Rotterdam Convention

Operation of the prior informed consent procedure
for banned or severely restricted chemicals

Decision Guidance Document

Methamidophos

Secretariat of the Rotterdam Convention
on the Prior Informed Consent
Procedure for
Certain Hazardous Chemicals and
Pesticides in International Trade

Food and Agriculture
Organization of the
United Nations

UNEP

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Introduction

The objective of the Rotterdam Convention is to promote shared responsibility and cooperative efforts among Parties in the international trade of certain hazardous chemicals in order to protect human health and the environment from potential harm and to contribute to their environmentally sound use, by facilitating information exchange about their characteristics, by providing for a national decision-making process on their import and export and by disseminating these decisions to Parties. The Secretariat of the Convention is provided jointly by the United Nations Environment Programme (UNEP) and the Food and Agriculture Organization of the United Nations (FAO).

Candidate chemicals[1] for inclusion in the prior informed consent (PIC) procedure under the Rotterdam Convention include those that have been banned or severely restricted by national regulatory actions in two or more Parties[2] in two different regions. Inclusion of a chemical in the PIC procedure is based on regulatory actions taken by Parties that have addressed the risks associated with the chemical by banning or severely restricting it. Other ways might be available to control or reduce such risks. Inclusion does not, however, imply that all Parties to the Convention have banned or severely restricted the chemical. For each chemical included in Annex III of the Rotterdam Convention and subject to the PIC procedure, Parties are requested to make an informed decision whether they consent or not to the future import of the chemical.

At its seventh meeting, held in Geneva from 4 to 15 May 2015, the Conference of the Parties agreed to list methamidophos in Annex III of the Convention and adopted the decision guidance document with the effect that this group of chemicals became subject to the PIC procedure.

The present decision guidance document was communicated to designated national authorities on 15 September 2015, in accordance with Articles 7 and 10 of the Rotterdam Convention.

Purpose of the decision guidance document

For each chemical included in Annex III of the Rotterdam Convention, a decision guidance document has been approved by the Conference of the Parties. Decision guidance documents are sent to all Parties with a request that they make a decision regarding future import of the chemical.

Decision guidance documents are prepared by the Chemical Review Committee. The Committee is a group of government-designated experts established in line with Article 18 of the Convention, which evaluates candidate chemicals for possible inclusion in Annex III of the Convention. Decision guidance documents reflect the information provided by two or more Parties in support of their national regulatory actions to ban or severely restrict the chemical. They are not intended as the only source of information on a chemical nor are they updated or revised following their adoption by the Conference of the Parties.

There may be additional Parties that have taken regulatory actions to ban or severely restrict the chemical and others that have not banned or severely restricted it. Risk evaluations or information on alternative risk mitigation measures submitted by such Parties may be found on the Rotterdam Convention website (www.pic.int).

Under Article 14 of the Convention, Parties can exchange scientific, technical, economic and legal information concerning the chemicals under the scope of the Convention including toxicological, ecotoxicological and safety information. This information may be provided directly to other Parties or through the Secretariat. Information provided to the Secretariat will be posted on the Rotterdam Convention website.

Information on the chemical may also be available from other sources.

Disclaimer

The use of trade names in the present document is primarily intended to facilitate the correct identification of the chemical. It is not intended to imply any approval or disapproval of any particular company. As it is not possible to include all trade names presently in use, only a number of commonly used and published trade names have been included in the document.

[1] According to the Convention, the term “chemical” means a substance, whether by itself or in a mixture or preparation and whether manufactured or obtained from nature, but does not include any living organism. It consists of the following categories: pesticide (including severely hazardous pesticide formulations) and industrial.

[2] According to the Convention, the term “Party” means a State or regional economic integration organization that has consented to be bound by the Convention and for which the Convention is in force.

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The designations employed and the presentation of material in this publication do not imply the expression of any opinion whatsoever on the part of FAO or UNEP concerning the legal status of any country, territory, city or area or of its authorities or concerning the delimitation of its frontiers or boundaries.

Standard core set of abbreviations

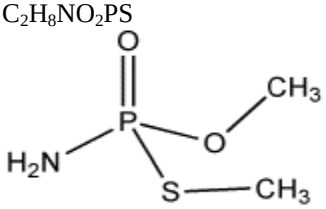
STANDARD CORE SET OF ABBREVIATIONS	
<	less than
≤	less than or equal to
>	greater than
≥	greater than or equal to
µg	microgram
µm	micrometre
ARfD	acute reference dose
a.i.	active ingredient
ADI	acceptable daily intake
ANVISA	National Health Surveillance Agency of Brazil
AOEL	acceptable operator exposure level
a.s.	active substance
b.p.	boiling point
bw	body weight
^{o}C	degree Celsius (centigrade)
CAS	Chemical Abstracts Service
cc	cubic centimetre
cm	centimetre
DNA	deoxyribose nucleic acid
DT_{50}	dissipation time 50%
EC	European Community
EC_{50}	median effective concentration
ED_{50}	median effective dose
EEC	European Economic Community
EHC	Environmental Health Criteria
EU	European Union
FAO	Food and Agriculture Organization of the United Nations
g	gram
GAP	Good Agricultural Practice
GHS	Globally Harmonized System of Classification and Labelling of Chemicals
h	hour
ha	hectare
i.m.	intramuscular
i.p.	intraperitoneal
IARC	International Agency for Research on Cancer
IC_{50}	median inhibitory concentration
ILO	International Labour Organization
IMO	International Maritime Organization
IPCS	International Programme on Chemical Safety
IPM	Integrated Pest Management
IUPAC	International Union of Pure and Applied Chemistry
iv	intravenous
JMPR	Joint FAO/WHO Meeting on Pesticide Residues (Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and a WHO Expert Group on Pesticide Residues)
k	kilo- (x 1000)
kg	kilogram

STANDARD CORE SET OF ABBREVIATIONS	
Koc	soil organic partition coefficient.
Kow	octanol–water partition coefficient
kPa	kilopascal
L	litre
LC_{50}	median lethal concentration
LD_{50}	median lethal dose
LOAEL	lowest-observed-adverse-effect level
LOEC	lowest-observed-effect concentration
LOEL	lowest-observed-effect level
m	metre
m.p.	melting point
mg	milligram
ml	millilitre
mPa	millipascal
MRL	maximum residue limit
MTD	maximum tolerated dose
ng	nanogram
NOAEC	no-observed-adverse-effect concentration
NOAEL	no-observed-adverse-effect level
NOEC	no-observed-effect concentration
NOEL	no-observed-effect level
OECD	Organisation for Economic Co-operation and Development
PEC	predicted environmental concentration
Pow	octanol-water partition coefficient, also referred to as Kow
PPE	personal protective equipment
ppm	parts per million (used only with reference to the concentration of a pesticide in an experimental diet. In all other contexts the terms mg/kg or mg/L are used).
RfD	reference dose (for chronic oral exposure; comparable to ADI)
sc	subcutaneous
SINAN	National System for Notified Diseases
SMR	standard(ized) mortality ratio
STEL	short-term exposure limit
TER	toxicity exposure ratio
TLV	threshold limit value
TV	trigger value
TWA	time-weighted average
UNEP	United Nations Environment Programme
USEPA	United States Environmental Protection Agency
UV	ultraviolet
VOC	volatile organic compound
w/w	weight for weight
WHO	World Health Organization
wt	weight

Decision guidance document for a banned or severely restricted chemical

Methamidophos **Published: September 2015**

1. Identification and uses (see Annex 1 for further details)

Common name	Methamidophos
Chemical name and other names or synonyms	IUPAC: O,S-Dimethyl phosphoramidothioate CA: O,S-Dimethyl phosphoramidothioate
Molecular formula	$C_2H_8NO_2PS$
Chemical structure	 (Pesticide Action Network database)
CAS-No.(s)	10265-92-6
Harmonized System Customs Code	2930.50
Other numbers	EINECS Number: 233-606-0 CIPAC Number: 355 Combined Nomenclature (CN) code of European Union: 2930 50 00
Category	Pesticide
Regulated category	Pesticide
Use(s) in regulated category	According to the European Union notification, methamidophos was used as an insecticide on the following crops: pome fruit, stone fruit (peach and apricot), tomato, flowering brassica (cauliflower and broccoli), head cabbage, cotton seed, soybean, potato, cereals, sugar/fodder beet, tobacco. According to the Brazilian notification, methamidophos was used as an insecticide/acaricide on the following crops: cotton, peanut, potato, bean, soybean, tomato, wheat.
Trade names	Trade names from EU Notification: Tamaron SL 200, Tamaron SL 600, Trade names from Brazilian Notification: Methamidophos Tecnico Agripec, Stron,Tamaron Tecnico BR, Tamaron BR, Tamaron Tecnico USA, Gladiador, Glent, Quasar, Rivat, Melamidofos Tecnico Fersol, Metamidofos Fersol 600, Melamidofos Tecnico Milenia, Metafos, Dinafos, Hamidop 600, Metasip. Trade names from other sources: Monitor, Tamaron, Filitox, Tamanox, Tarn, Patrole, Metamidofos Estrella, Methamidophos 60 WSC, Methedrin 60, Morithion, Red Star Alloran, Nitofol, Tamaron, Swipe, Nuratron, Vetaron, SRA 5172, Tam. *This is an indicative list. It is not intended to be exhaustive.*
Formulation types	SL (soluble concentrate). Content of technical active substance: 608 and 833 g/L (EU, 2000, p.10, item 1.3.3. and 1.3.5) Soluble and emulsifiable concentrates in various concentrations of active ingredient. Soluble liquid formulations of methamidophos which exceed 600 g a.i./L are included in the PIC procedure because of their acute hazard classification and concern as to their impact on human health under conditions of use in developing countries. (FAO/UNEP, 1997)
Uses in other categories	There is no reported use as an industrial chemical.

Basic manufacturers Bayer AG, Tomen Corp., Chevron Chemical Co., Cia-Shen Co., Crystal Chemical Inter-America, Eastchem, Fufong Agro-Chems Mfg, Golden Harvest Chemical Co., Ltd, Jiangmen, Jin Hung Fine Chemical Co., Linghu P.F., Mobay Corp., Productos OSA, Quimica Estrella S.A.C.I.e.I, Sanonda, SinoHarvest, Suzhou P.F., Taiwan Tainan Giant Industrial Co. (EU, 2000, p. 10, item 1.3.2; FAO/UNEP, 1997; Extension Toxicology Network; Pesticide Action Network database; IPCS,1993)

This is an indicative list of current and former manufacturers. It is not intended to be exhaustive.

2. Reasons for inclusion in the PIC procedure

Methamidophos is included in the PIC procedure as a pesticide. It is listed on the basis of the final regulatory actions taken by the European Union and Brazil to severely restrict and ban, respectively, methamidophos as a pesticide.
It should be noted that a severely hazardous pesticide formulation containing methamidophos (soluble liquid formulations of the substance that exceed 600 g active ingredient/l) is also listed in Annex III.
No final regulatory actions relating to industrial chemical uses have been notified.

2.1 Final regulatory action (see Annex 2 for further details)

Brazil

The legal reference for the pesticide management in Brazil is Law Nº 7.802/89 (Pesticide Law), regulated by Decree 4.074/02. The final regulatory action (Resolution-RDC No. 01 of 14 January 2011 of the National Health Surveillance Agency (ANVISA) - Technical regulation on the active ingredient methamidophos as a result of a toxicological re-evaluation) was based on results of a toxicological re-evaluation and resulted in a ban of all uses of methamidophos-based products in plant protection (as an agricultural pesticide). The decision was based on the Technical Note of Toxicological Reassessment on methamidophos commissioned by ANVISA. The decision entered into force on 17 January 2011 and prevents future registrations of this pesticide (UNEP-FAO-RC-CRC.9-8.En).

Reason: Human Health

European Union

Commission Directive 2006/131/EC of 11 December 2006 amending Directive 91/414/EEC severely restricted the placing on the market and use of plant protection products containing methamidophos. The Commission Directive amended Annex I to Directive 91/414/EEC (which was replaced by Regulation (EC) No 1107/2009 concerning the placing of plant protection products on the market) to permit the use of methamidophos from 1 January 2007 to 30 June 2008. It also set restrictions by limiting the application of methamidophos to only one specific crop (potato) and defined a maximum application rate and number of applications. It also prohibited specific uses and limited the period of inclusion of methamidophos in Annex I to Directive 91/414/EEC to 18 months after entry into force of Directive 2006/131/EEC on 1 January 2007. The Directive imposed on the Member States a requirement to review all authorizations of methamidophos to ensure that the restrictions set in Directive 2006/131/EC were respected as of 30 June 2007. It also required a re-evaluation of products containing methamidophos by 30 June 2008 (UNEP-FAO-RC-CRC.9-8.En).

Reason: Human Health and Environment

2.2 Risk evaluation (see Annex 1 for further details)

Brazil

Human Health

Methamidophos is an extremely toxic organophosphate (Class I), which causes serious adverse effects to human health, especially related to neurotoxicity, immunotoxicity and to the endocrine, reproductive systems and fetal development.

In studies with experimental animals, symptoms of toxicity were observed which were consistent with cholinesterase (AChE) inhibition, the typical effect of organophosphates together with other specific toxicity. Toxicity observed in experimental animals included generalized reduced organ weight including thyroid, heart, lung, pancreas, liver, kidney, adrenals, spleen, thymus, testes and ovaries. Methamidophos also caused some endocrine disruption in experimental studies and this may potentially lead to adverse effects on reproduction and development. Other toxicological concerns include immunotoxicity with effects on lymphocytes, monocytes and antibody formation, some studies showing genotoxic potential and psychiatric disorders including depression, cognitive impairment, suicide and Parkinsonism, which have been linked to organophosphate exposure.

A series of specific studies conducted within Brazil observed risks to human health arising from the use of methamidophos; in particular risks to operators, workers and consumers. These studies show that methamidophos is one of the most frequently used pesticides in Brazil. However, indiscriminate use is suspected in some cases, leading to the detection of residues above the legal maximum concentration in various foods (fresh tomato, strawberry and

lettuce) for which the use of methamidophos was not allowed or restricted. This was considered a public health problem as these foods are widely eaten raw in Brazil. The detection of residues suggested that more effective measures should be implemented. This led to the decision of ANVISA to reassess the risks posed by methamidophos.

A number of studies in Brazil have implicated methamidophos in contamination of drinking water and human toxicity:

- Contamination of drinking water and water retaining dams in Pernambuco State, where water concentrations of methamidophos have been detected above allowable levels.
- Cases of poisoning involving direct or indirect exposure to methamidophos in Brazil were analyzed using data collected from the National System for Notified Diseases (SINAN). Among the 128 active substances involved in the cases reported, glyphosate, paraquat and methamidophos were the main toxic agents, corresponding to 26.2% of the total cases.
- A study conducted in the rural centre of Vargem Bonita (Federal District), an area of intensive production of vegetables, showed that methamidophos poisoning occurred in five of the eight workers (62.5%) who applied the product. The same complaints were revealed by farmers in Nova Friburgo – Rio de Janeiro and in São Francisco Valley – Pernambuco State.
- A study of the production of processed tomato in sub-middle São Francisco River Valley (Pernambuco State) indicated that 1% of the samples were inappropriate for consumption due to the levels of methamidophos present in the product.
- In Culturama, a district of Fatima do Sul city (Mato Grosso do Sul State), 250 farmers responded to a survey focused on practices for the use of pesticides and symptoms after the application of the products. Over 90% of farmers reported the use of products containing methamidophos, and 149 farmers reported adverse effects after the use of pesticides.

Several studies showed that poisonings and deaths linked to occupational exposure to methamidophos are associated with the characteristics of toxicity of this active ingredient. Moreover, issues of social and economic situation (low level of education, low income) and biological conditions (age and gender) are factors that increase vulnerability to poisonings caused by methamidophos.

The risk evaluation took into account national studies, including studies on exposure under the prevailing conditions in Brazil, and the toxicological endpoints for methamidophos. The result was an unacceptable risk to human health. Therefore, a toxicological re-evaluation concluded that methamidophos should be banned according to Resolution RDC No 01 of 14 January 2011.

European Union

Human Health

It was concluded that it could be expected that plant protection products containing methamidophos would fulfil the safety requirements laid down in Article 5(1)(a) and (b) of Directive *91/414/EEC.* This conclusion was however subject to compliance with the particular requirements in sections 4, 5, 6 and 7 of the review report, as well as to the implementation of the provisions of Article 4(1) and the uniform principles laid down in Annex VI of Directive *91/414/EEC*, for each methamidophos-containing plant protection product for which Member States would grant or review the authorisation.

Therefore, Member States were requested to pay particular attention to the protection of operators who had to wear suitable protective clothing during mixing-loading and gloves, coveralls, rubber boots and face protection or safety glasses during application and cleaning of equipment. The above measures had to be applied, unless the exposure to the substance was adequately precluded by the design and construction of the equipment itself or by the mounting of specific protective components on such equipment.

Member States were requested to ensure that the authorisation holders report on any reported effect on operator health by December 31th of each year. Member States could require that elements, such as sales data and a survey of use patterns, are provided so that a realistic picture of the use conditions and the possible toxicological impact of methamidophos could be obtained.

Methamidophos is a cholinesterase inhibitor characterised by high acute toxicity.
Methamidophos is classified "T+ - Very toxic" (Directive *67/548/EEC)* and "Acute Tox. 2" (Regulation (EC) *1272/2008* implementing the GHS system).

The use of methamidophos may entail certain risks for consumers. Deterministic models indicated a high risk for chronic and acute dietary intake especially for toddlers (consumption values taken from UK diet). The highest contributions to chronic risk came from consumption of plum fruit and tomatoes and the acute risk (ARfD) was high for all crops except for broccoli, cauliflower, cabbage and potato. A probabilistic model showed no acute risk. Intended uses have been reduced and new processing factors added. Based on the new list of uses, the deterministic

model for estimating the chronic and acute intake of methamidophos through the diet did not show any risk for the general population.

Environment

A risk assessment revealed that toxicity/exposure ratios for a range of scenarios with aquatic and terrestrial organisms indicated acute and long-term risks for birds and acute risk for mammals for the use of methamidophos in potato fields. Furthermore acute and long-term risks were identified for aquatic invertebrates (*Daphnia magna)* associated with methamidophos use in field and orchard crops and vegetables. The risk to beneficial arthropods was also high. A risk to birds and mammals from consumption of dead insects and possibly other routes of exposure was also identified.

3. Protective measures that have been applied concerning the chemical

3.1 Regulatory measures to reduce exposure

Brazil

The final regulatory action (ANVISA Resolution RDC 01 of 14 January 2011) gradually reduced the use and banned the sale, import, export and use of methamidophos and finally cancelled the methamidophos registration. This established the definitive prohibition of registration of pesticides containing methamidophos. Authorizations for sale and use of plant protection products containing methamidophos had to be withdrawn by 31 December 2011 and 30 December 2012, respectively. As of 31 December 2012, registrations of all products containing methamidophos were cancelled and no longer allowed to be granted or renewed.

European Union

Commission Directive 2006/131/EC of 11 December 2006 amending Directive 94/414/EEC severely restricted the placing on the market and use of plant protection products containing methamidophos.

The Commission Directive amended Annex I to Directive 91/414/EEC (which was replaced by Regulation (EC) No 1107/2009 concerning the placing of plant protection products on the market) to permit the use of methamidophos from 1 January 2007 to 30 June 2008. It also set in place restrictions on the use of methamidophos. The Directive imposed on the Member States a requirement to review all authorizations of methamidophos to ensure that the restrictions set in Directive 2006/131/EC were respected as of 30 June 2007. It also required a re-evaluation of products containing methamidophos by 30 June 2008.

The restrictions limited the application of methamidophos to only one specific crop (potato) and defined a maximum application rate and number of applications. It also prohibited specific uses and limited the period of inclusion of methamidophos in Annex I to Directive 94/414/EEC to 18 months after entry into force of Directive 2006/131/EEC on 1 January 2007.

It should be noted that this period has now expired. As of 30 June 2008, methamidophos is no longer included in the list of authorized substances in Annex I. Hence, methamidophos is no longer allowed to be used as a plant protection product in the European Union.

3.2 Other measures to reduce exposure

Brazil

None reported.

European Union

None reported.

3.3 Alternatives

There are a number of alternative methods involving chemical and non-chemical strategies, including alternative technologies, available, depending on the individual crop-pest complex under consideration. Countries should consider promoting, as appropriate, integrated pest management (IPM) and organic strategies, agroecology and other ecosystem-based approaches to pest management as a means of reducing or eliminating the use of hazardous pesticides.

Advice may be available through National IPM focal points, the FAO, IFOAM (International Federation of Organic Movements) and agricultural research or development agencies. Where it has been made available by governments, additional information on alternatives to methamidophos may be found on the Rotterdam Convention website www.pic.int.

Brazil
The relevant substitutes for use on beans, soybeans and cotton are: abamectin, thiamethoxam, acephate, spinosad, triflumuron, fipronil, chlorpyrifos, indoxacarb, bifenthrin, lambda-cyhalothrin, methomyl, cypermethrin, diflebenzurom, imidacloprid, clothianidin, flufenoxuron, novalurom, triazophos, lufenuron and *Bacillus thuringiensi*s.

European Union
No information on alternatives was reported.

3.4 Socio-economic effects

Brazil
No assessment of socio-economic effects was reported.

European Union
No assessment of socio-economic effects was reported.

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4. Hazards and Risks to human health and the environment

4.1 Hazard Classification

WHO / IPCS	Highly hazardous (Class 1b)
IARC	Not classified
European Union	In accordance to Regulation (EC) No *1272/2008*, which implements the UN GHS in the EU: **Acute Tox. 2* - H330** - Fatal if inhaled. **Acute Tox. 2* - H300** - Fatal if swallowed. **Acute Tox. 3* - H311** - Toxic in contact with skin. **Aquatic acute 1 - H400** - Very toxic to aquatic life. (* = This classification shall be considered as a minimum classification.) In accordance with Council Directive *67/548/EEC:* **T+** - Very toxic. **R24** - Toxic in contact with skin. ***R26/28*** - Very toxic by inhalation and if swallowed. **N** - Dangerous for the environment. **R50** - Very toxic to aquatic organisms.
US EPA	Class I (highly toxic)

4.2 Exposure limits

CODEX MRLs in food (FAO/WHO Food Standards, 2012)

Commodity	MRL (mg/kg)	Year of adoption	
Artichoke, Globe	0.2 mg/Kg	2005	
Beans, except broad bean and soya bean	1 mg/Kg	2006	
Cotton seed	0.2 mg/Kg	2005	
Edible offal (mammalian)	0.01 mg/Kg	2005	(*)
Eggs	0.01 mg/Kg	2005	(*)
Fodder beet	0.02 mg/Kg	2005	
Meat (from mammals other than marine mammals)	0.01 mg/Kg	2005	(*)
Milks	0.02 mg/Kg	2005	
Potato	0.05 mg/Kg	2005	
Poultry meat	0.01 mg/Kg	2005	(*)
Poultry, Edible offal of	0.01 mg/Kg	2005	(*)
Rice straw and fodder, Dry	0.1 mg/Kg	2012	
Rice, Husked	0.6 mg/Kg	2012	
Soya bean (dry)	0.1 mg/Kg	2005	
Spices	0.1 mg/Kg	2005	(*)
Sugar beet	0.02 mg/Kg	2005	

(*) At or about the limit of determination

Acceptable Daily Intake (ADI)

The FAO/WHO Joint Meeting on Pesticide Residues (JMPR) set an ADI of 0-0.004 mg/kg bw/day (JMPR, 2002).

The EU established an ADI of 0.001 mg/kg bw/day, based on a 2-year rat study with a safety factor of 100 (EU, 2006).

Acute Reference Dose (ARfD)

The FAO/WHO Joint Meeting on Pesticide Residues (JMPR) set an ARfD of 0.01 mg/kg bw/day (JMPR, 2002).

The EU established an ARfD of 0.003 mg/kg bw/day, based on an acute neurotoxicity study with a safety factor of 100 (EU, 2006).

The US EPA set an oral Reference Dose (RfD) of 0.00005 mg/kg bw/day, based on a one-year dog feeding study with an uncertainty factor of 1000 (US EPA, 2002)

Acceptable Operator Exposure Level (AOEL)

The EU set an AOEL of 0.001 mg/kg bw/day, based on a 2-year rat study with a safety factor of 100 (EU, 2006).

WHO drinking water guideline

Methamidophos is excluded from guideline value derivation, as a review of the literature on occurrence or credibility of occurrence in drinking water has shown evidence that methamidophos is unlikely to occur in drinking water (WHO, 2011, p. 181).

4.3 Packaging and labelling	
The United Nations Committee of Experts on the Transportation of Dangerous Goods classifies the chemical in:	
Hazard Class and Packing Group:	The United Nations Committee of Experts on the Transportation of Dangerous Goods (UNDG) classifies methamidophos (pure substance) in: - Hazard Class 6.1 - Packing Group No. I (based on LD_{50} value in WHO, 2010) For further information on the classification of mixtures, special provisions and packing instructions see United Nations, 2013. It is recommended to follow the FAO Revised Guidelines on Good Labelling Practice for Pesticides (FAO, 1995;see also FAO/UNEP, 1997)
International Maritime Dangerous Goods (IMDG) Code	For methamidophos (pure substance): UN No. 2783 Organophosphorous pesticide, solid, toxic (methamidophos) Class 6.1 Marine pollutant (IMO, 2012)
Transport Emergency Card	TEC (R)-61G41b (IPCS, 1994)

4.4 First AID

NOTE: The following advice is based on information available from the World Health Organization and the notifying countries and was correct at the time of publication. This advice is provided for information only and is not intended to supersede any national first aid protocols.

The acute oral and dermal toxicities of methamidophos are high and it can be hazardous for human beings if incorrectly handled. On overexposure, typical signs and symptoms of organophosphorus poisoning may occur rapidly (IPCS, 1993). Early symptoms of poisoning may include excessive sweating, headache, weakness, giddiness, nausea, vomiting, hypersalivation, stomach pains, blurred vision and slurred speech. If these symptoms occur, the person should remove contaminated clothes, wash affected skin with soap and water, and flush with large quantities of water. If in the event of collapse artificial resuscitation is used, vomit may contain toxic amounts of the substance. In case of ingestion, the stomach should be emptied as soon as possible by careful gastric lavage. Do not induce vomiting if the formulation contained hydrocarbon solvents (FAO/UNEP, 1997).

Persons who have been poisoned (accidentally or otherwise) must be transported immediately to a hospital and put under the surveillance of properly trained medical staff. Antidotes are atropine sulphate and pralidoxime chloride. General surveillance and cardiac monitoring must be maintained for at least 14 days. (WHO, 1986)

1 Advice to physicians

For a more complete treatise on the effects of organophosphorus insecticides, especially their short- and long-term effects on the nervous system, please refer to EHC 63: Organophosphorus insecticides - a general introduction (WHO, 1986). See also the US EPA's publication, Recognition and Management of Pesticide Poisonings, 6th Edition (http://www2.epa.gov/pesticide-worker-safety/recognition-and-management-pesticide-poisonings).

1.1 Symptoms of poisoning

Signs and symptoms may include a feeling of exhaustion, headache, blurred vision, weakness, and confusion. Vomiting, abdominal pain, excessive sweating, and salivating may develop. The pupils are constricted. Difficulty in breathing may be experienced, due to congestion of the lungs and weakness of the respiratory muscles. Arrhythmias and cardiac failure have been reported. On severe poisoning, there will be muscle spasms, unconsciousness, and convulsion. Breathing may stop, followed by death.

1.2 Medical treatment

If a formulation that does not contain petroleum distillates is ingested, induce vomiting, or preferably perform gastric lavage using 5% sodium bicarbonate. In case of ingestion of liquid formulations containing hydrocarbon solvents, vomiting involves a risk of aspiration pneumonia. Instead, the stomach should be emptied, as soon as possible, by careful gastric lavage (using a cuffed endotracheal tube). If possible, identify the solvents present in the formulation and observe the victim for additional toxic effects. As early as possible, administer 2 mg of atropine sulfate iv and 1000-2000 mg pralidoxime chloride or 250 mg obidoxime chloride (adult dose) iv to patients suffering from severe respiratory difficulties, convulsions, and unconsciousness. Repeated doses of 2 mg of atropine sulfate should be given, as required, based on the respiration, blood pressure, pulse frequency, salivation, and convulsion conditions. Diazepam should be given in all but the mildest cases in doses of 10 mg, sc or iv, which may be repeated as required. For children, the doses are 0.04-0.08 mg of atropine/kg body weight, 250 mg of pralidoxime chloride per child or 4-8 mg of obidoxime chloride per kg body weight.

Artificial respiration should be applied if required.

Morphine, barbiturates, phenothiazine derivatives, tranquillizers, and all kinds of central stimulants are contraindicated in the absence of artificial respiration.

The diagnosis of intoxication should be confirmed, as soon as possible, by determination of the cholinesterase activity in venous blood.

In all cases of clinical poisoning with methamidophos and other organophosphorus insecticides, it is essential to maintain general surveillance and cholinesterase and cardiac monitoring for at least 14 days, and longer if necessary, and to adopt general supportive and specific therapy in accordance with the findings.

As stated earlier, more information on the treatment of organophosphorus insecticide poisoning can be obtained from EHC No. 63: Organophosphorus insecticides - a general introduction.

2 Health surveillance advice

In human beings exposed to methamidophos, the cholinesterase activity of the blood should be monitored regularly. Measurement of whole blood acetyl cholinesterase (AChE) is the most widely adopted method. Because physiological variations of blood cholinesterase (ChE) levels occur in a healthy person and among populations, it is preferable to compare the results with pre-exposure ChE levels (WHO, 1986).

4.5 Waste management

All waste and contaminated material associated with this chemical should be considered hazardous waste. The material should be destroyed by incineration in a special, high temperature chemical incinerator facility. However, it should be noted that the disposal/destruction methods recommended in the literature are often not available in, or suitable for, all countries; *e.g.*, high temperature incinerators may not be available. Consideration should be given to the use of alternative destruction technologies. Further information on possible approaches may be found in Technical Guidelines for the Disposal of Bulk Quantities of Obsolete Pesticides in Developing Countries (FAO, 1996).

In general, waste should be disposed of in accordance with the provisions of the Basel Convention on the Control of Transboundary Movements of Hazardous Wastes and Their Disposal (1996), any guidelines thereunder, and any other relevant regional agreements (Basel, 1996).

In addition the specific Technical Guidelines for the implementation of the International Code of Conduct on Pesticide Management on Prevention and Disposal of Obsolete Stocks should be followed. They are available at: http://www.fao.org/agriculture/crops/thematic-sitemap/theme/pests/code/list-guide-new/en/.

In the USA, any non-domestic waste containing methamidophos is considered a hazardous waste and should be notified. Permits are required for its handling, transport, treatment, storage, or disposal. Waste incinerators must achieve 99.99% destruction and removal of this substance (IPCS, 1993).

Annexes

Annex 1 **Further information on the substance**

Annex 2 **Details on Final regulatory action**

Annex 3 **Address of designated national authorities**

Annex 4 **References**

Annex 1	Further information on the substance

The information presented in this Annex reflects the conclusions of the notifying parties: Brazil and the European Union. The notification from Brazil was published in PIC Circular XXXVI of December 2012. The notification from the European Union was published in PIC Circular XXXVII of June 2013.

Where possible, information on hazards provided by the notifying parties has been presented together, while the evaluation of the risks, specific to the conditions prevailing in the notifying Parties are presented separately. This information has been taken from the documents referenced in the notifications in support of their final regulatory actions to ban or severely restrict methamidophos and includes the technical note on the toxicological review of methamidophos commissioned by the Brazilian National Health Surveillance Agency (ANVISA) and from the European Union (EU, 2000; 2004-A; 2004-B; 2006).

Annex 1 – Further information on *notified chemical*

1.	**Physico-Chemical properties**	
1.1	**Identity**	ISO: Methamidophos IUPAC: O,S-dimethyl phosphoramidothioate CAS: O,S-dimethyl phosphoramidothioate (EU, 2006)
1.2	**Formula**	$C_2H_8NO_2PS$
1.3	**Colour and Texture**	(a) Colourless crystals (IPCS, 1994) (b) Pure active ingredient: crystals Active substance as manufactured: liquid or crystal slurry (EU, 2000, p. 58)
1.4	**Melting Point**	45^{o}C (purity 99.5% and test material manufactured as waxy solid)
1.5	**Relative Density (g/cm^3)**	1.27 g/cm^3 at 20^{o}C (purity 99.5%) (EU, 2006)
1.6	**Boiling Point**	Exothermic decomposition between 160 and 215^{o}C (purity 99.7%)
1.7	**Vapour Pressure**	2.3 x 10^{-5} hPa at 20^{o}C
1.8	**Henry's Law Constant**	< 1.6 x 10^{-6} Pa.m^3/mole
1.9	**Solubility in Water**	>200 g/l at 20^{o}C (purity 99.5%)
2.0	**Solubility in Organic Solvents**	at 20^{o}C, 99.5% purity n-hexane: < 1 g/L toluene: 2-5 g/L dichloromethane: > 200 g/L 2-propanol: > 200 g/L acetone: >200 g/L dimethylformamide: > 200 g/L
2.1	**Dissociation Constant**	Methamidophos has neither basic nor acidic properties in water. Therefore a pK value cannot be determined.
2	**Toxicological properties**	
2.1	**General**	
2.1.1	**Mode of Action**	Methamidophos is an acutely toxic pesticide and belongs to the organophosphorus insecticides, which exert their acute effects in both insects and mammals by inhibiting acetylcholinesterase (AChE) in the nervous system with subsequent accumulation of toxic levels of acetylcholine (ACh), which is a neurotransmitter. In many cases, the organophosphorylated enzyme is fairly stable, so that recovery from intoxication may be slow (WHO 1986; IPCS, 1994).
2.1.2	**Symptoms of poisoning**	The organophosphate insecticides are cholinesterase inhibitors. They are highly toxic by all routes of exposure. When inhaled, the first effects are usually respiratory and may include bloody or runny nose, coughing, chest discomfort, difficult or short breath and wheezing due to constriction or excess fluid in the bronchial tubes. Skin contact with organophosphates may cause localised sweating and involuntary muscle contractions. Eye contact will cause pain, bleeding, tears, pupil constriction and blurred vision. Following exposure by any route, other systemic effects may begin within a few minutes or be delayed for up to 12 hours. These may include pallor, nausea, vomiting, diarrhoea, abdominal cramps, headache, dizziness, eye pain, blurred vision, constriction or dilation of the pupils, tears, salivation, sweating and confusion. Severe poisoning will affect the central nervous system, producing in coordination, slurred speech, loss of reflexes, weakness, fatigue, involuntary muscle contractions, twitching, tremors of the tongue or eyelids, and eventually paralysis of the body extremities and the respiratory muscles. In severe cases there may also be involuntary defecation or urination, psychosis, irregular heartbeat, unconsciousness, convulsions and coma. Respiratory failure or cardiac arrest may cause death (WHO 1986; IPCS, 1994).

2.1.3	**Absorption, distribution, excretion and metabolism in mammals**	Following administration, methamidophos is widely distributed in the body with no potential for accumulation. Methamidophos is metabolised to desamino-methamidophos, monomethyl phosphate, methylphosphoramidate, S-methylphosphoramidothioate, and phosphoric acid. Methamidophos is rapidly excreted, primarily in urine, with 50-60% being excreted after 24 hours. Twenty-eight days after administration via oral gavage, 80-90% of the initial dose of methamidophos was excreted, mainly via urine (60-70%) and the faeces (EU, 2006, p.5).
2.2	**Toxicology studies**	
2.2.1	**Acute toxicity**	Acute toxicity Rat LD_{50} oral: 9.1 mg/kg bw (79.95 mg/kg bw, refined estimation) Male rat LD_{50} oral: 11.8 mg/kg bw Female rat LD_{50} oral: 10.5 mg/kg bw Rat LD_{50} dermal: 50 mg/kg bw Male rat LC_{50} inhalation: 63.2 mg/m^3 Female rat LC_{50} inhalation: 76.5 mg/m^3 Skin irritation: Slightly irritating (rabbits) Eye irritation: Slightly irritating Skin sensitisation: Not sensitising (modified Buehler) (EU, 2006, p.5)
2.2.2	**Short term toxicity**	Target/critical effect: Nervous system/cholinesterase inhibition Lowest relevant oral NOEL: 0.03 mg/kg bw/day (56-day rat study) Lowest relevant dermal NOAEL/NOEL: 1 mg/kg bw/day (21-day rat study) Lowest relevant inhalation NOAEL/NOEL: 1.1 mg/m^3 (90-day rat study) (EU, 2006, p. 6)
2.2.3	**Genotoxicity (including mutagenicity)**	There is no concern for the mutagenicity of methamidophos (EU, 2006, p. 6). A number of *in vitro* studies have been conducted in bacterial and mammalian cells and *in vivo* studies that have not demonstrated genotoxicity (point mutations, chromosomal aberration and DNA damage studies). Weak positive results were reported in some *in vitro* and *in vivo* cytogenetic assays; however, these results were not confirmed in further experiments (EU notification, p. 23).
2.2.4	**Long term toxicity and carcinogenicity**	Target/critical effect: Cholinesterase inhibition Lowest relevant NOAEL: 2 mg/kg diet (0.1 mg/kg bw/day, 2-year rat study) Carcinogenicity: Negative (EU, 2006, p. 6)
2.2.5	**Effects on reproduction**	Target/critical effect: Reproductive toxicity: - Parental and pup cholinesterase inhibition - Lowest relevant reproductive NOEL: 0.1 mg/kg bw/day (rats) Target/critical effect: Developmental toxicity: None Lowest relevant developmental NOAEL: 2.5 mg/kg bw/day (highest dose tested) (EU, 2006, p. 6)
2.2.6	**Neurotoxicity/ delayed neurotoxicity, Special studies where available**	No potential for delayed neuropathy (rat). Delayed neuropathy only at very high doses (3-4 times higher than the LD_{50}) (hen) (EU, 2006, p. 6)
2.2.7	**Summary of mammalian toxicity and overall evaluation**	Methamidophos is an extremely toxic organophosphate (Class I, Brazil 1992), which causes serious adverse effects to human health, especially related to neurotoxicity, immunotoxicity and to the endocrine, reproductive systems and fetal development (Brazil, 2012-A, p. 1). Methamidophos is a cholinesterase inhibitor characterised by high acute toxicity. Methamidophos is classified "T+ - Very toxic" (Directive 67/548/EEC) and "Acute Tox. 2" (Regulation (EC) 1272/2008 implementing the GHS system) (EU, 2006).

Other studies

European Union

Human study: NOAEL: 0.3 mg/kg bw/day (21-day) (1:9 ratio methamidophos:acephate, plasma cholinesterase inhibition) (EU, 2000, p. 65)

Developmental neurotoxicity study in rats: NOAEL: 1 mg/kg diet (0.085 mg/kg bw/day) (no additional findings of concern) (EU, 2006, p. 6)

Safety values

European Union

Acceptable Daily Intake (ADI): 0.001 mg/kg bw/day

Acceptable Operator Exposure Level (AOEL): 0.001 mg/kg bw/day

Acute Reference Dose (ARfD): 0.003 mg/kg bw/day

Following its acute toxicity data Tamaron SL 200 is to be labelled as "toxic if swallowed", "harmful in contact with skin", "very toxic to aquatic organism" and "may cause long-term effects in the aquatic environment". Tamaron SL 600 is to be labelled as "very toxic if swallowed", "harmful in contact with skin", "very toxic to aquatic organisms" and "may cause long-term effects in the aquatic environment". Both products are non-irritating to skin; Tamaron SL 200 is slightly irritant to the eye, Tamaron SL 600 is not irritant to the eye. Both are not skin sensitizers. When used according to the proposed GAP, methamidophos poses no acute or long-term dietary risks to humans with the use of WHO European diet (EU, 2000, p. 28).

Residues

Metabolism studies in rats, lactating goats and laying hens revealed that methamidophos is rapidly excreted. Total ^{14}C residues in edible portions of goats and hens are very low and are likely to consist of natural products resulting from metabolism of methamidophos in the carbon-I pool. Comparing results from metabolism studies in rats, goats and hens, the two metabolites identified in farm animals are the desamino-methamidophos and S-methyl phosphoramidothioate, which are also identified in the rat. Therefore it can be concluded that this metabolite is not of toxicological relevance. The parent compound is regarded as the residue of concern (EU, 2000, p. 29).

3 Human exposure/Risk evaluation

3.1 Food

Use of methamidophos may result in low level residues; but there should be no health hazard if pre-harvest intervals are observed. Since 1987 in Hong Kong, there have been numerous cases of acute poisoning following the consumption of leafy vegetables imported from China. In Shenzen, where the bulk of these vegetables originates, it is strongly suspected that methamidophos has been used by some farmers and that the sprayed vegetables have been harvested too early before the residue levels have fallen to safe levels. In the USA, methamidophos was found at unacceptable levels in pre-schoolers diets in a 1989 study. The average intake as a percentage of ADI was 5.763%. Between 63-97.6% of 1-5 year old kids were estimated to be receiving average daily exposure above the ADI (FAO/UNEP, 1997).

Brazil

Studies show that methamidophos is one of the most frequently used pesticides in Brazil. However, indiscriminate use is suspected in some cases, leading to the detection of residues above the legal maximum concentration in various foods (fresh tomato, strawberry and lettuce) for which the use of methamidophos was not allowed or restricted. This was considered a public health problem as these foods are widely eaten raw in Brazil.

European Union

The use of methamidophos may entail certain risks for consumers. Deterministic models indicated high risk for chronic and acute dietary intake especially for toddlers (consumption values taken from UK diet). The highest contributions to chronic risk came from consumption of plum fruit and tomatoes and the acute risk (ARfD) was high for all crops except for broccoli, cauliflower, cabbage and potato. A probabilistic model showed no acute risk. Intended uses have been reduced and new processing factors added. Based on the new list of uses, the deterministic model for estimating the chronic and acute intake of methamidophos through the diet did not show any risk for the general population.

3.2 Air

The population is generally not exposed to methamidophos in the air (see section 4.1.3).

3.3 Water

The population is not generally exposed to methamidophos in water, although methamidophos has also been shown to contaminate drinking water in Brazil.

3.4 Occupational exposure

Higher occupational exposure (mainly through inhalation and dermal absorption) may occur in the case of accidents or as a result of incorrect handling. There are several reports on methamidophos indicating it may cause health problems during occupational use. In the US, methamidophos was judged third-highest among 28 pesticides on measures of occupational hazard. Methamidophos had the third-highest ratio of handler poisonings per 1000 applications in California when exposures in mixtures were included, and the second-highest overall for field workers. Methamidophos ranked second in percentage of cases displaying symptoms or life-threatening symptoms among occupational Poison Control Centre cases. In China, 27 provinces reported a total of 48377 poisoning cases, including 3204 fatalities in 1995. Fifteen-thousand three-hundred of these cases were caused by normal agricultural use and not by accidents or improper use. More than 50 % of these 15000 cases were attributed to parathion, methamidophos and omethoate (FAO/UNEP, 1997).

Brazil

A number of studies in Brazil have reported the presence of symptoms of organophosphate poisoning in farmers using methamidophos.

European Union

Member States were requested to pay particular attention to the protection of operators who had to wear suitable protective clothing during mixing-loading and gloves, coveralls, rubber boots and face protection or safety glasses during application and cleaning of equipment. The above measures had to be applied unless exposure to the substance was adequately precluded by the design and construction of the equipment itself or by the mounting of specific protective components on such equipment.

3.5 Medical data contributing to regulatory decision

European Union

It has been suggested that methamidophos would induce peripheral neuropathy starting a few days after severe overexposure ('intermediate syndrome'). The clinical, pathological and functional features of these neuropathies have been extensively discussed in the literature. The conclusion has been made that the existence of this disease as a separate nosological entity has not been demonstrated (EU, 2006, p. 6).

Dermal absorption: Results from the studies on dermal absorption in monkeys and humans in vivo could serve as a basis for estimating the extent of dermal absorption in humans. This will give a best estimated dermal absorption of about 5% for humans. The underlying assumption is that the disposition of methamidophos in the monkey is similar to that in humans. The value of about 5% is consistent with the 10 % value estimated from the monkey study and the fact that data with a number of compounds indicate a 2-3 fold higher skin absorption in monkeys than in humans.

3.6 Public exposure

In China, Hong Kong, Brazil and the European Union, a possible risk of toxicity has been identified due to the presence of methamidophos residues in food consumed by the public (see section 3.1). Contamination of drinking water by methamidophos has been observed in Brazil.

3.7 Summary-overall risk evaluation

Brazil

Methamidophos is an extremely toxic organophosphate (Class I), which causes serious adverse effects to human health, especially related to neurotoxicity, immunotoxicity and to the endocrine, reproductive systems and fetal development.

Symptoms of poisoning toxicity were observed in toxicity studies in experimental animals which were consistent with acetyl cholinesterase (AChE) inhibition, the typical effect caused by organophosphates.

A series of specific studies conducted within Brazil observed risks to human health arising from the use of methamidophos; in particular risks to operators, workers and consumers. The risk evaluation took into account national studies, including studies on exposure under the prevailing conditions in Brazil, and the toxicological endpoints for methamidophos. The result was an unacceptable risk to human health. In the light of the toxicity of methamidophos and observed risks to human health within Brazil, a toxicological re-evaluation concluded that the substance should be banned according to

Resolution RDC No 01 of 14 January 2011.

European Union
Methamidophos is a cholinesterase inhibitor characterised by high acute toxicity. Methamidophos is classified "T+ - Very toxic" (Directive 67/548/EEC) and "Acute Tox. 2" (Regulation (EC) 1272/2008 implementing the GHS system).
The use of methamidophos may entail certain risks for consumers. Deterministic models indicated high risk for chronic and acute dietary intake especially for toddlers (consumption values taken from UK diet). The highest contributions to chronic risk came from consumption of plum fruit and tomatoes and the acute risk (ARfD) was high for all crops except for broccoli, cauliflower, cabbage and potato. A probabilistic model showed no acute risk. Intended uses have been reduced and new processing factors added. Based on the new list of uses, the deterministic model for estimating the chronic and acute intake of methamidophos through the diet did not show any risk for the general population.

4 Environmental fate and effects

4.1 Fate

4.1.1 Soil

Under aerobic conditions, 49% mineralisation of methamidophos was reported to occur after 5 days, with 31% present in the soil as non-extractable residues.

S-methyl phosphoramidothioate and desamino-methamidophos were identified as major and minor metabolites, respectively. Both metabolites were rapidly degraded to carbon dioxide.

Methamidophos is rapidly degraded under anaerobic conditions. S-methyl phosphoramidothioate was identified as the major metabolite (35% at day 31). This metabolite did not appear to degrade under anaerobic conditions. After 61 days, non-extractable residues accounted for 22% of the initially applied concentration.

Photodecomposition of methamidophos on a thin layer of sandy loam soil under continuous lighting was reported to be rapid, with S-methyl phosphoramidothioate and desamino-methamidophos identified as the major and minor metabolites, respectively.

The DT_{90} for methamidophos in field studies has been determined to be less than 10 days (EU, 2006, p. 8-9).

4.1.2 Water

Hydrolysis of methamidophos readily occurs in neutral or alkaline conditions, with half-lives of 660, 5 and 3 days at pH 4, 7 and 9, respectively. Photolysis occurs according to first-order kinetics, with half-lives of 37 and 90 days under continuous simulated and natural sunlight, respectively, at latitude 38°49' and longitude 94°40'. Desamino-methamidophos and S-methyl phosphoramidothioate were identified as the major products of photo-degradation. Based on a water-sediment study, methamidophos is considered to be readily biodegradable both parent and its metabolites were >70% degraded within 28 days.
A water sediment study has identified the following DT_{50} values:
DT_{50} water (ditch): 4 days
DT_{50} water (pond): 7.8 days
DT_{50} whole system (ditch, loamy silt): 4.1 days (DT_{90} 13.8 days)
DT_{50} whole system (pond, loamy silt): 5.8 days (DT_{90}: 19.3 days) (EU, 2006, p. 11-12)

4.1.3 Air

The calculated half-life of methamidophos in air is 0.578 days and a value of 0.838 days for the chemical lifetime of methamidophos in the troposphere. Because of its short lifetime in air, methamidophos is unlikely to be transported in the gaseous phase over large distances or to accumulate in the air. On account of the relatively low trend to volatilise combined with the short life of methamidophos in air, an accumulation in the atmosphere and consequently a lasting contamination due to dry or wet deposition is not to be expected (EU, 2006, p. 13 and EU, 2000, p. 37).

4.1.4 Bioconcentration

Methamidophos lacks a potential for bioaccumulation, as indicated by a log P_{ow} of -0.8 (EU, 2006, p. 2 and 12).

4.1.5 Persistence

The half-life in soil is a few days. Degradation products are CO_2, mercaptan, dimethyl disulfide and dimethyl sulphide.

4.2 Effects on non-target organisms

4.2.1	**Terrestrial vertebrates**	**Birds** Bobwhite quail *(Colinus virginianus)* 5-day LC_{50}: 42 mg/kg diet Reproductive NOEL (species not stated): 0.29 mg/kg bw/day Short-term risk to bird was considered to be covered by acute exposure as it is not possible to derive a reliable daily dietary dose due to food avoidance at doses > 10 mg/kg diet (EU, 2006, p. 14 and EU, 2000, p. 37-39).
4.2.2	**Aquatic species**	**Algae** Green algae *(Scenedesmus subspicatus)* 96-hour EC_{50} (growth inhibition): >178 mg/L (technical methamidophos) Green algae *(Scenedesmus subspicatus)* 96-hour EC_{50} (growth inhibition): 202 mg/L (60 SL formulation) **Fish** Acute toxicity: Rainbow trout *(Oncorhynchus mykiss)* 96-hour LC_{50}: 40 mg/L (technical methamidophos) Golden orfe (*Leuciscus idus melanotus*) 96-hour LC_{50}: 112 mg/L (600 EC) Long-term toxicity: Rainbow trout *(Oncorhynchus mykiss)* 97-day NOEC: 2.15 mg/L (technical methamidophos) **Invertebrates** Acute toxicity: Waterflea *(Daphnia magna)* 48-hour EC_{50}: 0.27 mg/L (technical methamidophos) Chronic toxicity Waterflea *(Daphnia magna)* 21-day NOEC: 0.026 mg/L (technical methamidophos) (EU, 2006, p. 14 and EU, 2000, p. 39-40)
4.2.3	**Honeybees and arthropods**	**Honey bees** No hazard quotients for honey bees have been calculated, because only higher tier studies have been provided. From a cage field toxicity trial, toxicity to honey bees due to methamidophos proved to be very high, but decreased rapidly. Methamidophos 720 SL at 1.12 kg a.i./ha caused a reduction in bee visitation for 3 days and killed a moderately high number of bees for 1.5 days. The overall effect was considered to be a high toxicity level to honey bees. Methamidophos 720 SL at 0.56 kg a.i./ha caused a reduction in bee visitation for 2-3 days and killed a slightly higher number of bees than observed in water treated plots for 1 day. The overall effect was considered to be a moderately low toxicity level to honey bees. Methamidophos should not be used during flowering (EU, 2006, p. 15 and EU, 2000, p. 40). **Arthropods** Predatory mite *(Amblyseius potentillae)*: 100% mortality at 0.108 kg a.s./ha (Tamaron SL 600) Predatory mite *(Typhlodromus pyri)*: 100% mortality at 0.108 kg a.s./ha (Tamaron SL 600) Aphid parasite *(Aphidius rhopalosiphi)* LR_{50}: 2.52 g a.s./ha (Tamaron SL 200) Aphid parasite *(Aphidius rhopalosiphi)* LR_{50}: 1.29 g a.s./ha (Tamaron SL 600) (EU, 2006, p. 15 and EU, 2000, p. 41)
4.2.4	**Earthworms**	Earthworm *(Eisenia foetida)* LC_{50}: 28.8 mg formulation/kg dw soil (Tamaron 60%) Earthworm *(Eisenia foetida)* LC_{50}: 73 mg formulation/kg dw soil (Tamaron SL 600) Earthworm *(Eisenia foetida)* NOEC: 1 mg formulation/kg dw soil (EU, 2006, p. 16 and EU, 2000, p. 40-41)
4.2.5	**Soil microorganisms**	No significant influence on the mineralisation of carbon and nitrogen at 5.3 and 26.8 mg as/kg soil (EU, 2006, p.16).
4.2.6	**Terrestrial plants**	No data located

5 Environmental Exposure/Risk Evaluation

5.1	**Terrestrial vertebrates**	***European Union*** Toxicity/exposure ratios were calculated for a range of insectivorous and herbivorous birds and mammals based on methamidophos applied to potatoes in Europe. The Toxicity Exposure Ratio (TER) is a measure of the risk: it is calculated by dividing the toxicity values (LD_{50} or NOEL) of sensitive organisms by the predicted exposure to the substance. The Trigger Value (TV) represents a value above which the TER is considered to represent an acceptable risk and may include a margin of precaution. Birds: Acute TERs 0.25-64 (TV 10) Short-term TERs 0.004-0.32 (TV 10) Long-term TERs 0.02-2 (TV 5) Mammals: Acute and short-term TERs 0.004-64 (TV 10) Long-term TERs 0.07-6.41 (TV 5) The TERs indicated a potential high short- and long-term risk for both birds and mammals. Further assessment was conducted as to the consumption of methamidophos in the field by yellow wagtails and wood mice after reduction of insects by the insecticide. It was considered that consumption of dead insects would still take place. The role of avoidance by these animals (reduced consumption) of food treated with methamidophos was also considered but it appeared possible that feeding might be rapid enough for mortality to occur under field conditions. Preliminary consideration also suggested that other routes of exposure (drinking, dermal exposure and overspray of nesting birds) might be higher than risk from dietary exposure.
5.2	**Aquatic species**	***European Union*** The risk assessment (TER calculation) was based on the most sensitive toxic endpoints and Predicted Environmental Concentrations (PEC) for surface water at different distances from target crops. Acute TER: fish 339-66667 (TV 100), daphnids 2-450 (TV 100), green algae 1508-296667 (TV 10) Long-term TERs: fish 18-1194, daphnids 0.2-2.43 (TV 10) With buffer zones, the TERs for daphnids were raised to: short-term 103.8-177.6 and long-term 10.1-35 Overall it can be concluded that the risk from methamidophos use to fish and algae is quite low but the risk to daphnids is high. When a buffer zone is introduced the risk can be considered acceptable.
5.3	**Honey bees and Arthropods**	***European Union*** No hazard quotients (HQs) for honey bees have been calculated. Methamidophos is acutely toxic to a variety of beneficial arthropods.
5.4	**Earthworms**	***European Union*** Calculated Acute TERs of 36-270 were above the TV of 10 and this together with the rapid degradation of methamidophos in soil indicates that a negative impact on earthworms is not expected.
5.5	**Soil microorganisms**	***European Union*** Methamidophos does not have a negative influence on microbial mineralization processes in field soils.
5.6	**Summary – overall risk evaluation**	***European Union*** A risk assessment revealed that toxicity/exposure ratios for a range of scenarios with aquatic and terrestrial organisms indicated acute and long-term risk for birds and acute risk for mammals for the use of methamidophos in potato fields. Furthermore a high acute and long-term risk for aquatic invertebrates *(Daphnia magna)* was identified for methamidophos use in field and orchard crops and vegetables. The risk to beneficial arthropods was also high. There was also a potentially high risk to birds and mammals from consumption of dead insects and possibly other routes of exposure.

Annex 2 – Details on final regulatory actions reported

Country Name: BRAZIL

1	**Effective date(s) of entry into force of actions**	The Resolution-RDC No. 01 of 14 January 2011 of National Health Surveillance Agency (ANVISA) entered into force on 17 January 2011.
	Reference to the regulatory document	Resolution-RDC No. 01 of 14 January 2011 of National Health Surveillance Agency (ANVISA): Technical regulation on the active ingredient Methamidophos as a result of a Technical Note of Toxicological Reassessment commissioned by the ANVISA. Available at Document UNEP/FAO/RC/CRC.9/8/Add.1 (Focused summary - p. 31-33) or whole document in Portuguese (p. 34-143). Also available at http://www.in.gov.br/visualiza/index.jsp?data=17/01/2011&jornal=1&pagina=56&totalArquivos=104 or http://www.brasilsus.com.br/legislacoes/rdc/107157-1.html (in Portuguese)
2	**Succinct details of the final regulatory action(s)**	The final regulatory action prohibited all formulations containing methamidophos and all uses of methamidophos, including the sale, import and export. It also rejects future registrations of pesticides containing methamidophos.
3	**Reasons for action**	Health risks for agricultural workers, bystanders and consumers.
4	**Basis for inclusion into Annex III**	The final regulatory action to ban methamidophos was based on a risk evaluation taking into consideration local conditions in Brazil.
4.1	**Risk evaluation**	Methamidophos is an extremely toxic organophosphate (Class I), which causes serious adverse effects to human health, especially related to neurotoxicity, immunotoxicity and to the endocrine system, reproduction and fetal development. Toxicity studies in experimental animals observed symptoms of poisoning toxicity which were consistent with cholinesterase (AChE) inhibition, the typical effect of organophosphates. A series of specific studies conducted within Brazil observed risks to human health arising from the use of methamidophos; in particular risks to operators, workers and consumers. Cases of indiscriminate use of methamidophos and contamination in vegetable crops had been reported. Residues were found in various foods for which the use of methamidophos was not allowed (fresh tomato, strawberry and lettuce) or restricted. This was considered a public health problem, because these foods are usually eaten raw and are part of the eating habits in Brazil. Also in the production of processing tomato in sub-middle São Francisco River Valley, 11% of the samples were inappropriate for consumption due to the levels of methamidophos. At the rural centre of Vargem Bonita, methamidophos poisoning occurred in five of the eight workers (62.5%) who applied the product. In a survey on practices for the use of pesticides and symptoms after the application of the products, over 90% of 250 farmers reported the use of products containing methamidophos, and 149 farmers reported adverse effects after the use of pesticides. The risk evaluation took into account national studies, including studies on exposure under the prevailing conditions in Brazil, and the toxicological endpoints for methamidophos. The result was an unacceptable risk to human health. In the light of the toxicity of methamidophos and observed risks to human health within Brazil, a toxicological re-evaluation concluded that that the substance should be banned according to the Resolution RDC No 01 of 14 January 2011.
4.2	**Criteria used**	Risks to human health
	Relevance to other States and Region	None reported

5	**Alternatives**	The relevant substitutes for use on crops of beans, soybeans and cotton are: abamectin, thiamethoxam, acephate, spinosad ; triflumuron ; fipronil, chlorpyrifos, indoxacarb, bifenthrin, lambda-cyhalothrin, methomyl, cypermethrin; diflebenzurom; imidacloprid, clothianidin; flufenoxuron; novalurom; triazophos; lufenuron and *Bacillus thuringiensis*.
6	**Waste management**	None reported
7	**Other**	None reported

Country Name: EUROPEAN UNION		
1	**Effective date(s) of entry into force of actions**	Commission Directive *2006/131/EC* entered into force on 1 January 2007. However, Member States had to apply the provisions of this Directive from 1 July 2007.
	Reference to the regulatory document	Commission Directive *2006/131/EC* of 11 December 2006 amending Council Directive *91/414/EEC* to include methamidophos as an active substance (Official Journal of the European Union, L 349, 12.12.2006 p. 17 - 21). http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2006:349:0017:01:EN:HTML.
2	**Succinct details of the final regulatory action(s)**	Commission Directive *2006/131/EC* of 11 December 2006 amending Directive *94/414/EEC* severely restricted the placing on the market and use of plant protection products containing methamidophos. The Commission Directive amended Annex I to Directive *91/414/EEC* (which was replaced by Regulation (EC) No *1107/2009* concerning the placing of plant protection products on the market) to permit the use of methamidophos from 1 January 2007 to 30 June 2008. It also set in place restrictions on the use of methamidophos (for more details see Section 2.3.3). The Directive imposed on the Member States a requirement to review all authorisations of methamidophos to ensure that the restrictions set in Directive *2006/131/EC* were respected as of 30 June 2007. It also required a re-evaluation of products containing methamidophos by 30 June 2008. The restrictions limited the application of methamidophos to only one specific crop (potato) and defined a maximum application rate and number of applications. It also prohibited specific uses and limited the period of inclusion of methamidophos in Annex I to Directive *94/414/EEC* to 18 months after entry into force of Directive *2006/131/EEC* on 1 January 2007. It should be noted that this period has now expired. As of 30 June 2008, methamidophos is no longer included in the list of authorised substances in Annex I. Hence, methamidophos is no longer allowed to be used as plant protection product in the European Union.
3	**Reasons for action**	Human health: unacceptable risks for operators, workers and consumers. Environment: high risk for aquatic and terrestrial organisms.
4	**Basis for inclusion into Annex III**	The final regulatory action to ban methamidophos was based on a risk evaluation taking into consideration local conditions in the EU Member States.
4.1	**Risk evaluation**	**Human Health** It was concluded that it could be expected that plant protection products containing methamidophos would fulfil the safety requirements laid down in Article 5(1)(a) and (b) of Directive 91/414/EEC. This conclusion was however subject to compliance with the particular requirements in sections 4, 5, 6 and 7 of the review report, as well as to the implementation of the provisions of Article 4(1) and the uniform principles laid down in Annex VI of Directive 91/414/EEC, for each methamidophos containing plant protection product for which Member States would grant or review the authorisation. Therefore, Member States were requested to pay particular attention to the protection of operators who had to wear suitable protective clothing during mixing-loading and gloves, coveralls, rubber boots and face protection or safety glasses during application and cleaning of equipment. The above measures had to be applied, unless the exposure to the substance was adequately precluded by the design and construction of the equipment itself or by the mounting of specific protective components on such equipment. Member States were requested to ensure that the authorisation holders report at the latest on 31 December of each year on any reported effect on operator health. Member States could require that elements, such as sales data and a survey of use patterns, are provided so that a realistic picture of the use conditions and the possible toxicological impact of methamidophos could be obtained.

Methamidophos is a cholinesterase inhibitor characterised by high acute toxicity. Methamidophos is classified "T+ - Very toxic" (Directive 67/548/EEC) and "Acute Tox. 2" (Regulation (EC) 1272/2008 implementing the GHS system).

The use of methamidophos may entail certain risks for consumers. Deterministic models indicated high risk for chronic and acute dietary intake especially for toddlers (consumption values taken from UK diet). The highest contributions to chronic risk came from consumption of plum fruit and tomatoes and the acute risk (ARfD) was high for all crops except for broccoli, cauliflower, cabbage and potato. A probabilistic model showed no acute risk. Intended uses have been reduced and new processing factors added. Based on the new list of uses, the deterministic model for estimating the chronic and acute intake of methamidophos through the diet did not show any risk for the general population.

Environment
The risk assessment revealed that toxicity/exposure ratios for a range of scenarios with aquatic and terrestrial organisms indicated acute and long-term risk for birds and acute risk for mammals for the use of methamidophos in potato fields. Furthermore a high acute and long-term risk for aquatic invertebrates *(Daphnia magna)* was identified for methamidophos use in field and orchard crops and vegetables. The risk to beneficial arthropods was also high. There was also a risk to birds and mammals from consumption of dead insects and possibly other routes of exposure.

Therefore, Member States were requested to ensure that all appropriate risk mitigation measures were applied. Member States were requested to pay particular attention to the protection of:

- birds and mammals. Conditions of authorization needed to include risk mitigation measures, such as a judicious timing of the application and the selection of those formulations which, as a result of their physical presentation or the presence of agents that ensure an adequate avoidance, minimize the exposure of the concerned species,
- aquatic organisms and non-target arthropods. An appropriate distance had to be kept between treated areas and surface water bodies as well as margins of the crop. This distance could depend on the application or not of drift reducing techniques.

4.2	**Criteria used**	Risks to human health and the environment
	Relevance to other States and Region	Similar health and environmental problems are likely to be encountered in other countries where the substance is used particularly in developing countries.
5	**Alternatives**	None reported
6	**Waste management**	None reported
7	**Other**	None reported

Annex 3 – Addresses of designated national authorities

European Union

European Commission DG Environment BU-9, 06/164 B-1049 Brussels Belgium Dr. Juergen Helbig Policy Officer	**Phone** +32 2 298 8521 **Fax** +32 2 296 7617 **E-mail** Juergen.Helbig@ec.europa.eu

Brazil

Ministry of the Environment Department of Environmental Quality in Industry, Secretariat of Climate Change and Environmental Quality Esplanada dos Ministérios, Bloco B, 8º andar, Gabinete Sérgia de Souza Oliveira Director	**Phone** +55 61 2028 2073 **Fax** +55 61 2028 2074 **E-mail** sergia.oliveira@mma.gov.br, gsq@mma.gov.br

Annex 4 – References

Regulatory actions

European Union

Commission Directive 2006/131/EC of 11 December 2006 amending Council Directive 91/414/EEC to include methamidophos as an active substance (Official Journal of the European Union, L 349, 12.12.2006, p. 17 - 21). Available at: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2006:349:0017:01:EN:HTML or in Document UNEP/FAO/RC/CRC.9/8/Add.2, p. 215-219

Brazil

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Relevant guidelines and reference documents

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