety Authority
EU	European Union
f(twa)	time weighted average factor
g	gram
GAP	good agricultural practice
GS	growth stage
h	hour(s)
ha	hectare
HQ	hazard quotient
HR	highest residue
IEDI	international estimated daily intake
IESTI	international estimated short-term intake
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint Meeting on 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)
kg	kilogram
L	litre
LC_{50}	lethal concentration, median
LD_{50}	lethal dose, median; dosis letalis media
LOAEL	lowest observable adverse effect level
LOQ	limit of quantification (determination)
LR_{50}	lethal rate, median
MAF	multiple application factor
mg	milligram
mL	millilitre
MRL	maximum residue limit or level
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOER	no observed effect rate
ns	not surviving
NTE	neuropathy target esterase
OECD	Organisation for Economic Co-operation and Development
PD	proportion of different food types

PHI	pre-harvest interval
P_{ow}	partition coefficient between *n*-octanol and water
RBC	red blood cells (erythrocytes)
RMS	Rapporteur Member State
RUD	residue per unit dose
SETAC	Society of Environmental Toxicology and Chemistry
STMR	supervised trials median residue
TEF	toxicity equivalence factor
TER	toxicity exposure ratio
TRR	total radioactive residue