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

Chemical Review Committee
Ninth meeting
Rome, 22–25 October 2013
Item 5 (c) (iv) of the provisional agenda*

Technical work: review of notifications of final regulatory actions: methamidophos

Methamidophos: notifications of final regulatory action

Note by the Secretariat

I. Introduction

1. Under Article 5 of the Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade, when the Secretariat has received at least one notification of final regulatory action to ban or severely restrict a chemical from each of two prior informed consent (PIC) regions that it has verified as containing the information required in Annex I to the Convention, it shall forward the notifications and accompanying documentation to the members of the Chemical Review Committee. The Committee shall review the information provided in such notifications and, in accordance with the criteria set out in Annex II to the Convention, recommend to the Conference of the Parties whether the chemical in question should be included in Annex III to the Convention and whether a decision guidance document should be drafted.

2. The Secretariat has received such notifications of final regulatory action for methamidophos from two PIC regions: Latin America and the Caribbean (Brazil) and Europe (European Union). Summaries of the notifications from Brazil and the European Union were included in PIC Circular XXXVI of December 2012 and PIC Circular XXXVII of June 2013, respectively. The notifications, as received from the notifying parties, are set out in the annex to the present note and have not been formally edited.

3. The supporting documentation provided by Brazil and the European Union is set out in documents UNEP/FAO/RC/CRC.9/8/Add.1 and UNEP/FAO/RC/CRC.9/8/Add.2, respectively.

4. A list of other notifications for methamidophos previously considered by the Committee is set out in document UNEP/FAO/RC/CRC.9/INF/6.

II. Possible action by the Committee

5. The Committee may wish:

(a) To review the information provided in the notifications and the respective supporting documentation from Brazil and the European Union related to methamidophos in accordance with the criteria set out in Annex II to the Convention;

* UNEP/FAO/RC/CRC.9/1.

(b) To recommend to the Conference of the Parties that the chemical in question be included in Annex III to the Convention and to agree on a workplan to prepare a draft decision guidance document, if it concludes that the notifications meet the criteria of Annex II to the Convention.

Annex

Notifications of final regulatory action for methamidophos

A. Notification of final regulatory action for methamidophos submitted by Brazil

B. Notification of final regulatory action for methamidophos submitted by the European Union

ROTTERDAM CONVENTION

SECRETARIAT FOR THE ROTTERDAM CONVENTION
ON THE PRIOR INFORMED CONSENT PROCEDURE
FOR CERTAIN HAZARDOUS CHEMICALS AND PESTICIDES
IN INTERNATIONAL TRADE

UNEP

FORM FOR NOTIFICATION
OF FINAL REGULATORY ACTION TO BAN OR SEVERELY RESTRICT A CHEMICAL

Country: Brazil

SECTION 1 IDENTITY OF CHEMICAL SUBJECT TO THE FINAL REGULATORY ACTION

1.1	**Common name**	Methamidophos
1.2	**Chemical name according to an internationally recognized nomenclature (e.g. IUPAC), where such nomenclature exists**	O,S-dimethyl phosphoramidothioate
1.3	**Trade names and names of preparations**	Methamidophos Técnico Agripec, Stron, Tamaron Técnico BR, Tamaron BR, Tamaron Técnico USA, Gladiador, Glent, Quasar, Rivat, Metamidofos Técnico Fersol, Metamidofós Fersol 600, Metamidofós Técnico Milenia, Metafós, Dinafos, Hamidop 600, Metasip

1.4 Code numbers

1.4.1	CAS number	10265-92-6
1.4.2	Harmonized System customs code	
1.4.3	Other numbers (specify the numbering system)	

1.5 Indication regarding previous notification on this chemical, if any

1.5.1 ☒ This is a first time notification of final regulatory action

on this chemical.

1.5.2 ☐ This notification replaces all previously submitted notifications on this chemical.
Date of issue of the previous notification: _____

SECTION 2 FINAL REGULATORY ACTION

2.1 The chemical is: ☒ **banned** **OR** ☐ **severely restricted**

2.2 Information specific to the final regulatory action

2.2.1 Summary of the final regulatory action

Gradual reduction in methamidophos use until the ban of this pesticide.
*ban of use, sale, import and export

2.2.2 Reference to the regulatory document, e.g. where decision is recorded or published

Resolution RDC nº 01, of January 14, 2011 of the National Health Surveillance Agency (ANVISA)

2.2.3 Date of entry into force of the final regulatory action

January, 17, 2011

2.3 Category or categories where the final regulatory action has been taken

2.3.1 All use or uses of the chemical in your country prior to the final regulatory action

Methamidophos is an insecticide/acaricide used on the following crops in Brazil: Cotton, Peanut, Potato, Bean, Soybean, Tomato, Wheat

2.3.2 Final regulatory action has been taken for the category ☐ Industrial

Use or uses prohibited by the final regulatory action

Use or uses that remain allowed (only in case of a severe restriction)

2.3.3 Final regulatory action has been taken for the category ☒ Pesticide

Formulation(s) and use or uses prohibited by the final regulatory action

All formulations containing Methamidophos and all uses of this active ingredient will be prohibited in the end of the phase-out described below:

I - 31 de dezembro de 2011 – prohibition of the sale
II - 30 de junho de 2012 – prohibition of the use
III- 31 de dezembro de 2012- Cancel the registration of all products containing methamidophos

Formulation(s) and use or uses that remain allowed

(only in case of a severe restriction)

None

2.4 Was the final regulatory action based on a risk or hazard evaluation? ☒ **Yes**

☐ **No** (If no, you may also complete section 2.5.3.3)

2.4.1 If yes, reference to the relevant documentation, which describes the hazard or risk evaluation

Technical Note of the Toxicological Reassessment on Methamidophos - National Health Surveillance Agency (ANVISA)

2.4.2 Summary description of the risk or hazard evaluation upon which the ban or severe restriction was based.

2.4.2.1 Is the reason for the final regulatory action relevant to human health? ☒ Yes

☐ No

If yes, give summary of the hazard or risk evaluation related to human health, including the health of consumers and workers

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.

Toxicity studies observed symptoms of poisoning consistent with cholinesterase (AChE) inhibition, typical effect caused by organophosphates.

All animails tested had loss in their organ weights, such as thyroid, heart, lung, pancreas, liver, kidneys, adrenals, spleen, thymus, testes and ovaries. The decrease in

the concentration of AChE was observed in all groups treated with different doses.

The endocrine disruption caused by methamidophos in experimental studies should be valued, because they have the potential to interfere with reproduction, although few epidemiological studies have been reported in the literature. Endocrine disruption is a very worrying adverse effect because it can trigger serious debilitating effects and even death. Endocrine disruptors have the potential to interfere with reproduction, thus change the number of individuals of a given population. Studies showed that this substance can damage the sperm morphology and interfere with the fertility. It can lead to changes in reproductive performance of males and females and also cause infertility causes pronounced effects in fetuses, as embryolethality, malformations, change on the physical landmarks of development and on the behavior of puppies.

Methamidophos is also immunotoxic, inducing a number of immunological effects, including decrease numbers of lymphocytes, monocytes and inhibition of antibody formation. In parallel to the potential immunosuppressive effects, methamidophos induces genotoxic effects. Several studies report mutations, chromosomal aberrations and DNA damage.

Although few studies found on the carcinogenicity of methamidophos, it is important to note that the association of pesticide exposure and cancer induction is difficult because the lack of specific models for this purpose. It is noteworthy that the DNA mutation is a genuine indicator of the ocarcinogenesis process Data indicate that methamidophos induces metaphases with chromosomal aberrations at low doses.

Psychiatric disorders such as depression, which can lead to suicide, cognitive impairment, and parkinsonism are correlated with exposure to organophosphates. The neurotoxicity of methamidophos is also a consequence of the inhibition of acetylcholinesterase, essential enzyme for the transmission of nerve impulses. The main chronic neurotoxic effect manifested is delayed polyneuropathy.

Expected effect of the final regulatory action

Remove the human exposure to methamidophos

2.4.2.2 Is the reason for the final regulatory action relevant to the environment? ☐ Yes ☒ No

If yes, give summary of the hazard or risk evaluation related to the environment

Expected effect of the final regulatory action

2.5 Other relevant information regarding the final regulatory action

2.5.1 Estimated quantity of the chemical produced, imported, exported and used

Quantity per year (MT)	Year

produced	2010 (44.767 t), 2011 (33.970 t), 2012 (0 t)	
imported	2010 (5.772 t), 2011 (0 t), 2012 (0 t)	
exported	2010 (0 t), 2011 (0 t), 2012 (0 t)	
used		

2.5.2 Indication, to the extent possible, of the likely relevance of the final regulatory action to other states and regions

2.5.3 Other relevant information that may cover:

2.5.3.1 Assessment of socio-economic effects of the final regulatory action

2.5.3.2 Information on alternatives and their relative risks, e.g. IPM, chemical and non-chemical 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.

2.5.3.3 Basis for the final regulatory action if other than hazard or risk evaluation

2.5.3.4 Additional information related to the chemical or the final regulatory action, if any

SECTION 3 PROPERTIES

3.1 Information on hazard classification where the chemical is subject to classification requirements

International classification systems e.g. WHO, IARC, etc.	Hazard class
WHO	highly hazardous (Class 1b)

Other classification systems e.g. EU, USEPA	Hazard class
U.S. EPA PC Code:	Class I (higlhy toxic)

3.2 Further information on the properties of the chemical

3.2.1 Description of physico-chemical properties of the chemical

Formula $C_2H_8NO_2PS$

Solubility in water > 200 g/l at 20°C, highly soluble in alcohols and ketones, sparingly soluble in ether and petroleum ether

LogP_{ow} -0.8

Vapour Pressure 4.7 mPa (25°C)

Reference

3.2.2 Description of toxicological properties of the chemical

Acute toxicity	
Rat, LD_{50}, oral	13–23 mg/kg bw
Rat, LD_{50}, dermal	110–380 mg/kg bw
Rat, LC_{50}, inhalation	0.063–0.21 mg/l (4 h, nose-only)
Mouse LD_{50}, oral	10–30 mg/kg bw
Skin irritation	Mildly irritating
Eye irritation	Mildly irritating
Skin sensitization	Not sensitizing (modified Buehler test)
Short-term studies of toxicity	
Target /critical effect	Inhibition of cholinesterase activity
Lowest relevant oral NOAEL	2.1 ppm (equal to 0.1 mg/kg bw per day, 56-day study in rats)
	2 ppm (equal to 0.06 mg/kg bw per day, 1-year

	study in dogs)
Long-term studies of toxicity and carcinogenicity	
Target/critical effect	Inhibition of cholinesterase activity
Lowest relevant NOAEL	2 ppm (equal to 0.1 mg/kg bw per day, 2-year study in rats)
Carcinogenicity	Unlikely to pose a carcinogenic risk to hum
Reproductive toxicity	
Target/critical effect for reproductive toxicity	Reduced parental and pup weight and viability
Lowest relevant NOAEL for reproductive toxicity	1 ppm (equal to 0.1 mg/kg bw per day, rats)
Target/critical effect for developmental toxicity	Decreased fetal body weight only at maternally toxic doses
Lowest relevant NOAEL for developmental toxicity	1 mg/kg bw (rats)
Neurotoxicity	
Acute (rats)	NOAEL: 0.3 mg/kg bw for inhibition of cholinesterase activity
90-day	NOAEL: 1 ppm (equal to 0.067 mg/kg bw for inhibition of cholinesterase activity, rats)
Delayed polyneuropathy	Delayed polyneuropathy at doses well above the LD_{50}

Reference

Pesticide residues in food – 2002 - Joint FAO/WHO Meeting on Pesticide Residues

3.2.3 Description of ecotoxicological properties of the chemical

Fish LC_{50} 96 h: 25-100 mg/l (rainbow trout, goldfish, carp)
Aquatic invertebrates EC_{50} 48h: 0.27 mg/l (Daphnia)
Birds Oral LD_{50}: 8 - 50 mg/kg bw (mallard duck, Japanese quail, hen)
Bees Toxic to bees *(Tomlin, 1994; IPCS, 1993)*

Reference

DGD Methamidophos – UNEP / FAO

SECTION 4 DESIGNATED NATIONAL AUTHORITY

Institution	Ministry of the Environment
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Position of person in charge	Director of the Department of Environmental Quality
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Date, signature of DNA and official seal: Sérgia de Souza Oliveira
Diretora do Departamento de
Qualidade Ambiental na Indústria
15/Oct. 2012

PLEASE RETURN THE COMPLETED FORM TO:

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Food and Agriculture Organization
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Viale delle Terme di Caracalla
00153 Rome, Italy
Tel: (+39 06) 5705 2188
Fax: (+39 06) 5705 6347
E-mail: pic@pic.int

OR

Secretariat for the Rotterdam Convention
United Nations Environment
Programme (UNEP)
11-13, Chemin des Anémones
CH – 1219 Châtelaine, Geneva, Switzerland
Tel: (+41 22) 917 8296
Fax: (+41 22) 917 8082
E-mail: pic@pic.int

Definitions for the purposes of the Rotterdam Convention according to Article 2:

(a) '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;

(b) 'Banned chemical' means a chemical all uses of which within one or more categories have been prohibited by final regulatory action, in order to protect human health or the environment. It includes a chemical that has been refused approval for first-time use or has been withdrawn by industry either from the domestic market or

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FORM FOR NOTIFICATION
OF FINAL REGULATORY ACTION TO BAN OR SEVERELY RESTRICT A CHEMICAL

Country:

European Union

(Member States: Austria, Belgium, Bulgaria, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and United Kingdom)

SECTION 1 IDENTITY OF CHEMICAL SUBJECT TO THE FINAL REGULATORY ACTION

1.1	**Common name**	**Methamidophos**
1.2	**Chemical name according to an internationally recognized nomenclature (e.g. IUPAC), where such nomenclature exists**	**IUPAC: O,S-Dimethyl phosphoramidothioate** **CA: O,S-Dimethyl phosphoramidothioate**
1.3	**Trade names and names of preparations**	**Tamaron SL 200, Tamaron SL 600**

1.4 Code numbers

1.4.1	CAS number	10265-92-6
1.4.2	Harmonized System customs code	2930.50
1.4.3	Other numbers (specify the numbering system)	EINECS Number: 233-606-0 CIPAC Number: 355 Combined Nomenclature (CN) code of the European Union: 2930 50 00

1.5 Indication regarding previous notification on this chemical, if any

1.5.1 ☒ This is a first time notification of final regulatory action on this chemical.

1.5.2 ☐ This notification replaces all previously submitted notifications on this chemical.
Date of issue of the previous notification: _____

SECTION 2 FINAL REGULATORY ACTION

2.1 The chemical is: ☐ **banned** **OR** ☒ **severely restricted**

2.2 Information specific to the final regulatory action

2.2.1 Summary of the final regulatory action

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.

2.2.2 Reference to the regulatory document, e.g. where decision is recorded or published

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

2.2.3 Date of entry into force of the final regulatory action

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.

2.3 Category or categories where the final regulatory action has been taken

2.3.1 All use or uses of the chemical in your country prior to the final regulatory action

Methamidophos was used in plant protection products classified as insecticides on the following crops: pome fruit, stone fruit (peaches and apricots), tomatoes, flowering brassica (cauliflower and broccoli), head cabbage, cotton seed, soybeans, potatoes, cereals, sugar/fodder beet, tobacco.

2.3.2 Final regulatory action has been taken for the category ☐ Industrial

Use or uses prohibited by the final regulatory action

Not relevant

Use or uses that remain allowed (only in case of a severe restriction)

Nat relevant

2.3.3 Final regulatory action has been taken for the category ☒ Pesticide

Formulation(s) and use or uses prohibited by the final regulatory action

Part A of the Annex to Commission Directive 2006/131/EC provided for one single use on potato that was in principle allowed in the European Union and specified a maximum application rate and number of applications of the active substance, which means that Member States were allowed to grant national authorisations within those limits. All other uses not included in that list, i.e. other crops and higher rates of the active substance, were prohibited.

In addition, the following uses were not allowed to be authorised by Member States:

— air application,

— knapsack and all hand-held applications, neither by amateur nor by professional users,

— home gardening.

Formulation(s) and use or uses that remain allowed

(only in case of a severe restriction)

Methamidophos was only allowed to be used on potatoes.

The following conditions of use had to be respected:

- — At rates not exceeding 0.5 kg active substance per hectare per application,
- — Maximum 3 applications per season.

Member States were requested to ensure that all appropriate risk mitigation measures were applied. Particular attention had to be paid to the protection of:

— birds and mammals. Conditions of authorisation 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, minimise 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,

— operators, who needed to wear suitable protective clothing, in particular gloves, coveralls, rubber boots and respiratory protective devices during mixing and 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.

2.4 Was the final regulatory action based on a risk or hazard evaluation?

☒ **Yes**

☐ **No** (If no, you may also complete section 2.5.3.3)

2.4.1 If yes, reference to the relevant documentation, which describes the hazard or risk evaluation

A risk assessment was carried out on the basis of Directive 91/414/EEC (replaced by Regulation (EC) No 1107/2009), which provides for the European Commission to issue a work programme for the examination of existing active substances used in plant protection products with a view to their possible inclusion in Annex I to the Directive, and in accordance with the provisions laid down in Regulation (EEC) No 3600/92.

A Member State was designated to undertake the risk assessment based on the information submitted by the applicant and to establish a draft assessment report (monograph), which was subject to peer review by the Member States and the European Commission. This review revealed a number of open questions which were addressed by the Scientific Panel on Plant health, Plant protection products and their residues of the European Food Safety Authority (EFSA).

The European Commission examined methamidophos in accordance with the provisions laid down in Regulation (EEC) No 3600/92 and established a draft review report which was submitted to peer review by the Standing Committee on the Food Chain and Animal Health (SCFCAH), which 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.

The evaluation was based on a review of scientific data taking into account the conditions prevailing in the European Union (intended uses, recommended application rates, good agricultural practices). Only data that had been generated according to scientifically recognised methods were validated and used for the evaluation. Moreover, data reviews were performed and documented according to generally recognised scientific principles and procedures.

The risk assessment described above resulted in several documents, including:

- European Commission (2007): Review report for the active substance methamidophos finalised in the Standing Committee on the Food Chain and Animal Health at its meeting on XXX 2006 in view of the inclusion of methamidophos in Annex I of Directive 91/414/EEC
- Italy, Ministry of Health (2000): Monograph (including the addenda) prepared in the context of the inclusion of the following active substance in Annex I of the Council Directive 91/414/EEC – Methamidophos - Volume 1 - Report and Proposed Decision.

- EFSA (2004): Opinion of the Scientific Panel on Plant health, Plant protection Products and their Residues on a request from the Commission related to the evaluation of methamidophos in toxicology in the context of Council Directive 91/414/EEC (Question No. EFSA-Q-2004-60), the EFSA Journal 95, 1-15.
- EFSA (2004): Opinion of the Scientific Panel on Plant health, Plant protection Products and their Residues on a request from the Commission related to the evaluation of methamidophos in ecotoxicology in the context of Council Directive 91/414/EEC (Question No. EFSA-Q-2004-59), the EFSA Journal 144, 1-50.

2.4.2 Summary description of the risk or hazard evaluation upon which the ban or severe restriction was based.

2.4.2.1 Is the reason for the final regulatory action relevant to human health? ☒ Yes ☐ No

If yes, give summary of the hazard or risk evaluation related to human health, including the health of consumers and workers

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.

Expected effect of the final regulatory action

Reduction of risk from the use of plant protection products containing methamidophos.

2.4.2.2 Is the reason for the final regulatory action relevant to the environment? ☒ Yes ☐ No

If yes, give summary of the hazard or risk evaluation related to the environment

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 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 authorisation 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, minimise 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.

The risk assessment revealed that toxicity/exposure ratios for a range of scenarios and aquatic and terrestrial organisms indicated acute and long-term concern for birds and acute risk for mammals for the use of methamidophos in

potato fields. There was also acute and long-term risk for the aquatic organism, *Daphnia magna*, with methamidophos use in field and orchard crops and vegetables. The risk to beneficial arthropods was also high.

Further evaluation 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 in 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.

Expected effect of the final regulatory action

Reduction of risk to the environment (e.g. birds, mammals and aquatic organisms) from the use of plant protection products containing methamidophos.

2.5 Other relevant information regarding the final regulatory action

2.5.1 Estimated quantity of the chemical produced, imported, exported and used

	Quantity per year (MT)	Year
produced	No Information	
imported	No Information	
exported	No Information	
used	No Information	

2.5.2 Indication, to the extent possible, of the likely relevance of the final regulatory action to other states and regions

Similar health and environmental problems are likely to be encountered in other countries where the substance is used particularly in developing countries.

2.5.3 Other relevant information that may cover:

2.5.3.1 Assessment of socio-economic effects of the final regulatory action

No information

2.5.3.2 Information on alternatives and their relative risks, e.g. IPM, chemical and non-chemical alternatives

No information

2.5.3.3 Basis for the final regulatory action if other than hazard or risk evaluation

No information

2.5.3.4 Additional information related to the chemical or the final regulatory action, if any

No information

SECTION 3 PROPERTIES

3.1 Information on hazard classification where the chemical is subject to classification requirements

International classification systems **e.g. WHO, IARC, etc.**	**Hazard class**
WHO	2

Other classification systems **e.g. EU, USEPA**	**Hazard class**
Classification of the EU according to Regulation (EC) No 1272/2008, which implements the UN GHS in the European Union	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.)
Classification of the EU 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.

3.2 Further information on the properties of the chemical

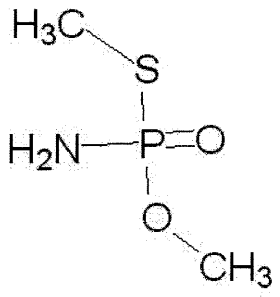
3.2.1 Description of physico-chemical properties of the chemical

Minimum Purity: 730 g/kg

Molecular formula: $C_2H_8NO_2PS$

Molecular Mass: 141.1

Structural Formula:



Appearance: Crystals (pure active ingredient), active substance manufactured as liquid or crystal slurry or waxy solid

Melting Point: 45°C (purity 99.5%),

45°C (test material manufactured as waxy solid)

Boiling Point: Exothermic decomposition between 160 and 215°C (purity 99.7%)

Vapour Pressure: 2.3 $x10^{-5}$ hPa at 20°C (purity 99.5%)

Henry's Law Constant: <1.6 $x10^{-6}$ $Pa.m^3/mole$

Solubility in Water: >200 g/l at 20°C (purity 99.5%)

Solubility in Organic Solvents: at 20°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

Relative Density: 1.27 at 20°C (purity 99.5%)

1.33 at 20°C (test material manufactured as waxy solid, not considered acceptable)

Dissociation Constant (pKa): Methamidophos has neither basic nor acidic properties in water. Therefore, a pK value cannot be determined.

Log Kow: -0.80 at 20°C (purity 99.7%)

0.32 at 20°C (test material manufactured as waxy solid, not considered acceptable)

Hydrolytic Stability:

Half-life in aqueous buffer at 22°C (extrapolated), purity 99.3%

pH 4: 660 days

pH 7: 5 days

pH 9: 3 days

Half-life in aqueous buffer at 25°C (extrapolated), purity 99.3%

pH 5: 309 days

pH 7: 27 days

pH 9: 3 days

Photostability in water DT_{50}:

Photodecomposition was first-order and yielded half-lives of 37 and 90 days under continuous simulated and natural sunlight, respectively, at latitude 38°49' and longitude 94°40'. The differences between the two systems were largely attributed to the length of irradiation (24-hours vs. 12-hours).

Reference

- European Commission (2007): Review report for the active substance methamidophos finalised in the Standing Committee on the Food Chain and Animal Health at its meeting on XXX 2006 in view of the inclusion of methamidophos in Annex I of Directive 91/414/EEC
- Italy, Ministry of Health (2000): Monograph (including the addenda) prepared in the context of the inclusion of the following active substance in Annex I of the Council Directive 91/414/EEC – Methamidophos - Volume 1 - Report and Proposed Decision.

3.2.2 Description of toxicological properties of the chemical

Toxicokinetics

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 the urine (60-70%) and the faeces.

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/m³

Female rat LC_{50} inhalation: 76.5 mg/m³

Skin irritation: Slightly irritating (rabbits)

Eye irritation: Slightly irritating

Skin sensitisation: Not sensitising (modified Buehler)

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/m³ (90-day rat study)

Genotoxicity

There is no concern for the mutagenicity of methamidophos. 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.

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

Reproductive toxicity

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)

Neurotoxicity/delayed neurotoxicity

No potential for delayed neuropathy (rat)

Delayed neuropathy only at very high doses (3-4 times higher than the LD_{50}) (hen)

Other studies

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

Developmental neurotoxicity study in rats: NOAEL: 1 mg/kg diet (0.085 mg/kg bw/day) (no additional findings of concern)

Medical data

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.

Dermal absorption: 10% estimate from monkey studies and from *in vivo / in vitro* data and approximately 5% in humans i.e. 2-3 fold higher skin absorption in monkeys than in humans.

Safety values

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

Reference

- European Commission (2007): Review report for the active substance methamidophos finalised in the Standing Committee on the Food Chain and Animal Health at its meeting on XXX 2006 in view of the inclusion of methamidophos in Annex I of Directive 91/414/EEC
- Italy, Ministry of Health (2000): Monograph (including the addenda) prepared in the context of the inclusion of the following active substance in Annex I of the Council Directive 91/414/EEC – Methamidophos - Volume 1 - Report and Proposed Decision.
- EFSA (2004): Opinion of the Scientific Panel on Plant health, Plant protection Products and their Residues on a request from the Commission related to the evaluation of methamidophos in toxicology in the context of Council Directive 91/414/EEC (Question No. EFSA-Q-2004-60). The EFSA Journal 95, 1-15.

3.2.3 Description of ecotoxicological properties of the chemical

Fate and Behaviour

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 of these 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.

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}s:

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)

Air

A photochemical oxidative degradation DT_{50} of 0.578 days in air has been calculated.

Ecotoxicity

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.

Aquatic organisms

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)

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)

Honey bees

No data

Earthworms

Earthworm (*Eisenia foetida*) LC_{50}: 28.8 mg formulation/kg dw soil

Earthworm (*Eisenia foetida*) LC_{50}: 73 mg formulation/kg dw soil

Earthworm (*Eisenia foetida*) NOEC: 1 mg formulation/kg dw soil

Arthropods

Predatory mite (*Amblyseius potentillae*) 100% mortality: 0.108 kg as/ha (Tamaron SL 600)

Predatory mite (*Typhlodromus pyri*) 100% mortality: 0.108 kg as/ha (Tamaron SL 600)

Aphid parasite (*Aphidius rhopalosiphi*) LR_{50}: 2.52 g as/ha (Tamaron SL 200)

Aphid parasite (*Aphidius rhopalosiphi*) LR_{50}: 1.29 g as/ha (Tamaron SL 600)

Soil micro-organisms

No significant influence on the mineralisation of carbon and nitrogen at 5.3 and 26.8 mg as/kg soil.

Reference

- European Commission (2007): Review report for the active substance methamidophos finalised in the Standing Committee on the Food Chain and Animal Health at its meeting on XXX 2006 in view of the inclusion of methamidophos in Annex I of Directive 91/414/EEC
- Italy, Ministry of Health (2000): Monograph (including the addenda) prepared in the context of the inclusion of the following active substance in Annex I of the Council Directive 91/414/EEC – Methamidophos - Volume 1 - Report and Proposed Decision.

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