CONCLUSION ON PESTICIDE PEER REVIEW

Conclusion on the peer review of the pesticide risk assessment of the active substance 1,4-diaminobutane (putrescine)[1]

European Food Safety Authority[2]

European Food Safety Authority (EFSA), Parma, Italy

SUMMARY

1,4-Diaminobutane (putrescine) is one of the 295 substances of the fourth stage of the review programme covered by Commission Regulation (EC) No 2229/2004,[3] as amended by Commission Regulation (EC) No 1095/2007.[4]

1,4-Diaminobutane was included in Annex I to Directive 91/414/EEC on 1 September 2009 pursuant to Article 24b of the Regulation (EC) No 2229/2004 (hereinafter referred to as 'the Regulation'), and has subsequently been deemed to be approved under Regulation (EC) No 1107/2009,[5] in accordance with Commission Implementing Regulation (EU) No 540/2011,[6] as amended by Commission Implementing Regulation (EU) No 541/2011.[7] In accordance with Article 25a of the Regulation, as amended by Commission Regulation (EU) No 114/2010,[8] the European Food Safety Authority (EFSA) is required to deliver by 31 December 2012 its view on the draft review report submitted by the European Commission in accordance with Article 25(1) of the Regulation. This review report was established as a result of the initial evaluation provided by the designated rapporteur Member State in the Draft Assessment Report (DAR). The EFSA therefore organised a peer review of the DAR. The conclusions of the peer review are set out in this report.

Austria being the designated rapporteur Member State submitted the DAR on 1,4-diaminobutane in accordance with the provisions of Article 22(1) of the Regulation, which was received by the EFSA on 28 November 2007. The peer review was initiated on 25 June 2008 by dispatching the DAR to the notifier Suterra LLC, and on 16 December 2010 to the Member States, for consultation and comments. Following consideration of the comments received on the DAR, it was concluded that there was no need to conduct an expert consultation and that the EFSA should deliver its conclusions on 1,4-diaminobutane.

The conclusions laid down in this report were reached on the basis of the evaluation of the representative uses of 1,4-diaminobutane as an insect attractant in orchards (fruit crops), citrus and other crops where *Ceratitis capitata* (Mediterranean fruit fly) causes damage, as proposed by the notifier at the time of submission. Full details of the representative uses can be found in Appendix A to this report.

[1] On request from the European Commission, Question No EFSA-Q-2009-00266, approved on 16 December 2012.
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[3] OJ L 379, 24.12.2004, p.13
[4] OJ L 246, 21.9.2007, p.19
[5] OJ L 309, 24.11.2009, p.1
[6] OJ L 153, 11.6.2011, p.1
[7] OJ L 153, 11.6.2011, p.187
[8] OJ L 37, 10.2.2010, p.12

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Data gaps were identified in the section on identity, physical and chemical properties and analytical methods.

No data gaps or critical areas of concern were identified in the mammalian toxicology section.

No data gaps or critical areas of concern were identified in the residue section.

Data gaps were identified for satisfactory information on the ready biodegradability of 1,4-diaminobutane and information on its hydrolytic stability under sterile conditions. Most importantly, there is a data gap for a comparison of the estimated quantity of 1,4-diaminobutane that may reach the different environmental compartments (primarily air but also soil, groundwater and surface water), consequent to the representative use assessed, compared to natural background levels. The environmental exposure assessment could not be finalised in the absence of this information.

Two data gaps were identified in the ecotoxicology section. Pending on the outcome of the fate and behaviour assessment, the risk of 1,4-diaminobutane to non-target species should be addressed. The mandatory toxicity studies with aquatic organisms should be submitted.

No critical areas of concern were identified.

KEY WORDS

1,4-diaminobutane, putrescine, peer review, risk assessment, insect attractant

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BACKGROUND

1,4-Diaminobutane is one of the 295 substances of the fourth stage of the review programme covered by Commission Regulation (EC) No 2229/2004,[9] as amended by Commission Regulation (EC) No 1095/2007.[10]

1,4-Diaminobutane was included in Annex I to Directive 91/414/EEC on 1 September 2009 pursuant to Article 24b of the Regulation (EC) No 2229/2004 (hereinafter referred to as 'the Regulation'), and has subsequently been deemed to be approved under Regulation (EC) No 1107/2009,[11] in accordance with Commission Implementing Regulation (EU) No 540/2011,[12] as amended by Commission Implementing Regulation (EU) No 541/2011.[13] In accordance with Article 25a of the Regulation, as amended by Commission Regulation (EU) No 114/2010,[14] the European Food Safety Authority (EFSA) is required to deliver by 31 December 2012 its view on the draft review report submitted by the European Commission in accordance with Article 25(1) of the Regulation (European Commission, 2008). This review report was established as a result of the initial evaluation provided by the designated rapporteur Member State in the Draft Assessment Report (DAR). The EFSA therefore organised a peer review of the DAR. The conclusions of the peer review are set out in this report.

Austria being the designated rapporteur Member State submitted the DAR on 1,4-diaminobutane in accordance with the provisions of Article 22(1) of the Regulation, which was received by the EFSA on 28 November 2007 (Austria, 2007). The peer review was initiated on 25 June 2008 by dispatching the DAR to the notifier Suterra LLC, and on 16 December 2010 to the Member States, for consultation and comments. In addition, the EFSA conducted a public consultation on the DAR. The comments received were collated by the EFSA and forwarded to the rapporteur Member State for compilation and evaluation in the format of a Reporting Table. The notifier was invited to respond to the comments in column 3 of the Reporting Table. At that time the notifier indicated that they have withdrawn support for the substance. . The comments were evaluated by the rapporteur Member State in column 3 of the Reporting Table.

The scope of the peer review was considered in a telephone conference between the EFSA, the rapporteur Member State, and the European Commission on 5 April 2011. On the basis of the comments received and the rapporteur Member State's evaluation thereof it was concluded that there was no need to conduct an expert consultation.

The outcome of the telephone conference, together with EFSA's further consideration of the comments is reflected in the conclusions set out in column 4 of the Reporting Table. All points that were identified as unresolved at the end of the comment evaluation phase and which required further consideration were compiled by the EFSA in the format of an Evaluation Table.

The conclusions arising from the consideration by the EFSA, and as appropriate by the rapporteur Member State, of the points identified in the Evaluation Table were reported in the final column of the Evaluation Table.

A final consultation on the conclusions arising from the peer review of the risk assessment took place with Member States via a written procedure in November/December 2011.

This conclusion report summarises the outcome of the peer review of the risk assessment on the active substance and the representative formulation evaluated on the basis of the representative uses as an insect attractant in orchards (fruit crops), citrus and other crops where *Ceratitis capitata* (Mediterranean fruit fly) causes damage, as proposed by the notifier. A list of the relevant end points

[9] OJ L 379, 24.12.2004, p.13
[10] OJ L 246, 21.9.2007, p.19
[11] OJ L 309, 24.11.2009, p.1
[12] OJ L 153, 11.6.2011, p.1
[13] OJ L 153, 11.6.2011, p.187
[14] OJ L 37, 10.2.2010, p.12

for the active substance as well as the formulation is provided in Appendix A. In addition, 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 initial commenting phase to the conclusion. The Peer Review Report (EFSA, 2011) comprises the following documents, in which all views expressed during the course of the peer review, including minority views, can be found:

- the comments received on the DAR,
- the Reporting Table (5 April 2011),
- the Evaluation Table (9 December 2011),
- the comments received on the draft EFSA conclusion.

Given the importance of the DAR including its addendum (compiled version of May 2011 containing all individually submitted addenda (Austria, 2011)) and the Peer Review Report, both documents are considered respectively as background documents A and B to this conclusion.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Butane-1,4-diamine (IUPAC) notified as 1,4-diaminobutane or putrescine is considered by the International Organization for Standardization not to require a common name.

The representative formulated product for the evaluation was 'BioLure Med Fly', a vapour releasing product, (VP) consisting of three individual, retrievable, polymeric, hand-applied dispensers used in combination to make one plant protection preparation, containing 2.7 g/kg 1,4-diaminobutane, 91 g/kg trimethylamine hydrochloride and 211.3 g/kg ammonium acetate, registered under different trade names in several EU countries.

The representative uses evaluated comprise application by hand of the dispensers into physical traps in orchards, where *Ceratitis capitata* (Mediterranean fruit fly) causes damage, as an insect attractant. It should be emphasized however that the product is not used alone for mass trapping, but in combination with insecticides for the control of *C. capitata.* Full details of the GAP can be found in the list of end points in Appendix A.

CONCLUSIONS OF THE EVALUATION

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

The following guidance document was followed in the production of this conclusion: SANCO/3030/99 rev.4 (European Commission, 2000).

The minimum purity of 1,4-diaminobutane is open as a data gap was identified for five batch data according to GLP. No FAO specification exists.

The assessment of the data package revealed no issues that need to be included as critical areas of concern with respect to the identity of the active substance, however data gaps were identified for additional information concerning the starting materials of the manufacturing process and the analytical method used for the determination of the specified impurity in the batch analysis. With respect to the physical, chemical and technical properties of 1,4-diaminobutane and the representative formulation, data gaps were identified for the vapour pressure of the active substance, Henry's law constant, and a shelf-life study of the preparation.

Data gaps were also identified for validated methods for the determination of the active substance in the technical material and for the determination of the content of active substance in the respective dispenser for monitoring purposes.

The need for methods of analysis for monitoring this compound in food of plant and animal origin have been waived due to the specific kind of application. Data gaps need to be filled (see section 4) before a conclusion on the need for monitoring methods in the environment can be finalised. A method for body fluids and tissues is not required as the active substance is not classified as toxic or very toxic.

2. Mammalian toxicity

The toxicological database submitted for 1,4-diaminobutane was mainly composed of published studies, with limited applicability for regulatory use.

1,4-Diaminobutane is harmful if swallowed and in contact with skin (R22 and R21 proposed). As no acute inhalation studies were available, the notifier proposed classification as R20 ("Harmful by inhalation"). It is corrosive to skin and eyes (R34 proposed). No studies were submitted to test the skin sensitisation potential. The relevant short-term oral toxicity No Observed Adverse Effect Level (NOAEL) is 180 mg/kg bw/day, based on decreased food consumption (male rats), decreased body weight, and increased alanineaminotransferase and relative brain weight in females. 1,4-Diaminobutane did not show any genotoxic potential, however no long-term toxicity and

carcinogenicity studies were submitted. In a developmental study of limited validity no teratogenicity was observed. In an intraperitoneal acute toxicity study in rats, reversible neurological effects (locomotor hyperactivity and wet dog shakes at 100 mg/kg bw; coordination deficits, atony and sedation at 150 and 200 mg/kg bw) were fully reversible at non-lethal doses (up to 150 mg/kg bw).

For the representative use, the vapour releasing dispensers of the preparation 'BioLure Med Fly' are placed inside physical traps and the active substances, which are fully contained within the polymeric dispensers, do not come into contact with crops, therefore, an Acceptable Daily Intake (ADI) and an Acute Reference Dose (ARfD) were not established. Because of the very limited available data set, it was considered not possible to set an AOEL for 1,4-diaminobutane, however, due to the limited exposure to 1,4-diaminobutane arising from the representative use, an AOEL is not needed for a risk assessment for the operator. Similarly, no worker and bystander exposure is expected.

3. Residues

This conclusion is based on the guidance documents listed in the document 1607/VI/97 rev.2 (European Commission, 1999).

According to the representative uses, 1,4-diaminobutane (putrescine) is contained in a vapour releasing dispenser with two other individual active substances (i.e trimethylamine hydrochloride and ammonium acetate) in the preparation 'BioLure Med Fly'. The active substances are placed inside hand-applied physical traps in the canopy of the trees, and, held within the dispensers, never come into direct contact with the crops. It can also be reasonably assumed that residues of 1,4-diaminobutane on fruits through volatilisation and deposition will be insignificant. Therefore a quantitative consumer dietary risk assessment can be waived due to the specific kind of application.

4. Environmental fate and behaviour

Satisfactory data on the vapour pressure and consequently estimates of the Henry's Law constant of 1,4-diaminobutane were not available. 1,4-Diaminobutane is reported by the notifier to be volatile, and in order to be effective in the way described it would need to be volatile. Information on hydrolysis under sterile conditions (water solubility is 883g/L) and ready biodegradability in the presence of a sewage sludge inoculum were not available. Consequently, data gaps were identified for this missing information. As 1,4-diaminobutane is placed as an attractant in traps for mass trapping, the primary route of exposure to the environment is via volatilisation to air. In the upper atmosphere 1,4-diaminobutane will not be expected to be subject to long-range atmospheric transport as it was estimated to have a half-life in the upper atmosphere of < 2 days as a consequence of indirect photodegradation reactions with hydroxyl radicals (0.162 days estimated by quantitative structure activity relationship calculation). The notifier made the case that exposure to the environmental compartments including air would be low and within the range of naturally occurring background levels. Consequently further data on the route and rate of degradation of 1,4-diaminobutane in soil and natural surface water systems and an assessment of the potential for the exposure of groundwater were proposed to be unnecessary. However, as the dossier provided no estimates of the naturally occurring background levels of 1,4-diaminobutane (neither in air nor the other compartments), it was not possible to validate that this was in fact the case. Therefore a data gap was identified for the provision of a comparison of the estimated quantity of 1,4-diaminobutane that may reach the different environmental compartments, consequent to the representative use assessed, compared to natural background levels.

5. Ecotoxicology

The risk to non-target organisms could be considered as low for the representative use providing the exposure is below the background level of 1,4-diaminobutane. However, in view of the data gap identified in section 4 for information on the background level, the ecotoxicology risk assessment could not be finalised. A data gap is identified to re-consider the risk assessment to non-target organisms once such information is available. Additionally a data gap was identified for the acute toxicity studies with aquatic organisms to fulfil the Annex II data requirements.

6. Overview of the risk assessment of compounds listed in residue definitions triggering assessment of effects data for the environmental compartments

6.1. Soil

Compound (name and/or code)	Persistence	Ecotoxicology
1,4-Diaminobutane alone, but provisional in the absence of a comparison with natural background concentrations.	Data Gap. Not relevant if it is demonstrated that levels in soil consequent to the use would not be above natural background concentrations.	Data gap pending on the information on the background level.

6.2. Ground water

Compound (name and/or code)	Mobility in soil	>0.1 µg/L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)[(a)]	Pesticidal activity	Toxicological relevance	Ecotoxicological activity
1,4-Diaminobutane alone, but provisional in the absence of a comparison with natural background concentrations.	Data Gap. Not relevant if it is demonstrated that levels in soil consequent to the use would not be above natural background concentrations.	Data gap. Not relevant if it is demonstrated that levels in soil consequent to the use would not be above natural background concentrations.	–	Yes	Data gap pending on the information on the background level.

(a): EFSA's reading of the Council Directive 98/83/EC[15] on the quality of drinking water intended for human consumption is that, as an attractant, 1,4-diaminobutane is not considered a pesticide under this directive, so the parametric drinking water limit of 0.1µg/L for pesticides, usually used as a decision-making criteria regarding groundwater exposure, does not apply. However a groundwater exposure estimate to enable a risk assessment from the human consumption of groundwater as drinking water and an aquatic risk assessment, in the situation that groundwater becomes surface water, would be appropriate if soil exposure would be demonstrated to be above natural background concentrations.

[15] OJ L 330, 5.12.1998, p.32

6.3. Surface water and sediment

Compound (name and/or code)	**Ecotoxicology**
1,4-Diaminobutane alone, but provisional in the absence of a comparison with natural background concentrations.	Data gap pending on the information on the background level

6.4. Air

Compound (name and/or code)	**Toxicology**
1,4-Diaminobutane	Harmful by inhalation (no data available).

7. List of studies to be generated, still ongoing or available but not peer reviewed

This is a complete list of the data gaps identified during the peer review process, including those areas where a study may have been made available during the peer review process but not considered for procedural reasons (without prejudice to the provisions of Article 7 of Directive 91/414/EEC concerning information on potentially harmful effects).

- Five batch data according to GLP (relevant for all representative uses evaluated; submission date proposed by the notifier: the notifier has indicated that they have withdrawn their support for this substance; see section 1).

- Additional information concerning the starting materials of the manufacturing process (relevant for all representative uses evaluated; submission date proposed by the notifier: the notifier has indicated that they have withdrawn their support for this substance; see section 1)

- Additional information concerning the analytical method used for the determination of the specified impurity in the batch analysis (relevant for all representative uses evaluated; submission date proposed by the notifier: the notifier has indicated that they have withdrawn their support for this substance; see section 1).

- Validated method for the determination of the active substance in the technical material and for the determination of the content of active substance in the respective dispenser for monitoring purposes (relevant for all representative uses evaluated; submission date proposed by the notifier: the notifier has indicated that they have withdrawn their support for this substance; see section 1).

- Vapour pressure of 1,4-diaminobutane, and Henry's law constant (relevant for all representative uses evaluated; submission date proposed by the notifier: the notifier has indicated that they have withdrawn their support for this substance; see section 1).

- Shelf life study of the preparation (relevant for all representative uses evaluated; submission date proposed by the notifier: the notifier has indicated that they have withdrawn their support for this substance; see section 1).

- Information on the hydrolysis of 1,4-diaminobutane under sterile conditions at pH 5, 7 and 9 (relevant for all representative uses evaluated; submission date proposed by the notifier: the notifier has indicated that they have withdrawn their support for this substance; see section 4).

- Satisfactory information on the 'ready biodegradability' of 1,4-diaminobutane (relevant for all representative uses evaluated; submission date proposed by the notifier: the notifier has indicated that they have withdrawn their support for this substance; see section 4).

- A comparison of the estimated quantity of 1,4-diaminobutane that may reach the different environmental compartments consequent to the representative use assessed compared to natural background levels that can occur (relevant for all representative uses evaluated; submission date proposed by the notifier: the notifier has indicated that they have withdrawn their support for this substance; see sections 4 and 5).

- Acute toxicity studies with aquatic organisms to fulfil the Annex II data requirements (relevant for all representative uses evaluated; submission date proposed by the notifier: the notifier has indicated that they have withdrawn their support for this substance; see section 5).

- Ecotoxicology risk assessment should be re-considered based on the information on the background levels of 1,4-diaminobutane (relevant for all representative uses evaluated; submission date proposed by the notifier: the notifier has indicated that they have withdrawn their support for this substance; see section 5).

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

None.

9. Concerns

9.1. 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 environmental exposure assessment to air and consequently due to potential wet and dry deposition, the exposure assessment for soil, groundwater and surface water. Consequently the risk assessment for non-target organisms could not be finalised.

9.2. 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.

9.3. Overview of the concerns for each representative use considered

(If a particular condition proposed to be taken into account to manage an identified risk, as listed in section 8, has been evaluated as being effective, then 'risk identified' is not indicated in this table.)

Representative use		**Fruit crops, citrus and other crops where *C. capitata* causes damage**
Operator risk	Risk identified	
	Assessment not finalised	
Worker risk	Risk identified	
	Assessment not finalised	
Bystander risk	Risk identified	
	Assessment not finalised	
Consumer risk	Risk identified	
	Assessment not finalised	
Risk to wild non target terrestrial vertebrates	Risk identified	
	Assessment not finalised	X[1]
Risk to wild non target terrestrial organisms other than vertebrates	Risk identified	
	Assessment not finalised	X[1]
Risk to aquatic organisms	Risk identified	
	Assessment not finalised	X[1]
Groundwater exposure active substance	Legal parametric value breached	
	Assessment not finalised	X[1]
Groundwater exposure metabolites	Legal parametric value breached	
	Parametric value of 10µg/L[(a)] breached	
	Assessment not finalised	X[1]
Comments/Remarks		

The superscript numbers in this table relate to the numbered points indicated in sections 9.1 and 9.2. Where there is no superscript number see sections 2 to 6 for further information. A column is greyed out if there is a concern for that specific use.

(a): Value for non-relevant metabolites prescribed in SANCO/221/2000-rev 10-final, European Commission, 2003

REFERENCES

Austria, 2007. Draft Assessment Report (DAR) on the active substance 1,4-diaminobutane (putrescine) prepared by the rapporteur Member State Austria in the framework of Directive 91/414/EEC, November 2007.

Austria, 2011. Final Addendum to Draft Assessment Report on 1,4-diaminobutane, compiled by EFSA, May 2011.

EFSA (European Food Safety Authority), 2011. Peer Review Report to the conclusion regarding the peer review of the pesticide risk assessment of the active substance 1,4-diaminobutane.

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, 10/6/1999.

European Commission, 2000. Technical Material and Preparations: Guidance for generating and reporting methods of analysis in support of pre- and post-registration data requirements for Annex II (part A, Section 4) and Annex III (part A, Section 5) of Directive 91/414. SANCO/3030/99.

European Commission, 2003. Guidance document on assessment of the relevance of metabolites in groundwater of substances regulated under council directive 91/414/EEC. SANCO/221/2000-rev 10-final, 25 February 2003.

European Commission, 2008. Review report for the active substance 1,4-Diaminobutane (Putrescine). Finalised in the Standing Committee on the Food Chain and Animal Health at its meeting on 28 October 2008 in view of the inclusion of 1,4-Diaminobutane (Putrescine) in Annex I of Directive 91/414/EEC. SANCO/2626/08 – rev. 1. 12 August 2008.

APPENDICES

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

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

Active substance (ISO Common Name) ‡	1,4-diaminobutane (putrescine) (No ISO common name)
Function (*e.g.* fungicide)	food attractant

Rapporteur Member State	Austria
Co-rapporteur Member State	Not relevant

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	butane-1,4-diamine
Chemical name (CA) ‡	1,4-diaminobutane
CIPAC No ‡	854
CAS No ‡	110-60-1
EC No (EINECS or ELINCS) ‡	203-782-3
FAO Specification (including year of publication) ‡	No specification exists at the time of evaluation
Minimum purity of the active substance as manufactured ‡	Open
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	No relevant impurities are identified
Molecular formula ‡	$C_4H_{12}N_2$
Molecular mass ‡	88.15 g/mol
Structural formula ‡	

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	26.8°C ± 0.4 (998 g/kg)
Boiling point (state purity) ‡	167°C ± 3.5 (998 g/kg)
Temperature of decomposition (state purity)	Not relevant
Appearance (state purity) ‡	White solid or colourless liquid Clear liquid > 27 °C; Crystalline < 27 °C (998 g/kg)
Vapour pressure (state temperature, state purity) ‡	Data gap
Henry's law constant ‡	Data gap
Solubility in water (state temperature, state purity and pH) ‡	883.2 g/L ± 7.36 at 23 °C
Solubility in organic solvents ‡ (state temperature, state purity)	Solubility in ether (998 g/kg) 47.49 g/L ± 0.37 at 23 °C
Surface tension ‡ (state concentration and temperature, state purity)	Not required
Partition co-efficient ‡ (state temperature, pH and purity)	- 0.64 No information with respect to temperature, pH and purity
Dissociation constant (state purity) ‡	Not required
UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	Not required as section fate and behaviour does not indicate any concern
Flammability ‡ (state purity)	Not required Flash point: 63 - 64 °C
Explosive properties ‡ (state purity)	Not required Lower (LEL): 0.7 vol % Upper (UEL): 11.2 vol %
Oxidising properties ‡ (state purity)	Not oxidising (statement)

Summary of representative uses evaluated [1,4-Diaminobutane (Putrescine)]

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 (days) (l)	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)	kg as/hL**) min max	water L/ha**) min max	kg as/ha**) min max		
Orchards (Fruit Crops)	Southern Europe	BioLure® Med Fly	F	Mediterranean Fruit Fly *(Ceratitis capitata)*	VP	0.27 % (0.05 g as per trap)	Ground application by hand of dispensers into physical traps	Monitoring: Begin of flight of *C. capitata* Monitoring and Mass Trapping: Begin of flight of *C. capitata* or specifically when fruits become susceptible to damage	Monitoring Orchards: 3 Citrus: 5 Other: 2 Mass Trapping: Orchards: 1 Citrus: 2 Other: 1	Approx: 6 – 8 weeks Depends upon environ-mental factors such as climate and topography	--	--	Orchards: 75 – 100 traps/ha Emission rate*): 0.0031 to 0.0041 mg a.s./m^3/day	0	
Citrus													Citrus: Min: 50 traps/ha Emission rate*): 0.0021 mg a.s./m^3/day		
Other crops where *C. capitata* causes damage													Other crops: 50-100 traps/ha Emission rate*): 0.0021 to 0.0041 mg a.s./m^3/day		

*) Calculated on the base of the medium height of crops where BioLure® Med Fly is applied (citrus and orchards) is 2.5 m, resulting in a volume of 25 000 m^3 air/ha.
The dispensers release the active substances over a period of 6 to 8 weeks (average 49 days).
**) does not apply

Remarks:

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

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

(c) eg. biting and suckling insects, soil born insects, foliar fungi, weeds

(d) eg. wettable powder (WP), emulsifiable concentrate (EC), granule (GR)

(e) GCPF Codes - GIFAP Technical Monograph No 2, 1989

(f) All abbreviations used must be explained

(g) Method, eg. high volume spraying, low volume spraying, spreading, dusting, drench

(h) Kind, eg. overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated

(i) g/kg or g/l

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

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

(l) PHI - minimum pre-harvest interval

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

Methods of Analysis

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

Technical as (analytical technique)	Validated method is required
Impurities in technical as (analytical technique)	Open
Plant protection product (analytical technique)	Validated methods are required

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		No residue definition is required.
Food of animal origin		No residue definition is required.
Soil		Data gaps need to be filled before this can be finalised
Water	surface	Data gaps need to be filled before this can be finalised
	drinking/ground	Data gaps need to be filled before this can be finalised
Air		1,4-diaminobutane

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	Not relevant as no MRLs are required.
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	Not relevant as no MRLs are required.
Soil (analytical technique and LOQ)	Open
Water (analytical technique and LOQ)	Open
Air (analytical technique and LOQ)	Open
Body fluids and tissues (analytical technique and LOQ)	Not relevant, active substance is not classified toxic or very toxic.

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

	RMS/peer review proposal
Active substance	None

Impact on Human and Animal Health

The toxicological database was considered of limited validity

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

Rate and extent of oral absorption ‡	No data available, not needed
Distribution ‡	Widely distributed, highest levels found in muscle, liver and kidney (i.p. application in rats, oral administration in chicks)
Potential for accumulation ‡	No evidence for bioaccumulation
Rate and extent of excretion ‡	No data available, not needed
Metabolism in animals ‡	Intracellular putrescine levels are tightly regulated by de novo synthesis, interconversion, terminal degradation and transport
Toxicologically relevant compounds ‡ (animals and plants)	Parent compound
Toxicologically relevant compounds ‡ (environment)	Parent compound

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	463 mg/kg bw (females)	R22
Rat LD_{50} dermal ‡	1576 mg/kg bw (males)	R21
Rat LC_{50} inhalation ‡	No data available, not needed notifier proposed R20	R20
Skin irritation ‡	Corrosive	R34
Eye irritation ‡	Severe damage to eyes (R41 is overruled by R34)	-
Skin sensitisation ‡	No data available, not needed	

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	food consumption ↓ (males); body weight ↓, ALAT ↑ and relative brain weight ↑ (females)	
Relevant oral NOAEL ‡	5 weeks, rat: 180 mg/kg bw/d	
Relevant dermal NOAEL ‡	No data available – not needed	
Relevant inhalation NOAEL ‡	No data available - not needed	

Genotoxicity ‡ (Annex IIA, point 5.4)

	no genotoxic potential	

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

Target/critical effect ‡	No data available - not needed	
Relevant NOAEL ‡	No data available - not needed	
Carcinogenicity ‡	No data available - not needed	

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	No data available - not needed	
Relevant parental NOAEL ‡	No data available - not needed	
Relevant reproductive NOAEL ‡	No data available - not needed	
Relevant offspring NOAEL ‡	No data available - not needed	

Developmental toxicity

Developmental target / critical effect ‡	Decreased fetal weight, no teratogenicity (study of limited validity)	
Relevant maternal NOAEL ‡	Not reported	
Relevant developmental NOAEL ‡	Mouse: < 314 mg/kg bw (i.p., 1 day dosing)	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	i.p. administration to rats: locomotor hyperactivity and wet dog shakes at 100 mg/kg bw; coordination deficits, atony and sedation at 150 and 200 mg/kg bw, fully reversible at non-lethal doses (up to 150 mg/kg bw)	
Repeated neurotoxicity ‡	No data available - not needed	
Delayed neurotoxicity ‡	No data available - not needed	

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	No relevant data available - not needed
Studies performed on metabolites or impurities ‡	No data available - not needed

Medical data ‡ (Annex IIA, point 5.9)

	No case of toxicological concern has been registered in production, manipulation, transport and application of the preparation BioLure® Med Fly.

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	Not allocated - not needed		
AOEL ‡	Not allocated - not needed		
ARfD ‡	Not allocated - not needed		

Dermal absorption ‡ (Annex IIIA, point 7.3)

Formulation BioLure® Med Fly	No data available - not needed (no relevant dermal exposure to be expected)

Exposure scenarios (Annex IIIA, point 7.2)

Operator	Negligible (qualitative risk assessment)
Workers	Negligible (qualitative risk assessment)
Bystanders	Negligible (qualitative risk assessment)

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

	RMS/peer review proposal
Substance classified (Putrescine)	Xn; R20/21/22 - C; R34

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

Plant groups covered Rotational crops Metabolism in rotational crops similar to metabolism in primary crops? Processed commodities Residue pattern in processed commodities similar to residue pattern in raw commodities? Plant residue definition for monitoring Plant residue definition for risk assessment Conversion factor (monitoring to risk assessment)	No data available. Not required according to the representative uses.

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

Animals covered Time needed to reach a plateau concentration in milk and eggs Animal residue definition for monitoring Animal residue definition for risk assessment Conversion factor (monitoring to risk assessment) Metabolism in rat and ruminant similar (yes/no) Fat soluble residue: (yes/no)	No data available. Not required according to the representative uses.

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

No data available. Not required according to the representative uses.

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

No data available. Not relevant.

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)	No data available. Not required according to the representative uses.		

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

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

No data available. Not required according to the representative uses.

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

ADI TMDI (% ADI) according to WHO European diet TMDI (% ADI) according to national (to be specified) diets IEDI (WHO European Diet) (% ADI) NEDI (specify diet) (% ADI) Factors included in IEDI and NEDI ARfD IESTI (% ARfD) NESTI (% ARfD) according to national (to be specified) large portion consumption data Factors included in IESTI and NESTI	A quantitative consumer dietary risk assessment can be waived due to the specific kind of application.

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

Crop/ process/ processed product	Number of studies	Processing factors		Amount transferred (%) (Optional)
		Transfer factor	Yield factor	
No data available. Not required according to the representative uses.				

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

Not required.

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

Not relevant in the situation that exposure to air is demonstrated to be comparable to natural background levels, but there is a data gap to demonstrate this.

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

Not relevant in the situation that exposure to air is demonstrated to be comparable to natural background levels, but there is a data gap to demonstrate this.

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

Not relevant in the situation that exposure to air is demonstrated to be comparable to natural background levels, but there is a data gap to demonstrate this.

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Not relevant in the situation that exposure to air is demonstrated to be comparable to natural background levels, but there is a data gap to demonstrate this.

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

Not relevant in the situation that exposure to air is demonstrated to be comparable to natural background levels, but there is a data gap to demonstrate this.

PEC (soil) (Annex IIIA, point 9.1.3)

Not relevant in the situation that exposure to air is demonstrated to be comparable to natural background levels, but there is a data gap to demonstrate this.

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

Hydrolytic degradation of the active substance and metabolites > 10 % ‡	pH 5: No information available, data required
	pH 7: No information available, data required
	pH 9: No information available, data required
Photolytic degradation of active substance and metabolites above 10 % ‡	Not relevant in the situation that exposure to air is demonstrated to be comparable to natural background levels, but there is a data gap to demonstrate this.

Quantum yield of direct phototransformation in water at Σ > 290 nm	Not relevant in the situation that exposure to air is demonstrated to be comparable to natural background levels, but there is a data gap to demonstrate this.
Readily biodegradable ‡ (yes/no)	No satisfactory information available, data required

Degradation in water / sediment

	Not relevant in the situation that exposure to air is demonstrated to be comparable to natural background levels, but there is a data gap to demonstrate this.

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

Not relevant in the situation that exposure to air is demonstrated to be comparable to natural background levels, but there is a data gap to demonstrate this.

PEC (ground water) (Annex IIIA, point 9.2.1)

Not relevant in the situation that exposure to air is demonstrated to be comparable to natural background levels, but there is a data gap to demonstrate this.

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

Direct photolysis in air ‡	Not studied - no data requested
Quantum yield of direct phototransformation	Not relevant
Photochemical oxidative degradation in air ‡	0.162 d (Atkinson calculation, 12 hr day, 1.5 x10^6 OH^-/cm^3)
Volatilisation ‡	Not relevant
Metabolites	None

PEC (air)

Method of calculation	A calculation was provided, but as it was based on an assumed average daily emission from traps and not a measured rate of volatilisation, the results of the available calculation are uncertain.

$PEC_{(a)}$

Maximum concentration	Data gap, a comparison with the natural background levels was not available

Residues requiring further assessment

Environmental occurring residues requiring further	Soil: 1,4-Diaminobutane

assessment by other disciplines (toxicology and ecotoxicology) and or requiring consideration for groundwater exposure..	Groundwater: 1,4-Diaminobutane Surface water/ sediment: 1,4-Diaminobutane Air: 1,4-Diaminobutane

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

Soil (indicate location and type of study)	Not required
Surface water (indicate location and type of study)	Not required
Ground water (indicate location and type of study)	Not required
Air (indicate location and type of study)	Not required

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

Candidate for R53 as a satisfactory ready biodegradability study is not available.

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

[1] A general data gap is identified in the ecotoxicology section: pending on the outstanding data in the fate and behaviour section, the risk assessment of 1,4-diaminobutane to non-target organisms for the representative uses should be re-considered.

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

Species	Test substance	Time scale	Endpoint (mg/kg bw/d)	Endpoint (mg/kg feed)
Birds				
Not required[1]				
Mammals				
Rat	putrescine	Acute	463 mg/kg bw (females)	/
		Long-term	Not required[1]	
Additional higher tier studies				
Not required[1]				

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

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
Not required[1]				

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

Group	Test substance	Time-scale (Test type)	Endpoint	Toxicity (mg/L)
Data gap[2].				

[2] Data gap identified for acute toxicity studies with aquatic organisms to fulfil the Annex II data requirement

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

Test substance	Organism	Toxicity endpoint (mg/L)	Time scale	maximum PEC (mg/L)	TER	Annex VI Trigger
Not required[1].						

Bioconcentration
Not applicable

Effects on honeybees (Annex IIA, point 8.7, Annex IIIA, point 10.4)

Test substance	Acute oral toxicity (LD 50 µg ai/bee)	Acute contact toxicity (LD50 µg ai/bee)
Not required [1]		

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

Test substance	Route	Hazard quotient	Annex VI Trigger
Not required[1]			

Effects on other arthropod species (Annex IIA, point 8.8, Annex IIIA, point 10.5)

Laboratory tests with standard sensitive species

Species	Test Substance	Endpoint	Effect (LR50 g ai/ha)
Not required[1]			

HQ

Test substance	Species	Effect (LR50 g ai/ha)	HQ in-field	HQ off-field	Trig-ger
Not required[1]					

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

Test organism	Test substance	Time scale	Endpoint
Not required[1]			

Toxicity/exposure ratios for soil organisms

Test organism	Test substance	Time scale	endpoint mg/kg dw	max.PEC_{S}i	TER	Trigger
Not required[1]						

Effects on non target plants (Annex IIA, point 8.12, Annex IIIA, point 10.8)

Laboratory dose response tests

Most sensitive species	Test substance	ER50 (g ai/ha)[2] vegetative vigour	ER50 (g ai/ha)[2] emergence	Exposure[1] (g ai/ha)[2]	TER	Trigger
Not required[1]						

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

Test type/organism	endpoint
Not required[1]	

Residues definition (consider all relevant metabolites requiring further assessment from the fate section)

Compartment	Ecotoxicologically relevant residue
soil	Data gaps need to be filled before this can be finalised
water	Data gaps need to be filled before this can be finalised
sediment	Data gaps need to be filled before this can be finalised
groundwater	Data gaps need to be filled before this can be finalised

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

	RMS/EPCO proposal	ECB decision
Active substance	Data gap	--
Product	no classification	--

ABBREVIATIONS

1/n	slope of Freundlich isotherm
λ	wavelength
°C	degree Celsius (centigrade)
µg	microgram
µm	micrometer (micron)
a.s.	active substance
AChE	acetylcholinesterase
ADE	actual dermal exposure
ADI	acceptable daily intake
AF	assessment factor
AOEL	acceptable operator exposure level
AP	alkaline phosphatase
AR	applied radioactivity
ARfD	acute reference dose
AST	aspartate aminotransferase (SGOT)
AV	avoidance factor
BCF	bioconcentration factor
BUN	blood urea nitrogen
bw	body weight
CAS	Chemical Abstracts Service
CFU	colony forming units
ChE	cholinesterase
CI	confidence interval
CIPAC	Collaborative International Pesticides Analytical Council Limited
CL	confidence limits
cm	centimetre
d	day
DAA	days after application
DAR	draft assessment report
DAT	days after treatment
DM	dry matter
DT_{50}	period required for 50 percent disappearance (define method of estimation)
DT_{90}	period required for 90 percent disappearance (define method of estimation)
dw	dry weight
EbC_{50}	effective concentration (biomass)
EC_{50}	effective concentration
ECHA	European Chemical Agency
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINCS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
ER_{50}	emergence rate/effective rate, median
ErC_{50}	effective concentration (growth rate)
EU	European Union
EUROPOEM	European Predictive Operator Exposure Model
f(twa)	time weighted average factor
FAO	Food and Agriculture Organisation of the United Nations
FIR	Food intake rate
FOB	functional observation battery
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
g	gram
GAP	good agricultural practice
GC	gas chromatography

GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GGT	gamma glutamyl transferase
GM	geometric mean
GS	growth stage
GSH	glutathion
h	hour(s)
ha	hectare
Hb	haemoglobin
Hct	haematocrit
hL	hectolitre
HQ	hazard quotient
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)
K_{doc}	organic carbon linear adsorption coefficient
kg	kilogram
K_{Foc}	Freundlich organic carbon adsorption coefficient
L	litre
LC_{50}	lethal concentration, median
LD_{50}	lethal dose
LDH	lactate dehydrogenase
LEL	lower explosive limit
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification (determination)
m	metre
M/L	mixing and loading
MAF	multiple application factor
MCH	mean corpuscular haemoglobin
MCHC	mean corpuscular haemoglobin concentration
MCV	mean corpuscular volume
mg	milligram
mL	millilitre
mm	millimetre
MRL	maximum residue limit or level
MS	mass spectrometry
MSDS	material safety data sheet
MTD	maximum tolerated dose
MWHC	maximum water holding capacity
NESTI	national estimated short-term intake
ng	nanogram
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
OM	organic matter content
Pa	pascal
PD	proportion of different food types
PEC	predicted environmental concentration
PEC_{air}	predicted environmental concentration in air
PEC_{gw}	predicted environmental concentration in ground water

PEC_{sed}	predicted environmental concentration in sediment
PEC_{soil}	predicted environmental concentration in soil
PEC_{sw}	predicted environmental concentration in surface water
pH	pH-value
PHED	pesticide handler's exposure data
PHI	pre-harvest interval
PIE	potential inhalation exposure
pK_a	negative logarithm (to the base 10) of the dissociation constant
P_{ow}	partition coefficient between *n*-octanol and water
PPE	personal protective equipment
ppm	parts per million (10^{-6})
ppp	plant protection product
PT	proportion of diet obtained in the treated area
PTT	partial thromboplastin time
QSAR	quantitative structure-activity relationship
r^2	coefficient of determination
RPE	respiratory protective equipment
RUD	residue per unit dose
SC	suspension concentrate
SD	standard deviation
SFO	single first-order
SSD	species sensitivity distribution
STMR	supervised trials median residue
$t_{1/2}$	half-life (define method of estimation)
TER	toxicity exposure ratio
TER_A	toxicity exposure ratio for acute exposure
TER_{LT}	toxicity exposure ratio following chronic exposure
TER_{ST}	toxicity exposure ratio following repeated exposure
TK	technical concentrate
TLV	threshold limit value
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
TSH	thyroid stimulating hormone (thyrotropin)
TWA	time weighted average
UDS	unscheduled DNA synthesis
UEL	upper explosive limit
UV	ultraviolet
W/S	water/sediment
w/v	weight per volume
w/w	weight per weight
WBC	white blood cell
WG	water dispersible granule
WHO	World Health Organisation
wk	week
yr	year