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

Chemical Review Committee
Fourteenth meeting
Rome, 11–14 September 2018
Agenda item 4 (a) (iii)

Technical work: consideration of draft decision guidance documents: phorate

Draft decision guidance document for phorate

Note by the Secretariat

I. Introduction

1. At its fifth and thirteenth meetings, the Chemical Review Committee reviewed notifications of final regulatory action for phorate submitted by Canada and Brazil, together with the supporting documentation referenced therein, and concluded that the notifications met all the criteria of Annex II to the Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade.

2. In its decision CRC-13/4, the Committee recommended that the Conference of the Parties list phorate in Annex III to the Convention as a pesticide. In the same decision, the Committee adopted a rationale for its conclusions, decided to prepare a draft decision guidance document for phorate and also decided on the composition of the intersessional drafting group to prepare the document. A detailed workplan for the development of the decision guidance document was prepared by the Committee, in line with the process adopted by the Conference of the Parties by decision RC-2/2 and amended by decisions RC-6/3 and RC-7/3. The recommendation, the rationale in respect of the Brazilian notification and the workplan were annexed to the report of the Committee on the work of its thirteenth meeting (UNEP/FAO/RC/CRC.13/19, annexes I and III). The rationale for its conclusion that the notification of final regulatory action submitted by Canada in respect of phorate met the criteria of Annex II to the Rotterdam Convention is set out in part B of Annex III of the report of the Chemical Review Committee on the work of its fifth meeting (UNEP/FAO/RC/CRC.5/16).

3. The material available to the intersessional drafting group included a summary of the outcome of the fifth and thirteenth meetings of the Committee, a copy of the working paper on the preparation of internal proposals and decision guidance documents for banned and severely restricted chemicals and the notifications of final regulatory action and associated supporting documentation available to the Committee at its fifth and thirteenth meetings.

4. In accordance with the agreed workplan, Ms. Johanna Peltola-Thies (United Kingdom of Great Britain and Northern Ireland), the chair of the intersessional drafting group, and Mr. Jack Holland (Australia), the vice-chair, prepared an internal proposal based on the notifications and the supporting documentation. That internal proposal was circulated to the members of the drafting group for comment on 15 December 2017. It was amended in the light of the comments received and was circulated, on 19 February 2018, to all Committee members and to the observers who had attended the thirteenth meeting. Responses were received from Committee members and observers and taken into consideration in the preparation of the draft decision guidance document.

5. The draft decision guidance document and a compilation of the comments received were circulated to the members of the drafting group on 7 May 2018.

6. At its fourteenth meeting, the Committee further revised and, by its decision CRC-14/3, adopted the draft decision guidance document for phorate and decided to forward it, together with the related tabular summary of comments (UNEP/FAO/RC/CRC.14/INF/8/Rev.1), to the Conference of the Parties for its consideration. The text of the draft decision guidance document is set out in the annex to the present note. It has not been formally edited.

Annex

Rotterdam Convention

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

Draft Decision Guidance Document

Phorate

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

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 […] meeting, held in […] on […], the Conference of the Parties agreed to list phorate in Annex III of the Convention and adopted the decision-guidance document with the effect that this chemical became subject to the PIC procedure.

The present decision-guidance document was communicated to designated national authorities on […], 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.

Standard core set of abbreviations[3]

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
b.p.	boiling point
bw	body weight
°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
h	Hour
ha	Hectare
i.m.	Intramuscular
i.p.	Intraperitoneal
IARC	International Agency for Research on Cancer
IC_{50}	median inhibitory concentration
IBAMA	Brazilian Institute for the Environment and the Renewable Resources
ILO	International Labour Organization
IPCS	International Programme on Chemical Safety
IPM	Integrated Pest Management
IUPAC	International Union of Pure and Applied Chemistry
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)

[3] *This core list should serve as the basis for DGDs for industrial chemicals, pesticides and severely hazardous pesticide formulations. It should be augmented by abbreviations used in the individual DGDs relevant to the chemical(s) in question.*

Definitions and spelling should, as far as practicable, follow the IUPAC glossary of terms in toxicology and the IUPAC glossary of terms relating to pesticides in their current editions.

As a general rule it is preferable that acronyms used only once in the text be spelled out rather than included in the list of abbreviations.

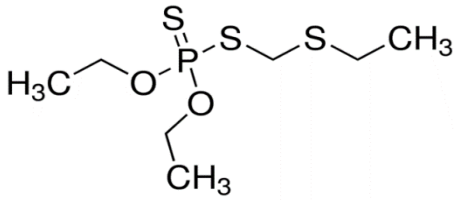
STANDARD CORE SET OF ABBREVIATIONS

k	kilo- (x 1000)
kg	Kilogram
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
LOEL	Lowest-observed-effect level
MAPA	Ministry of Agriculture, Livestock and Food Supply
m	Metre
m.p.	melting point
mg	Milligram
ml	Millilitre
MOE	Margin of Exposure
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
PMRA	Pest Management Regulatory Agency, Canada
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)
SMR	standard(ized) mortality ratio
STEL	short-term exposure limit
TER	toxicity exposure ratio
TLV	threshold limit 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

Phorate **Published:**

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

Common name:	Phorate
Chemical name and other names or synonyms	IUPAC: O,O-diethyl S-ethylthiomethyl phosphorodithioate; diethyl {[(ethylsulfanyl)methyl]sulfanyl}(sulfanylidene)phosphonate; CAS: O,O-diethyl S-[(ethylthio)methyl]phosphorodithioate. Also: O,O-diethyl S-[(ethylthio)methyl]ester of phosphorodithioic acid; phosphorodithioic acid, O,O-diethyl S-(ethylthio)methylester; O,O-diethyl S-ethylmercaptomethyl phosphorodithioate. Manufacturers Code names: AC 8911, CL 35,024; EI 3911; AC 3911; ENT 24042
Molecular formula	$C_7H_{17}O_2PS_3$
Chemical structure	
CAS-No.(s)	298-02-2
Harmonized System Customs Code	
Other numbers	EC No.: 206-052-2, OSHA IMIS Code Number: 2064, Caswell Number 660, CCOHS Record Number 502, RCRA Waste Number TD9450000
Category	Pesticide
Regulated category	Pesticide
Use(s) in regulated category	Phorate was authorized in Brazil as an insecticide exclusively for agricultural use in cotton, potatoes, coffee, beans and corn. Phorate is a systemic insecticide, which at the time of regulatory action was registered in Canada for use on potatoes, beans, corn, lettuce and rutabagas.
Trade names	Trade names listed by Brazil: Granutox and Granutox 150 G. Trade names listed by Canada at the time of regulatory action: Thimet 15G Soil & Systemic Insecticide Granular. Other trade names: (manufacturer indicated in brackets): Thimet 15G Soil & Systemic Insecticide, Cecurafox (Cequisa), Dhan (Dhanuka), Granural, Granutox, Granutox 150 G; Kurunal (Ramcides), Umet (United Phosphorus), Volphor (Voltas), Warrant (Searle India), Agromet, Geomet, Phorate 10G, Rampart, Thimenox, Thimet (Cyanamid), Vegfru Foratox, Timet and Vegfru. This is an indicative list of trade names. It is not intended to be exhaustive.
Formulation types	Granutox and Granutox 150 G are granules. The Canadian notification indicates type “G”: granular.
Uses in other categories	There is no reported use as an industrial chemical.
Basic manufacturers	AMVAC Chemical Corporation, BASF, Paramount Pesticides Ltd., Insecticides (India) Ltd., P. I. Industries Ltd., Gujarat Pesticides Pvt. Ltd., Vimal Crop Care Pvt. Ltd., Modern Chemicals Pvt. Ltd., Sanova Pharma Chem Pvt. Ltd., Prime Agro Industries Pvt. Ltd., , Insecticides India Ltd., Sudarshan Fertilisers, Sunray Chemical Industries, Trans Yamuna Fertilizers Pvt. Ltd., P. I. Industries Limited, Balaa Pesticides, Jai Chemicals

(source: e-World Trade Fair), American Cyanamid Co. One Cyanamid Plaza (source: Toxnet, 2017), United Phosphorus, Cequisa, Dhanuka, Ramcides, Voltas, Searle India (Pesticide Manual 11th edition in (UNEP/FAO/RC/CRC.5/9/Add.1)).

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

Phorate is included in the PIC procedure as a pesticide. It has been listed on the basis of the final regulatory actions to ban its use, notified by Brazil, and to severely restrict its use, notified by Canada.

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

Brazil

According to the Law No. 7.802/89 (pesticide Law), the legal reference for pesticide management, regulated by Decree No 4.074/02, no pesticide shall be manufactured, imported, exported, traded or used unless it has been registered in Brazil.

Resolution RDC No. 12 of 13 March 2015, issued by the National Health Surveillance Agency (ANVISA), prohibits the use of all technical and formulated products based on the phorate active ingredient in Brazil. Therefore, the production, use, trade, import and export of products based on phorate was banned. The Resolution cancelled the toxicological evaluation reports of all the technical and formulated products based on phorate and excluded the monograph of the active ingredient phorate from the date of publication of the Resolution. It obligated companies that held stocks of products based on phorate to provide adequate final disposal.

The Resolution was based on the Technical Note of Toxicological Re-evaluation of the Active Ingredient Phorate prepared by ANVISA with the collaboration of the Oswaldo Cruz Foundation.

The final regulatory action has been taken for the pesticide category to protect human health.

Reason: Human Health

Canada

The Pest Management Regulatory Agency (PMRA) performed a re-evaluation of the active ingredient phorate, carrying out an assessment of available information, and concluded that the use of phorate and associated end-use products (EP) entail an unacceptable risk of harm to the environment pursuant to Section 20 of the Canadian Pest Control Product (PCP) Regulation. As a result, PMRA determined that all uses of phorate were to be phased out. Uses of phorate and associated end-use products on corn, lettuce, beans and rutabagas were phased out at the end of December 2004.

Due to the lack of alternatives to phorate for control of wireworm on potatoes, the use of phorate, for this use only, could be continued until 1 August 2008, with interim mitigation measures to protect workers (engineering controls, requirements regarding additional Personal Protective Equipment (PPE)) and the environment (environmental statements on the label). The use on potatoes was subsequently extended to August 2015. A new phorate product, paired with application equipment to reduce environmental exposure, was registered in 2015.

Relevant regulatory documents are:

- Health Canada (2003): Proposed Acceptability for Continuing Registration (PACR 2003-01), Pest Management Regulatory Agency (PMRA) Re-evaluation of Phorate, January 24 , 2003 (see UNEP/FAO/RC/CRC.5/9/Add.1)
- Health Canada (2004): Re-evaluation Decision Document (RRD 2004-11) Phorate, 13 May 2004 (see UNEP/FAO/RC/CRC.5/9/Add.1)
- Health Canada (2007): Re-evaluation note, REV2007-07, Update on the Use of Phorate on Potatoes, 5 June 2007 (see UNEP/FAO/RC/CRC.5/9/Add.1)
- Health Canada (2008): REV2008-05: Update on the Use of Phorate on Potatoes.
- Health Canada (2012): Re-evaluation Note REV2012-01: Update of the Use of Phorate on Potatoes. Pest Management Regulatory Agency, 28 May 2012.

The final regulatory action has been taken for the pesticide category to protect the environment.

Reason: Environment

2.2 Risk evaluation (see Annex 1 for further details)

Brazil

The final regulatory action was based on a risk or hazard evaluation.

In accordance with the Brazilian Pesticide Law, governmental agencies responsible for pesticides registration (ANVISA, IBAMA (Brazilian Institute for the Environment and the Renewable Resources) or MAPA(Ministry of Agriculture, Livestock and Food Supply) can re-evaluate the registration of a pesticide, when there is evidence of reduction of agronomic efficiency and/or change of risks to human health or environment. Technical Notes on the toxicology and/or potential environmental hazards of the active ingredient are developed based on data collected from studies and surveys conducted by national and international accredited institutions as well as information provided by the National System of Toxic-Pharmacological Intoxications and Poisonings (SINITOX), Pesticide Residues in Food Analysis Programme or pesticide registrants. After the re-evaluation, measures to restrict, suspend or prohibit the production and import of pesticides could be taken as well as to cancel the registration, if a criterion of prohibition of registration is fulfilled.

Human health

Brazil's risk evaluation of phorate took into account toxicology and public health, occupational health and safety, conditions of use, environmental impact and availability of lower-risk alternatives. An extensive review of relevant data on hazard and risk of phorate using reviewed documents, published reports and literature was undertaken.

On the basis of available data, phorate and its metabolites were shown to be easily absorbed through skin and mucous membranes and to irreversibly block the catalytic activity of acetylcholinesterase (AChE), the enzyme responsible for mediating the hydrolysis of acetylcholine into acetic acid and choline acid. Thus, phorate and its metabolites interrupt the transmission of nerve impulses in the cholinergic synapses of the central nervous system (CNS), autonomic nervous system (ANS) and neuromuscular junction. Inactivation of AChE causes cholinergic hyperstimulation by acetylcholine accumulation in the synaptic cleft.

Experimental and epidemiological studies involving the respiratory tract demonstrate that phorate has a high toxicity for this system.

Data confirm that phorate can cause complex neurological clinical manifestations in humans, such as encephalopathy, intermediate syndrome and delayed polyneuropathy. However, in laboratory animals that were exposed to phorate there were no cases of intermediate syndrome or late polyneuropathy, that was concluded in ANVISA to show this pesticide is more toxic to humans than it is demonstrated in tests with laboratory animals.

As stated in the Brazilian notification, besides its neurotoxic effects, phorate demonstrated potential to cause adverse effects to the endocrine regulation processes of steroid hormones in humans (Usmani, 2003), which may contribute to increased cancer cases (Alavanja et al., 2002; Mahajan et al, 2006; Koutros et al, 2010).

Several studies analysed by Brazil showed that agricultural workers exposed to phorate were victims of poisonings and deaths related to the toxicity of the active ingredient. The exposure becomes even more dangerous due to the difficulties related to the availability and/or ineffectiveness of personal protective equipment (PPE). A comprehensive study on the conditions of pesticide use carried out in municipalities of the state of Amazonas in Brazil concluded that farmers were not prepared for the proper use of pesticides, ignoring the risks of these products to human health and the environment. PPE is not used because it is expensive, uncomfortable and unsuitable for the hot climate of the region. Lack of training and poor knowledge of the hazards of pesticides contribute to incorrect handling during the preparation and application of the pesticide, and the disposal of empty containers. In these conditions, the exposure of farmers, their families, consumers and the environment is high.

The decision to ban phorate was taken on the basis of the evaluation of its hazardous properties as well as on the basis of the expected exposure of agricultural workers to pesticides in general and also to phorate under the known conditions of pesticide use in Brazil. ANVISA concluded that this active ingredient has the potential to cause hormonal disturbances in humans and is more toxic to humans than demonstrated in tests with laboratory animals, which are prohibitive criteria for registration of pesticides in Brazil.

Canada

As per Section 16 of the *Pest Control Products Act*, the PMRA re-evaluates all pesticides registered prior to 1995, and also conducts re-evaluations of all pesticides on a 15-year cycle. In addition, a re-evaluation may be initiated if there have been changes to the information requirements or the procedures used to evaluate risk. Re-evaluation uses current scientific approaches to assess the potential risks consider the r*isks to human health and the environment, and to determine if registered uses of pesticides continue to be acceptable.*

Environment

On the basis of a deterministic assessment of the environmental risk of pest control products containing phorate, conducted by the PMRA, phorate was found to be highly toxic to all terrestrial and aquatic species tested. Incident reports of bird and mammal fatalities in Canada, the United States of America and the United Kingdom of Great Britain and Northern Ireland support the conclusion that phorate presents a significant risk to birds and wildlife. Surface broadcast application presents the greatest risk owing to the large number of exposed granules on the surface. Although soil incorporation is expected to lower the risk of terrestrial and aquatic exposure, it nevertheless presents a very high risk owing to unincorporated granules remaining exposed on the surface. The risk to small and moderate-sized birds and small or moderate-sized mammals remains high to very high with either method of application. Owing to its extreme toxicity to all organisms tested, the very high risk to moderate and smaller-sized birds and mammals, the incident reports of bird and mammal mortalities (including large raptors in Canada), in addition to the persistence and mobility of the toxic sulfoxide and sulfone transformation products, Canada has concluded that the use of phorate in the country presents a high risk to the environment.

3. Protective measures that have been applied concerning the chemical

3.1 Regulatory measures to reduce exposure

Brazil Resolution RDC No.12 of 13 March 2015 from ANVISA prohibited production, use, trade, import and export of products based on phorate. Complete entry into force of the final regulatory action was 16 March 2015.

Canada Use of phorate and associated end-use products on corn, lettuce, beans and rutabagas where phased out at the end of December 2004. No further use was allowed after December 2004, except on potatoes, where use for controlling wireworms was allowed to be continued until 1 August 2008. The use on potatoes was subsequently extended to August 2015. A new phorate product, paired with application equipment to reduce environmental exposure, was registered in 2015.

Relevant regulatory documents are provided in section 2.1.

3.2 Other measures to reduce exposure

Brazil
None reported.

Canada
For the exempted use for controlling wireworm on potatoes, the use of interim mitigation measures to protect workers (engineering controls, requirements regarding additional Personal Protective Equipment (PPE) and the environment (environmental statements on the label) was required.

General
None.

3.3 Alternatives

Brazil

Prior to the final regulatory action, phorate was used in insecticides authorized exclusively for agricultural use for the following crops: cotton, potatoes, coffee, beans and corn.

The alternatives to phorate applied to cotton in Brazil are: acephate, acetamiprid, benfuracarb, methidathion, esfenvalerate, imidacloprid, thiacloprid, permethrin, cypermethrin, azadirachtin, cyfluthrin, pymetrozine, methomyl, beta-cyfluthrin, flonicamid, chlorpyrifos, bifenthrin, deltamethrin, dimethoate, carbosulfan, clothianidin, zetacypermethrin, triazophos, fenthion, malathion, diafenthiuron, furathiocarb, thiodicarb, fenvalerate and fenitrothion.

The alternatives to phorate applied to potatoes in Brazil are: acephate, acetamiprid, benfuracarb, esfenvalerate, imidacloprid, thiacloprid, alpha-cypermethrin, pymetrozine, methomyl, beta-cyfluthrin, chlorpyrifos, bifenthrin, deltamethrin, carbosulfan, betacypermethrin, piridafenthion, diafenthiuron, fipronil, chlorantraniliprole, cadusafos, tebupirimfos, lambda cyhalothrin, gamma-cyhalotrin and chlorfenapyr.

The alternatives to phorate applied to coffee in Brazil are: esfenvalerate, imidacloprid, permethrin, cypermethrin, azadirachtin, cyfluthrin, beta-cyfluthrin, chlorpyrifos, zeta-cypermethrin, alpha-cypermethrin, beta-cypermethrin, novaluron, abamectin, chlorantraniliprole, teflubenzuron, lufenuron, cyantraniliprole, pyriproxyfen, fenpropathrin, gamma-cyhalothrin, lambda-cyhalothrin and fluvalinate.

The alternatives to phorate applied to beans in Brazil are: thiodicarb, imidacloprid, malathion, chlorpyrifos, esfenvalerate, acetate, acetamiprid, bifenthrin, beta-cyfluthrin, thiacloprid, phenopopation, clothanidine, carbosulfan, permethrin and etofenprox.

The alternatives to phorate applied to corn in Brazil are: chlorpyrifos, fipronil, bifenthrin and imidacloprid.

Canada

Phorate was registered on rutabagas for the control of cabbage maggot (CM). Other organophosphate insecticides, azinphos-methyl, chlorpyrifos, diazinon and terbufos, were also registered as a prophylactic treatment at planting to control CM.

Phorate was registered for corn rootworm control. Alternative soil insecticides that were registered for control of this insect include carbaryl, chlorpyrifos, diazinon, terbufos and tefluthrin.

General

It is essential that before a country considers substituting a substance with alternatives, it ensures that the use is relevant to its national needs, and the anticipated local conditions of use. The hazards of the substitute materials and the controls needed for safe use should also be evaluated.

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 as a means of reducing or eliminating the use of hazardous pesticides.

SAICM's Fourth International Conference on Chemicals Management recommended that in replacing highly hazardous pesticides the focus should be on agroecologically-based practices. Information on such practices can be found at the following websites:

FAO Agroecology hub: http://www.fao.org/agroecology/en/
IPAM (International Peoples Agroecology Multiversity): http://ipamglobal.org/
OISAT (Online Information Service for Non-Chemical Pest Management in the Tropics): http://www.oisat.org/
Replacing Chemicals with Biology: Phasing out Highly Hazardous Pesticides with Agroecology: http://panap.net/2015/11/replacing-chemicals-biology-phasing-highly-hazardous-pesticides-agroecology/

3.4 Socio-economic effects

Brazil

No assessment of socio-economic effects was reported.

Canada

A significant challenge for PMRA was a regulatory decision that moved towards the goal of eliminating phorate in a manner that was the least disruptive to the need to protect agricultural crops from pests. To meet its challenge, the PMRA considered the availability of alternatives and the need for a transition period for those uses for which no or limited alternatives were available. A significant challenge for industry was to develop alternatives in the relatively short time frame of the proposed phase-outs. A significant challenge for the agricultural sector was to reduce the use during the transition period and be open to using alternatives.

4. Hazards and Risks to human health and the environment

4.1 Hazard Classification

WHO / IPCS	I a – Extremely Hazardous
European Union	**Classification according to Regulation (EC) No 1272/2008 of the European Parliament and of the Council (CLP-Regulation)** Acute Toxicity (oral) 2* - H300 (Fatal if swallowed) Acute Toxicity 1 - H310 (Fatal in contact with skin) Aquatic Acute 1 - H400 (Very toxic to aquatic life) Aquatic Chronic 1 - H410 (Very toxic to aquatic life with long lasting effects)
US EPA	I – Highly toxic (acute oral, dermal and inhalation)

4.2 Exposure limits

Canadian risk evaluation:

Acute reference dose (ARfD): 0.00025 mg/kg bw

In animal studies, the adverse effects noticeable at the lowest dose (i.e. the toxicity end point) were clinical signs observed in an acute rat neurotoxicity study (NOAEL = 0.25 mg/kg body weight (bw)). The uncertainty factor was 100 (10x for interspecies extrapolation x 10x intraspecies variability). An additional safety factor of 10x was applied to account for the steepness of the dose-response and the high degree of potency (based on lethality at very low doses). The acute reference dose was calculated to be 0.00025 mg/kg bw (0.25 mg/kg bw / 1000). This value was considered to be protective for infants and children.

Acceptable Daily Intake (ADI): 0.00025 mg/kg bw/d

As the ARfD value was lower than any acceptable daily intake derived from any of the repeat-dose toxicity studies (reflecting the high acute toxicity and use of the additional safety factor), the ADI was established at the same value as the ARfD. Thus, the ADI is 0.00025 mg/kg bw/d.

JMPR Report 2004, JMPR Report 2012

Acute reference dose (ARfD): 0.003 mg/kg bw

An ARfD of 0.003 mg/kg bw was established based on the NOAEL of 0.25 mg/kg bw for miosis in the study with single doses in rats. Although inhibition of acetylcholinesterase activity is a C_{max}-dependent phenomenon, a safety factor of 100 was used in view of the steep dose–response curve and the slow recovery of brain acetylcholinesterase activity because of irreversibility of its inhibition. This ARfD includes the metabolites of phorate, phorate sulfone and phorate sulfoxide.

Acceptable Daily Intake (ADI): 0–0.0007 mg/kg bw

An ADI of 0–0.0007 mg/kg bw was established on the basis of an overall NOAEL of 0.07 mg/kg bw per day for inhibition of brain acetylcholinesterase activity in rats and dogs and a safety factor of 100. This ADI includes the phorate metabolites, phorate sulfone and phorate sulfoxide.

Occupational exposure limits (NIOSH, 2000):

OSHA PELhttps://www.cdc.gov/niosh/npg/pgintrod.html - exposure: none
NIOSH REL: TWA 0.05 mg/m^3 ST 0.2 mg/m^3 skin
NIOSH IDLH: N.D. See: IDLH INDEX (https://www.cdc.gov/niosh/idlh/intridl4.html)
TLV: (inhalable fraction & vapour) 0.05 mg/m^3 as TWA; (skin); A4 (not classifiable as a human carcinogen); BEI issued; (ACGIH 2008).
MAK not established.

MRL values

Canadian values (additional information, not provided in the notification):

https://www.canada.ca/content/dam/hc-sc/migration/hc-sc/cps-spc/alt_formats/pdf/pest/part/consultations/_pmrl2015-47/pmrl2015-47-eng.pdf

This link indicates that the use of phorate on potatoes in Canada was approved for a new formulation Thimet 20-G in 2015 (see Section 2.1 above) with proposed MRLs of 0.6 ppm for potato flakes and granules, 0.2 ppm for potatoes and 0.024 ppm for all food crops (other than those listed in this item).

EU values

http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=pesticide.residue.CurrentMRL&language=EN&pestResidueId=179
This link provides 378 individual entries with values ranging from 0.01 to 0.5 mg/kg phorate (sum of phorate, its oxygen analogue and their sulfones expressed as phorate). Many of the values are at the lower limit of analytical determination.

WHO drinking water guideline

Phorate is excluded from guideline value derivation.

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:	UN Hazard Class: 6.1 UN Packing Group: I
International Maritime Dangerous Goods (IMDG) Code	For phorate (pure substance) UN number 3018 Organophosphorus pesticide, liquid, toxic (phorate) Class 6.1 Marine pollutant Source: IMO (1996) http://www.imo.org/en/OurWork/Legal/HNS/Documents/IMDG%20Code%201996_searchable.pdf
Transport Emergency Card	TEC (R)-61GT6-I

Further specific guidance on appropriate symbols and label statements applicable for phorate products may be available in the FAO *Guidelines on Good Labelling Practice for Pesticides* (FAO, 2015).

4.4 First aid

Safety and first aid recommendations extracted from the IPCS/WHO safety data sheet (see whole safety data sheet at http://www.inchem.org/documents/icsc/icsc/eics1060.htm **)**

Fire and explosion
Acute hazard: Combustible. Prevention: no open flames. First aid: Use water spray, foam, powder, carbon dioxide

STRICT HYGIENE! IN ALL CASES CONSULT A DOCTOR!

Inhalation symptoms
Laboured breathing. Pupillary constriction, muscle cramp, excessive salivation. Sweating. Prevention: Use ventilation, local exhaust or breathing protection. First aid: Fresh air, rest. Refer for medical attention.

Skin:
Symptoms: MAY BE ABSORBED! See Inhalation. Prevention: Protective gloves. Protective clothing. First aid: Rinse and then wash skin with water and soap. Refer for medical attention.

Eyes:
Symptoms: See Inhalation. Prevention: Wear safety goggles, face shield or eye protection in combination with breathing protection. First aid: First rinse with plenty of water for several minutes (remove contact lenses if easily possible), then refer for medical attention.

Ingestion:
Symptoms: See Inhalation. Abdominal cramps. Diarrhoea. Vomiting. Prevention: Do not eat, drink, or smoke during work. Wash hands before eating. Rinse mouth. First aid: Give one or two glasses of water to drink. Refer for medical attention.

SPILLAGE DISPOSAL

Collect leaking and spilled liquid in sealable containers as far as possible. Absorb remaining liquid in sand or inert absorbent. Then store and dispose of according to local regulations. Do NOT let this chemical enter the environment. Personal protection: gas-tight chemical protection suit including self-contained breathing apparatus.

PubChem (2017a)

Note: Phorate is a cholinesterase inhibitor.

Signs and Symptoms of Acute Phorate Exposure: Acute exposure to phorate may produce the following signs and symptoms: pinpoint pupils, blurred vision, headache, dizziness, muscle spasms, and profound weakness. Vomiting, diarrhoea, abdominal pain, seizures, and coma may also occur. The heart rate may decrease following oral exposure or increase following dermal exposure. Chest pain may be noted. Hypotension (low blood pressure) may occur, although hypertension (high blood pressure) is not uncommon. Dyspnea (shortness of breath) may be followed by respiratory collapse. Giddiness is common.

Emergency Life-Support Procedures: Acute exposure to phorate may require decontamination and life support for the victims. Emergency personnel should wear protective clothing appropriate to the type and degree of contamination. Air-purifying or supplied-air respiratory equipment should also be worn, as necessary. Rescue vehicles should carry supplies such as plastic sheeting and disposable plastic bags to assist in preventing spread of contamination.

Inhalation Exposure: 1. Move victims to fresh air. Emergency personnel should avoid self-exposure to phorate. 2. Evaluate vital signs including pulse and respiratory rate, and note any trauma. If no pulse is detected, provide CPR. If not breathing, provide artificial respiration. If breathing is laboured, administer oxygen or other respiratory support. 3. Obtain authorization and/or further instructions from the Localized hospital for administration of an antidote or performance of other invasive procedures. 4. Transport to a health care facility.

Dermal/Eye Exposure: 1. Remove victims from exposure. Emergency personnel should avoid self-exposure to phorate. 2. Evaluate vital signs including pulse and respiratory rate, and note any trauma. If no pulse is detected, provide CPR. If not breathing, provide artificial respiration. If breathing is laboured, administer oxygen or other respiratory support. 3. Remove contaminated clothing as soon as possible. 4. If eye exposure has occurred, eyes must be flushed with lukewarm water for at least 15 minutes. 5. Wash exposed skin areas three times with soap and water. 6. Obtain authorization and/or further instructions from the localized hospital for administration of an antidote or performance of other invasive procedures. 7. Transport to a health care facility.

Ingestion Exposure: 1. Evaluate vital signs including pulse and respiratory rate, and note any trauma. If no pulse is detected, provide CPR. If not breathing, provide artificial respiration. If breathing is laboured, administer oxygen or other respiratory support. 2. Obtain authorization and/or further instructions from the localized hospital for administration of an antidote or performance of other invasive procedures. 3. Vomiting may be induced with syrup of Ipecac. If elapsed time since ingestion of phorate is unknown or suspected to be greater than 30 minutes, do not induce vomiting and proceed to Step 4. Ipecac should not be administered to children under 6 months of age. Warning: Ingestion of phorate may result in sudden onset of seizures or loss of consciousness. Syrup of Ipecac should be administered only if victims are alert, have an active gag-reflex, and show no signs of impending seizure or coma. If ANY uncertainty exists, proceed to Step 4. The following dosages of Ipecac are recommended: children up to 1 year old, 10 mL (1/3 oz); children 1 to 12 years old, 15 mL (1/2 oz); adults, 30 mL (1 oz). Ambulate (walk) the victims and give large quantities of water. If vomiting has not occurred after 15 minutes, Ipecac may be re-administered. Continue to ambulate and give water to the victims. If vomiting has not occurred within 15 minutes after second administration of Ipecac, administer activated charcoal. 4. Activated charcoal may be administered if victims are conscious and alert. Use 15 to 30 g (1/2 to 1 oz) for children, 50 to 100 g (1-3/4 to 3-1/2 oz) for adults, with 125 to 250 mL (1/2 to 1 cup) of water. 5. Promote excretion by administering a saline cathartic or sorbitol to conscious and alert victims. Children require 15 to 30 g (1/2 to 1 oz) of cathartic; 50 to 100 g (1-3/4 to 3-1/2 oz) is recommended for adults. 6. Transport to a health care facility. (PubChem, 2017a)

Safety Data Sheet of Central Pollution Control Board of India (2017)

Fire

Fire Extinguishing Media:

Special Procedure: Keep containers cool by spraying water, if exposed to heat or flame.

Unusual hazard: Shock can shatter containers, releasing the contents. When heated to decomposition, toxic fumes of sulfur oxides, phosphorus oxides, and nitrogen oxides are emitted.

EXPOSURE: First Aid Measures:

Inhalation: Remove the person to fresh air area and atropine powder or tablet may be given.

Skin: Remove the contaminated clothes and wash the affected area with plenty of water and soap. The affected area may be decontaminated with 5-10% soln. of ammonia or 2-5% soln. of chloramine.

Eyes: Flush eyes with water for at least 15 mins

Ingestion: Induce vomiting. Give half a glass of a 2% $Na_2CO^4_3$, soln. with 2-3 table spoonfuls triturated activated charcoal to drink.
Antidote/dosages: See "Additional Information"

Spills
Steps to be taken: Spills should be washed with water and soda ash. May also be absorbed with dry sand or vermiculite.

Safety Data Sheet of Sigma-Aldrich (2015) (link)

General advice: Consult a physician. Show this safety data sheet to the doctor in attendance.
If inhaled: If breathed in, move person into fresh air. If not breathing, give artificial respiration. Consult a physician.

In case of skin contact: Wash off with soap and plenty of water. Take victim immediately to hospital. Consult a physician.

In case of eye contact: Flush eyes with water as a precaution.
If swallowed: Never give anything by mouth to an unconscious person. Rinse mouth with water. Consult a physician.

Firefighting measures

Suitable extinguishing media: Use water spray, alcohol-resistant foam, dry chemical or carbon dioxide.
Special hazards arising from the substance or mixture: Carbon oxides, Sulphur oxides, Oxides of phosphorus
Advice for firefighters: Wear self-contained breathing apparatus for firefighting if necessary.
Further information: No data available

Accidental release measures

Personal precautions, protective equipment and emergency procedures:
Wear respiratory protection. Avoid breathing vapours, mist or gas. Ensure adequate ventilation.
Evacuate personnel to safe areas.

Environmental precautions:

Prevent further leakage or spillage if safe to do so. Do not let product enter drains. Discharge into the environment must be avoided.

Methods and materials for containment and cleaning up

Soak up with inert absorbent material and dispose of as hazardous waste. Keep in suitable, closed containers for disposal.

4.5 Waste management

Regulatory actions to ban a chemical should not result in creation of a stockpile requiring waste disposal. For guidance on how to avoid creating stockpiles of obsolete pesticides the following guidelines are available: *FAO Guidelines on Prevention of Accumulation of Obsolete Pesticide Stocks (FAO, 1995b), The Pesticide Storage and Stock Control Manual (FAO, 1996a)* and *Guidelines for the management of small quantities of unwanted and obsolete pesticides (FAO, 1999).*

In all cases waste should be disposed 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.

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, 1996b).*

Disposal Methods for this chemical as cited in PubChem (2017b)

[4] Note: original reference provides “NaIICO”, but this was not considered plausible by the CRC and the correct chemistry in this context has been provided in the text.

Recycle any unused portion of the material for its approved use or return it to the manufacturer or supplier. Ultimate disposal of the chemical must consider: the material's impact on air quality; potential migration in soil or water; effects on animal, aquatic, and plant life; and conformance with environmental and public health regulations.

Potential candidate for liquid injection incineration with a temperature range of 650-1600ºC and residence time of 0.1 to 2 seconds. Also, a candidate for rotary kiln incineration with a temperature range of 820 to 1600ºC with residence times for liquids and gases: seconds; solids: hours. Also, a candidate for fluidized bed incineration with a temperature range of 450 to 980ºC with residence times for liquids and gases: seconds; solids: longer.
USEPA; Engineering Handbook for Hazardous Waste Incineration p.3-10 (1981) EPA 68-03-3025

Mix phorate with excess calcium oxide or sodium hydroxide and sand or other adsorbent. Sodium hydroxide (or sodium carbonate) can also be added to the mixture to help speed the reactions when calcium oxide is used as the main alkali. The amount of calcium oxide or sodium hydroxide to use depends on the amount of pesticide to be disposed of and, to some extent, the concentration of active ingredient in the pesticide and the actual chemical nature of the active ingredient. For safety, a preliminary test should be made in which a very small amount of the pesticide and alkali are mixed and observed briefly to make sure it does not react too vigorously. Sizable quantities of pesticides can be disposed of in several smaller batches, rather than all at once, for added safety. Recommendable methods: Incineration and hydrolysis. Peer-review: For large amount: Incineration in a unit with effluent gas scrubbing is recommendable. (Peer-review conclusions of an IRPTC expert consultation (May 1985)).

United Nations. Treatment and Disposal Methods for Waste Chemicals (IRPTC File). Data Profile Series No. 5. Geneva, Switzerland: United Nations Environmental Programme, Dec. 1985., p. 241
Hydrolysis: Alkaline hydrolysis leads to complete degradation. Alkaline salts of O,S-diethylphosphorodithioate, formaldehyde, and ethyl mercaptan are non-toxic. Acid hydrolysis leads to complete degradation. Essentially the same products as alkaline hydrolysis. *United Nations. Treatment and Disposal Methods for Waste Chemicals (IRPTC File). Data Profile Series No. 5. Geneva, Switzerland: United Nations Environmental Programme, Dec. 1985., p. 242*

Annexes

Annex 1 Further information on phorate

The information presented in this Annex reflects the conclusions of the notifying parties: Brazil and Canada. The notification of Canada was published in PIC Circular XXVIII of December 2008. The notification from Brazil was published in PIC Circular XLV of June 2017.

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 the final regulatory actions to ban or severely restrict phorate.

Furthermore, information from the FAO/WHO Joint Meeting on Pesticide Residues (JMPR) monographs of toxicological evaluation of phorate in reports of the year 2004[5] and of the year 2012[6], as well as other sources such as PubChem, has been taken into account.

1. Identity and Physico-Chemical properties

1.1	**Identity:**	ISO: phorate IUPAC: O,O-diethyl S-ethylthiometyl phosphorodithioate; diethyl {[(ethylsulfanyl)methyl]sulfanyl}(sulfanylidene)phosphonite CAS: O,O-diethyl S-[(ethylthio)methyl]phosphorodithioate
1.2	**Formula**	$C_7H_{17}O_2PS_3$
1.3	**Molecular weight**	260.4
1.4	**Colour and Texture**	Technical phorate is a clear liquid at room temperature (Extoxnet, 1996) Phorate is a relatively stable clear to yellow liquid at room temperature (Toxipedia) Pale straw to light brown; colorless to very light yellow liquid with skunk-like odor (PubChem, 2017c)
1.5	**Melting point**	<-15ºC (technical grade) [(7)]
1.6	**Boiling Point**	118-120ºC/0.8 mmHg (technical grade) [(6)]
1.7	**Relative Density (g/cm3)**	1.167 (technical grade at 25ºC) [(6)] 1.156 at 25°C (Toxnet, 2017)
1.8	**Vapour Pressure**	85 mPa at 25ºC [(6)]
1.9	**Henry's Law Constant**	5.9 X 10^{-1} Pa m^3/mol [(6)] 4.368 X 10^{-6} atm.m^3/mol [(6)]
1.10	**Solubility in Water**	50 (mg/L) at 25ºC [(6)]
1.11	**Solubility in Organic Solvents**	Miscible with alcohols, ketones, ethers, esters, aromatic, aliphatic and chlorinated hydrocarbons, dioxane, vegetable oils, and other organic solvents. [(6)]
1.12	**Partition co-efficient**	$LogK_{ow}$: 3.92 [(6)]
1.13	**Dissociation Constant**	Not available, no pKa expected in the environmentally relevant pH range.
1.14	**Surface tension**	Not available
1.15	**Hydrolytic stability (DT_{50})**	2.6 d (pH 5), 3.2 d (pH 7), 3.9 d (pH 9) [(6)]

[5] http://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/JMPR/Reports_1991-2006/report2004jmpr.pdf.

[6] http://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/JMPR/Report12/JMPR_2012_Report.pdf.

[7] Canadian notification and supporting documentation

1.16	**Decomposition temperature**	No information available
1.17	**Resistance to acids**	Phorate is subject to hydrolysis under alkaline conditions, but is stable under neutral and acidic conditions. (PubChem, 2017c)
1.18	**Resistance to alkalis**	Phorate is subject to hydrolysis under alkaline conditions, but is stable under neutral and acidic conditions. (PubChem, 2017c)
1.19	**Tensile strength (10^3 kg/cm^2)**	Not applicable
1.20	**Storage stability**	Stable under normal storage conditions for at least 2 years (6)

2 Toxicological properties

2.1	**General**	
2.1.1	**Mode of Action**	Acetylcholinesterase (AChE) inhibition. The main feature of the toxic mechanism of organophosphorus pesticides is inhibition of the esterase enzyme activity, in particular of cholinesterase, which plays an important physiological role. Organophosphorus pesticides can also indirectly interact with the biochemical receptors of acetylcholine. (PubChem, 2017c) Systemic with contact and stomach action (PPDB, 2018).
2.1.2	**Symptoms of poisoning**	Phorate demonstrated to be extremely toxic, causing lethality at low doses, for different exposure conditions. The studies show that agricultural workers exposed to phorate are victims of poisonings and deaths related to toxicity characteristics of the active ingredient. Signs and symptoms of phorate poisoning are characteristic of AChE inhibition and may include vomiting, dizziness, abdominal pain, tachycardia, excessive salivation miosis and hypotension were observed in cases of intentional intoxication, occupational and accidental exposure to phorate. More severe symptoms such as convulsions, spasms, tremors, loss of muscle coordination, increased muscle tone of the limbs, respiratory distress, cerebral edema, loss of consciousness and deep coma have also been described. Findings in some patients were consistent with brain death, including absence of corneal, oculocephalic, pupillary and muscular reflexes, absence of reactions to pain or heat stimuli, and absence of spontaneous respiration, with global suppression of cortical activity. Some intoxication cases have evolved to death. Phorate can cause complex neurological manifestations such as encephalopathy, intermediate syndrome and delayed polyneuropathy in humans. Furthermore, the experimental and epidemiological studies involving the respiratory tract demonstrate that phorate has high toxicity for this system. At doses similar to occupational human exposure, signs and symptoms may include emphysema, bronchopneumonia, inflammatory changes and respiratory distress as main effects that were shown to be irreversible for the observation period even after the exposure ceased. It is known that these effects may cause increased pulmonary vascular resistance, overwhelm the heart and even cause heart failure. (Brazilian notification and supporting documentation). <u>Targeted organs</u> Eyes, skin, respiratory system, central nervous system, cardiovascular system, blood cholinesterase. (PubChem, 2017c). Further information on symptoms can be found in Toxnet (2017): under the section ”Clinical effects”.
2.1.3	**Absorption, distribution, excretion and metabolism in mammals**	**<u>Brazilian notification</u>** Rate and extent of oral absorption: Rapid, approximately 90% within 24 h. Dermal absorption: Extensive based on acute toxicity. Distribution: Rapid and extensive. Potential for accumulation: None.

Rate and extent of excretion: 89% within 24 h; urinary excretion predominated (77%); faecal excretion (12%).

PubChem (2017c)
Phorate is absorbed by all routes, oral, respiratory, and dermal. About 77% of an oral dose was excreted in the urine of rats within 24 hr, and 12% was excreted in the feces. Rats given oral phorate at 2 mg/kg or 6 daily doses at 1 mg/kg/day eliminated up to 35% of the dose in urine and up to 6% in feces in 6 days. Rats treated at the rate of 1 mg/kg/day for 6 days excreted only 12% in the urine and 6% in the feces within 7 days.

Brain, liver and kidney tissues from the latter animals contained unidentified and largely unextractable residues (IPCS INCHEM, undated).

Metabolism
Metabolism in animals - Major pathway: cleavage of phosphorus–sulfur bond, methylation of the liberated thiol group and oxidation of the resulting divalent moiety to the sulfoxide and sulfone.

Toxicologically significant compounds (plants, animals and the environment): parent, phorate sulfoxide and phorate sulfone (Brazilian notification).

The urine of male rats given daily oral doses of 1 mg/kg bw contained 17% diethyl phosphoric acid, 80% *O,O*-diethyl phosphorothioic acid and 3% *O,O*-diethyl phosphorodithioic acid. Phorate sulfoxide, phorate sulfone, phoratoxon sulfoxide and phoratoxon sulfone were formed (IPCS INCHEM, undated).

Metabolites of phorate were quantified in daily urine specimens obtained from employees of a pesticide formulating plant. The predominant alkyl phosphates found in urine were diethyl phosphate, diethyl phosphorothiolate, and diethyl thiophosphate (PubChem, 2017c).

2.2 Toxicology studies

2.2.1 Acute toxicity

Rat, LD_{50}, oral for male and female 3.7 mg/kg bw, 1.4 mg/kg bw, respectively (Brazilian notification).
Rat LD_{50} oral for male and female 3.7 and 1.6 mg/kg bw, respectively (Canadian notification).
Rat LD_{50} oral for male and female 2 and 1.1 mg/kg bw, respectively (PubChem, 2017c).
Mice LD_{50} oral 6 mg/kg bw (Canadian notification).
Mouse male LD_{50} oral 2.25 mg/kg bw (PubChem, 2017c).
Mouse male LD_{50} ip 2.1 mg/kg (PubChem, 2017c).
Mice LD_{50} range from 1.4 to 10 mg/kg bw (Brazilian notification, section 2.4.2.1).
Rat, LD_{50}, dermal for male and female 9.3 mg/kg bw and 3.9 mg/kg bw, respectively.
Rat, LC_{50}, inhalation for male and female 0.06 mg/L of air (1 h) and 0.011 mg/L of air (1 h), respectively (Brazilian notification).
Skin and eye acute percutaneous LD_{50} for male rats 6.2, female rats 2.5, male rabbits 5.6, female rabbits 2.9, Guinea pigs 30.0 mg/kg (Canadian notification).

2.2.2 Short term toxicity

Target/critical effect: brain and erythrocyte acetylcholinesterase activity, and miosis (rats).
Lowest relevant oral NOAEL: 0.07 mg/kg bw per day (Brazilian notification).
Lowest relevant dermal NOAEL: 0.41 mg/kg bw from 28-day dermal toxicity study for short- and intermediate-term dermal risk assessment in which there was inhibition of cholinesterase activity at the next level (Canadian notification).
Lowest relevant inhalation NOAEC: No data (Brazilian notification).
NOAEL = 0.25 mg/kg body weight derived from acute rat neurotoxicity study findings consistent with acetylcholinesterase inhibition (Brazilian notification).

2.2.3 Genotoxicity (including mutagenicity)

Negative results in vivo and in vitro (Brazilian notification).

2.2.4	**Long term toxicity and carcinogenicity**	Target/critical effect: Inhibition of erythrocyte and brain cholinesterase activity Lowest relevant NOAEL: 0.07 mg/kg per day (rat, Brazilian notification) Carcinogenicity: Not carcinogenic in mice and rats (Brazilian notification). A rat study is available. The LEL in this study was 2.0 ppm (0.1 mg/kg/day); the NOEL was 0.66 ppm (0.033 mg/kg/day). - Chronic toxicity: Dog study is available (NOEL and LEL for systemic toxicity were 50 and 250 µg/kg/day, respectively). Mouse study is available (NOEL and LEL were .45 and .9 µg/kg/day, respectively). Rat study is available (LEL was 0.05 mg/kg/day, NOEL was not determined). Source: Extoxnet (2017)
2.2.5	**Effects on reproduction**	Reproduction target/critical effect: Reduced pup growth at maternally toxic dose. Lowest relevant reproductive NOAEL: 2 ppm, equivalent to 0.17 mg/kg bw per day Developmental target/critical effect: Decreased pup weights and delayed ossification at maternally toxic doses (rats). Lowest relevant developmental NOAEL: 0.3 mg/kg bw per day (rats). (Brazilian notification)
2.2.6	**Neurotoxicity/ delayed neurotoxicity, Special studies where available**	Single dose study of neurotoxicity: Target/critical effect: Signs consistent with acetylcholinesterase inhibition; no neuropathological effects. Relevant NOAEL: 0.25 mg/kg bw. Delayed neuropathy: No delayed neurotoxicity in hens. Medical data: Findings consistent with inhibition of acetylcholinesterase activity; no record of permanent sequelae. (Brazilian notification)
2.2.7	**Summary of mammalian toxicity and overall evaluation**	**Canadian notification** **In laboratory animals, phorate was found to be extremely acutely toxic following acute oral, dermal and inhalation exposures. Following both single and repeated dosing, the most sensitive indicator of toxicity was the inhibition of acetylcholinesterase, an enzyme necessary for the proper functioning of the nervous system or clinical signs of cholinergic toxicity. Female animals were more sensitive to the toxic effects of phorate. Phosphorylated phorate metabolites (phorate sulfoxide and phorate sulfoxone) are of comparable toxicity to phorate. Phorate did not cause any apparent delayed neurotoxicity and there was no evidence of histopathologic effects on the central nervous system in any of the available studies. Phorate was not found to be genotoxic nor was it carcinogenic to either rats or mice. Phorate did not cause fetal malformations in either rats or rabbits, nor did it cause reproductive toxicity in rats other than reduced viability of the young at doses that were maternally toxic. The developmental and reproductive toxicity studies did not demonstrate any sensitivity of young animals relative to adult animals although lack of cholinesterase measurements in these studies precluded a definitive assessment of this issue. On the basis of the available toxicity studies, phorate is anticipated to have a high dermal absorption potential. One of the most remarkable features of phorate was the steepness and potency of the dose-response with acute and short-term dosing. No observed adverse effect levels (NOAELs) were very close to dose levels that elicited mortality in the test animals.** **Brazilian notification** Phorate and its metabolites were found to be easily absorbed through skin and mucous membranes and irreversibly block the catalytic activity of acetylcholinesterase (AChE). Thus, it interrupts the transmission of nerve impulses in the cholinergic synapses of the central nervous system (CNS), autonomic nervous system (ANS) and neuromuscular junction. Inactivation of AChE causes cholinergic hyperstimulation by acetylcholine accumulation in the synaptic cleft. Phorate is considered one of the most toxic organophosphate AChE inhibitors (with mean oral LD_{50} for mice ranging from 1.4 to 10 mg/kg body weight). Phorate can cause complex neurological clinical manifestations in humans, such as encephalopathy, intermediate syndrome and delayed polyneuropathy. In laboratory animals that received phorate there were no cases of intermediate syndrome or late

polyneuropathy, which suggests this pesticide is more toxic to humans than demonstrated in tests with laboratory animals.

The experimental and epidemiological studies involving the respiratory tract demonstrate that phorate has high toxicity for this system.

Phorate demonstrated the potential to cause adverse effects to the endocrine regulation processes of steroid hormones in humans, which may contribute to increased cancer cases.

Several studies showed that agricultural workers exposed to phorate are victims of poisonings and deaths related to toxicity characteristics of the active ingredient. The exposure becomes even more dangerous due to the difficulties related to the availability and/or ineffectiveness of personal protective equipment.

3	**Human exposure/Risk evaluation**	
3.1	**Food**	Monitoring data indicate that the general population may be exposed to phorate via ingestion of food.
3.2	**Air**	Monitoring data indicate that the general population may be exposed to phorate via inhalation in ambient air.
3.3	**Water**	Monitoring data indicate that the general population may be exposed to phorate via drinking water.
3.4	**Occupational exposure**	Occupational exposure to phorate may occur through inhalation and dermal contact with this compound at workplace where phorate is produced or used.

Brazil

The notification refers to several studies that have shown that pesticide poisonings, especially with organophosphorous pesticides, occurred in different regions of Brazil. In addition, the technical note (ANVISA, 2009) indicates that many pesticide poisoning incidents were not reported in Brazil.

According to a study from the Amazonas area of Brazil, agricultural workers were not prepared to use pesticides correctly. They were not sufficiently aware of the risks of pesticides to human health and the environment. This study further concludes that farmers did not use protective clothing or equipment because it was expensive and not suitable for a tropical climate. Due to lack of training and poor knowledge of pesticide hazards, pesticides were handled carelessly during preparation, application and disposal of empty packages. Exposure of farmers, their families, consumers and the environment was thus high.

Although no poisoning incidents with phorate itself have been reported from Brazil, the decision to ban phorate was taken on the basis of the evaluation of its hazardous properties as well as the expected exposure of agricultural workers to phorate under conditions of use in Brazil. . ANVISA concluded this active ingredient has the potential to cause hormonal disturbances in humans and is more toxic to humans than demonstrated in tests with laboratory animals, which are prohibitive criteria for registration of pesticides in Brazil.

Canada

Occupational risk assessment

Workers can be exposed to a pesticide through loading or applying the pesticide, and re-entering a treated site. Worker risk is estimated by an MOE that determines how close the occupational exposure comes to the NOAEL taken from animal studies. For workers entering a treated site, re-entry intervals are calculated where required, to determine the minimum length of time required before workers or others are allowed to enter.

The risks from loading and applying the clay-based granular Thimet 15-G (15% active ingredient) using a Lock'n Load closed handling system and other mitigation measures, are below the PMRA's level of concern. Approximately 60% of Thimet 15-G is sold in Lock'n Load packaging, according to the registrant. The risk of loading Thimet 15-G in paper bags (open loading) exceeds the PRMA's level of concern.

Chemical-specific exposure information was used to assess the closed handling system scenario (Lock'n Load). The Pesticide Handlers Exposure Database (PHED) was used to assess the open mixing and loading scenario. For Thimet 15-G, adequate worker protection would be afforded under the following conditions: for loading activities: Lock'n Load packaging, and personal protective equipment including chemical resistant apron and gloves; and for application activities: closed cab. As an interim measure pending implementation of closed cabs, chemical resistant coveralls over long pants and long sleeves, chemical resistant gloves and a respirator are recommended for application activities.

Adequate MOEs were not obtained for open loading activities with Thimet 15-G packaged in paper.

The PMRA concluded that exposure to persons entering treated sites after application is considered minimal due to the application method (soil incorporation at planting). A Re-entry interval of 48 h based on acute toxicity is sufficient to protect workers who may re-enter treated areas.

Toxnet (2017):

Phorate was detected in farmer's cotton coveralls, worn during pesticide application (1985-1987).

3.5 Medical data contributing to regulatory decision

Poisoning incidents

Usha and Harikrishnan (2004) reported several cases of acute poisoning in communities of Kerala, India. Among these, 5 cases (occurred between 1999 and 2002), were associated to exposure to phorate.

According to the authors, in July 1999, about 12 people living in banana crop areas were severely poisoned by phorate. After the product use, it rained on the region, causing the product evaporate quickly and spread to nearby area, reaching the homes. Shortly after application of the product, the symptoms appeared and the affected required hospitalization. In June 2001, a 16-year-old boy died as a result of occupational exposure to phorate for a period of one week. That same year, 40 rural women workers in a tea plantation were intoxicated during harvesting. Symptoms appeared within 30 minutes after exposure, featured by light-headedness, dizziness, blurred vision, vomiting. Thirty-seven women had more severe symptoms and remained hospitalized for two days. The authors point out that in July 2002, 31 children from an upper primary school were poisoned by phorate applied in plantation nearby school.

The children showed persistent headache, chest pain, breathing difficulty, nausea, giddiness, blurring of vision and stomach pain, and one of them showed uncontrolled muscle twitching and convulsions even after 24 hours of treatment.

On 21 July 2006, 20 residents of Salkiana village, district Jalandhar, India, had to be rushed to a hospital when neurotoxic symptoms of acute exposure to phorate were observed. The product was used in a nearby sugarcane field. The worst affected were the schoolchildren of an Elementary School. Teachers and students started complaining of a strange smell and breathlessness. Suddenly one student fell unconscious and then students started to faint. Within ten minutes, 16 students fainted after inhaling something that was toxic. In addition to difficulty breathing, the most frequent symptoms were feeling poorly, headache, eye irritation, dizziness, nausea, vomiting, lacrimation, salivation excessive, muscle cramps and pain. Six days after exposure to phorate, several patients still had symptoms such as eye irritation, dermal reactions and general uneasiness. (Mission, 2006).

3.6 Public exposure

Toxnet (2017):

"Phorate was detected on the hands of farmer' children at the level of 15 ng, following application of the pesticide in the fields" and "Secondary exposure of children through contact with their parent's contaminated clothing can also occur".

3.7	**Summary-overall risk evaluation**	**Brazil** has conducted a risk evaluation of the human health effects of phorate. Based on the hazardous properties of phorate as well as on conditions of use in Brazil, the expected risks resulting from the exposure of agricultural workers, bystanders and the general population to phorate were considered too high.

4 Environmental fate and effects

4.1 Fate

4.1.1 Soil

Brazil

Breakdown in soil and groundwater: Phorate is of moderate persistence in the soil environment, with reported field half-lives of 2 to 173 days. A representative value may be approximately 60 days. Actual residence times may be influenced by soil clay and organic matter content, rainfall, and soil pH. Soil treatments often leave more residues in plants than foliar treatments, because the compound persists in the soil and is readily taken up by plant roots. Phorate binds moderately well to most soils and is slightly soluble in water. It should therefore not be highly mobile in most soils, and should mainly be transported with runoff via sediment and water. Phorate has minimal potential to leach through the soil and contaminate groundwater. This is most likely where soils are sandy and aquifers are shallow.

Field studies indicate that leaching is very low in soils high in clay and organic matter content, and low in sandy soils.

Canada

Phorate is transformed by chemical and microbial action. It is moderately persistent in soil (time required for 50% dissipation (DT_{50}) = 49-75 d) under field conditions, as seen in field studies in British Columbia. The major transformation products phorate sulfoxide and phorate sulfone, that are formed as a result of microbial action, are moderately persistent (DT_{50} = 65-137 d) in soil under laboratory conditions. These transformation products retain the phosphorylated structure and are expected to exhibit cholinesterase inhibition, and therefore be as toxic as the parent compound phorate.

Phorate is strongly sorbed to soil and is classified as having slight (Koc = 2000-3000) to moderate mobility (Koc = 224-450). Phorate sulfoxide and phorate sulfone partition preferentially into water and are both classified as having moderate (Koc = 172-210) to high mobility (Koc = 71-91) in a range of soil types. Phorate and its major transformation products can enter aquatic systems through run-off, however, the latter are more mobile than the parent compound.

4.1.2 Water

Brazil

Breakdown in water: The half-life of phorate in acidic water solutions is between a few days and a few weeks, depending on temperature; the half-life in alkaline (basic) water may be much shorter. Phorate is degraded by waterborne microorganisms and hydrolysis. As it breaks down in water, nontoxic, water-soluble products are formed.

Canada

Phorate is soluble in water at 50 mg/L and highly volatile with a vapour pressure of 85 mPa at 25°C. **The** Henry's law constant is 4.368 x 10^{-6} atm.m^3/mol, which indicates there is potential to volatilize from water or moist soil.

Although there may be contamination of surface water through run-off, phorate is not persistent in water owing to rapid hydrolysis. In sterile water at pH 5, 7 and 9, the half-lives are 2.6, 3.2 and 3.9 d, respectively. Photolysis is also an important route of transformation (dark control adjusted half-life of 1.9 d in pH buffer solutions after 7 d of continuous irradiation). Formaldehyde, phorate sulfoxide and phorate sulfone are the major transformation products formed during hydrolysis and aqueous photolysis. Aerobic aquatic biotransformation studies with non-sterile pond water showed the parent compound and transformation products did not persist in the water (phorate DT_{50} of 0.5 d, phorate sulfoxide DT_{50} of 9 d, phorate sulfone DT_{50} of 21 d) and formaldehyde reached 17% of applied by 14 d after treatment).

4.1.3 Air

Canada

Phorate is highly volatile with a vapour pressure of 85 mPa at 25ºC. The Henry's law constant of 4.368 X 10^{-6} indicates there is potential to volatilise from soil and water. However, as outlined below the literature indicates that phorate is not persistent in air.

Literature

According to a model of gas/particle partitioning of semivolatile organic compounds in the atmosphere, phorate, which has a vapour pressure of 0.000638 mm Hg at 25ºC, is expected to exist solely as a vapour in the ambient atmosphere. Vapour-phase phorate is degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals; the half-life for this reaction in air is estimated to be 1.5 hours, calculated from its rate constant of 2.5 X 10^{-10} cc/molecule-sec at 25ºC that was derived using a structure estimation method. Laboratory experiments indicated rapid gas-phase photolysis of phorate under midsummer sunlight conditions with observed half-lives <30 minutes (PubChem, 2017c).

4.1.4 Bioconcentration

Canada

The n-octanol-water partition co-efficient (log Kow) is 3.92, which indicates there is potential for bioaccumulation. However, the rapid degradation in water to more water soluble products shown above in both the Brazilian and Canadian notifications would suggest the bioconcentration potential is low. Further Canada concluded that phorate is not bioaccumulative by the federal Toxic Substances Management Policy (TSMP) Track-1 cut-off criterion (log *Kow* ~ 3.92)

Juvenile sheepshead minnows, *Cyprinodon variegatus*, after 28 days exposure to phorate had a BCF of 90. According to a classification scheme, this BCF suggests the potential for bioconcentration in aquatic organisms is moderate. Bioconcentration of phorate from culture media by the blue green algae *Anabaena sp*. (ARM 310) and *Aulosira fertilissima* (ARM 68) was studied. Bioconcentration factors for phorate in *Anabaena sp.* were 3, 6 and 12 at 2.5, 5 and 10 µg/mL, respectively. *Elodea nuttallii* plants grown for 2 weeks in water with a deposit of C14-phorate in the bottom soil accumulated 30% of the originally soil-applied radiocarbon in their tissues; 56% of phorate accumulated in plant tissues when the insecticide was applied directly to the water (PubChem, 2017c).

4.1.5 Persistence

Canada

Phorate in soil is moderately persistent (time required for 50% dissipation (DT_{50}) = 49-75 d) under field conditions, as seen in field studies in British Columbia. The major transformation products phorate sulfoxide and phorate sulfone, that are formed as a result of microbial action, are moderately persistent (DT_{50} - 65-137 d) in soil under laboratory conditions.

Although there may be contamination of surface water through run-off, phorate is not persistent in water owing to rapid hydrolysis. In sterile water at pH 5, 7 and 9, the half-lives are 2.6, 3.2 and 3.9 d, respectively. Aerobic aquatic biotransformation studies with nonsterile pond water showed that the parent compound and transformation products did not persist in the water (phorate DT_{50} of 0.5 d, phorate sulfoxide DT_{50} of 9 d, phorate sulfone DT_{50} of 21 d and formaldehyde reached 17% of applied by 14 d after treatment).

After phorate (Thimet 15-G) was assessed in regard to the federal Toxic Substances Management Policy (TSMP) it was concluded that phorate does not meet the TSMP criteria for persistence.

4.2 Effects on non-target organisms

4.2.1 Terrestrial vertebrates

Brazil

Effects on birds: Phorate is very highly toxic to birds. The reported acute oral LD_{50} values are:

		12.8 mg/kg in chukar, 7.5 mg/kg in starlings, 0.6 to 2.5 mg/kg in mallards, 7 to 21 mg/kg in northern bobwhite quail, 1 mg/kg in red-winged blackbirds, and 7 mg/kg in ring-neck pheasants. The 5- to 8-day dietary LC_{50} values are reported as 370 to 580 ppm in Japanese quail, mallard, northern bobwhite quail, and ring-neck pheasant. **Canada** Studies have shown that phorate is very highly toxic to birds on an acute oral basis (mallard duck mean lethal dose (LD_{50}) = 0.62 mg a.i./kg), and is highly toxic to birds on a dietary basis (mallard duck LD_{50} = 248 mg a.i./kg). Phorate is very highly toxic to small mammals on an acute oral basis (rat LD_{50} = 1.1-3.7 mg a.i./kg) and on a dietary basis (rat LD_{50} = 28 mg a.i./kg).
4.2.2	**Aquatic species**	**Brazil** **Effects on aquatic organisms**: Phorate is very highly toxic to fish. Reported 96-hour LC_{50} values range from 2 to 13 µg/L in cutthroat trout, bluegill sunfish and largemouth bass. Other 96-hour LC_{50} values are 110 µg/L in northern pike and 280 µg/L in channel catfish. Reported 96-hour LC_{50} values for the compound in freshwater invertebrates such as stoneflies and scuds are 4 µg/L, also indicating very high toxicity. Other LC_{50} values are 0.006 µg/L for amphipods and 0.11 to 1.9 µg/L in other freshwater invertebrates. The acute oral LD_{50} of phorate is 85 mg/kg in bullfrogs. **Canada** Phorate is very highly toxic on an acute basis to fish (rainbow trout mean lethal concentration (LC_{50}) = 13 µg a.i./L) and to aquatic invertebrates (*Gammarus fasciatus* LC_{50} = 4 µg a.i./L). **Pesticide Properties DataBase** (PPDB, 2018) Fish - Acute 96 hour LC_{50} = 0.013 mg/L *Oncorhynchus mykiss.* Fish - Chronic 21 day NOEC = 0.0002 mg/L *Oncorhynchus mykiss.* Aquatic invertebrates - Acute 48 hour EC_{50} = 0.004 mg/L *Daphnia magna.* Aquatic crustaceans - Acute 96 hour LC_{50} = 0.00033 mg/L *Americamysis bahia.* Sediment dwelling organisms - Acute 96 hour LC_{50} = 0.081 mg/L *Chironomus riparius.* **Algae - Acute 72 hour EC_{50}, growth 0.13 mg/L. Unknown species.**
4.2.3	**Honeybees and other arthropods**	**Brazil** Phorate is toxic to bees, with a reported topical application LD_{50} of 10 µg per bee. **Canada** Phorate is moderately to highly toxic to bees on an acute contact basis (0.32-10.1 µg a.i./bee).
4.2.4	**Earthworms**	**Pesticide Properties DataBase** (PPDB, 2018) Earthworms - Acute 14 day LC_{50} (mg kg^{-1}) 20.8 *Eisenia foetida.*
4.2.5	**Soil microorganisms**	No data available
4.2.6	**Terrestrial plants**	No data available

5	**Environmental Exposure/Risk Evaluation**	
5.1	**Terrestrial vertebrates**	The Brazilian notification does not contain any information or summary of the environmental risk assessment conclusions for terrestrial vertebrates. **Canada** Extremely high risks to terrestrial organisms have been identified from registered uses of phorate. This assessment is supported by reports of incidents in Canada and the U.S. Estimated exposure concentrations for terrestrial organisms exceed acute

		effects levels for both birds and mammals. For in-furrow applications, the estimated surface exposure is 1%. For banded subsurface emplacement to corn and rutabagas, the estimated surface exposure is 15%. The acute risk from direct consumption of granules is greatest for smaller species. The number of lethal doses (LD_{50}s) that are available within one square metre immediately after application ($LD_{50}s/m^2$) is used as the risk quotient (RQ) for granular products. Risk quotients for acute effects in mammals were greater than 1 LD_{50}/m^2, the threshold of concern for tested species, for use on potatoes and beans. Risk quotients ranged from 198 to 13 112 $LD_{50}s/m^2$ for surface broadcast applications to beans and 98 to 6 481 $LD_{50}s/m^2$ for in-furrow applications to potatoes, depending upon the size of the mammal. For applications to lettuce, risk quotients ranged from 99 to 6556 $LD_{50}s/m^2$, for corn from 101 to 6782 $LD_{50}s/m^2$ and for rutabagas from 417 to 55 340 $LD_{50}s/m^2$. These are classified as high to extremely high risk. Risk quotients for acute effects in birds were greater than 1 LD_{50}/m^2, the threshold of concern for tested species, for use on beans and potatoes. Risk quotients ranged from 170 to 21 623 $LD_{50}s/m^2$ for surface broadcast applications to beans and 84 to 10 687 $LD_{50}s/m^2$ for in-furrow applications to potatoes depending upon the size of the bird. For applications to lettuce risk quotients ranged from 85 to 10 811 $LD_{50}s/m^2$, for corn from 88 to 11 184 $LD_{50}s/m^2$ and for rutabagas from 358 to 91 263 $LD_{50}s/m^2$. These risk quotients are classified as high risk to extremely high risk. Birds may also be exposed by other routes, such as by walking on exposed granules and bathing, drinking water contaminated by granules and by eating tainted prey.
5.2	**Aquatic species**	Extremely high risks to aquatic organisms have been identified from all registered uses of phorate. This assessment is supported by reports of incidents of adverse effects in the U.S. Similar effects may have occurred in Canada, but there is no equivalent reporting system in this country. Estimated environmental concentrations exceed acute and chronic effects levels in both fish and aquatic invertebrates: Risk quotients for acute and chronic effects on the majority of freshwater aquatic invertebrates tested were greater than 1, the threshold of concern. Risk quotients exceeded 1000 for use on potatoes (RQ = 1476), beans (RQ = 1495), lettuce (RQ = 1917), corn (RQ = 2650) and rutabagas (RQ = 4500) and are classified as extremely high risk. Risk quotients for acute and chronic effects on freshwater fish were greater than 1, the threshold of concern. Values exceeded 100 for applications to beans (RQ = 165), corn (RQ = 122) and rutabagas (RQ = 415) and are classified as very high risk. For applications to lettuce (RQ = 89), the acute and chronic risks were classified as high risk, as the RQ was greater than 10. For estuarine and marine fish and invertebrates, the acute and chronic risk quotients exceeded 1000, which is classified as extremely high risk.
5.3	**Honey bees**	The Brazilian or Canadian notifications do not contain any information or summary of the environmental risk assessment conclusions for honey bees.
5.4	**Earthworms**	The Brazilian or Canadian notifications do not contain any information or summary of the environmental risk assessment conclusions for earthworms.
5.5	**Soil microorganisms**	The Brazilian or Canadian notifications do not contain any information or summary of the environmental risk assessment conclusions for soil microorganisms.
5.6	**Summary – overall risk evaluation**	Risk quotients and margins of safety calculated for applications of Thimet 15-G indicate risks for all groups of organisms (birds, mammals, fish and aquatic invertebrates) for all application scenarios. Based on the available toxicity data, risk is classified as high to extremely high risk for freshwater aquatic organisms and high to extremely high risk for birds. Similarly, risk to mammals is classified as high risk for large mammals to extremely high risk to small mammals. The identified risks to birds and fish are supported by reported incidents arising from labelled use of the products. The use of phorate and associated end-use products (EP) entails an unacceptable risk to the environment pursuant to Section 20 of the Canadian Pest Control

Product (PCP) Regulations. As a result, the Pest Management Regulatory Agency (PMRA) determined that all uses of phorate were to be phased out[8].

[8] The use on potato was subsequently extended to August 2015. Furthermore, it should be noted that a new phorate product, paired with application equipment to reduce environmental exposure, was registered in 2015.

Annex 2 – Details on final regulatory actions reported

Country Name: Brazil

1	**Effective date(s) of entry into force of actions**	March 16th, 2015
	Reference to the regulatory document	Resolution RDC No. 12 of 13 March 2015, issued by the National Health Surveillance Agency (ANVISA)
2	**Succinct details of the final regulatory action(s)**	Pursuant to resolution RDC No. 12 of 13 March 2015, issued by ANVISA, all technical and formulated products based on phorate active ingredient are prohibited. Consequently, production, use, trade, import and export of phorate are banned. Before the final regulatory action entered into force, phorate was used in Brazil as an insecticide authorized exclusively for agricultural use.
3	**Reasons for action**	Human health: unacceptable risk for workers, consumers and general population.
4	**Basis for inclusion into Annex III**	The final regulatory action to ban phorate was based on a risk evaluation taking into consideration local conditions in Brazil.
4.1	**Risk evaluation**	The final regulatory action was based on a risk and hazard evaluation. In accordance with the Brazilian Pesticide Law, one or more of the governmental agencies responsible for the pesticides registration (IBAMA, ANVISA or MAPA) can re-evaluate the registration of a pesticide, when there is evidence of reduction of agronomic efficiency and/or change of risks to human health or environment. In order to carry out the re-evaluation a Technical Committee is established. The Committee develops Technical Notes on the toxicology and/or potential environmental hazards of the active ingredient in addition to an economic analysis of pesticide substitutes, based on data collected from studies and surveys conducted by national and international accredited institutions as well as information provided by the National System of Toxic-Pharmacological Intoxications and Poisonings (SINITOX), the Pesticide Residues in Food Analysis Programme or the pesticide registrants. The Technical Notes in the re-evaluation process assess the potential exposure and exposure and the hazard in accordance with the parameters and methodologies adopted internationally, especially by the World Health Organization (WHO),), the Food and Agriculture Organization (FAO), the Organization for Economic Cooperation and Development (OECD), the USA Environmental Protection Agency and the European Union. After the re-evaluation, measures to restrict, suspend or prohibit the production and import of pesticides could be taken as well as to cancel the registration, if a criterion of prohibition of registration is fulfilled. The Brazil risk evaluation of phorate took into account toxicology and public health, occupational health and safety, the environmental impact and availability of lower-risk alternatives. An extensive review of relevant data on hazard and risk of phorate using reviewed documents, published reports and literature was undertaken. The re-evaluation took into account *inter alia* the study carried out by Waichman (2008) in municipalities of the state of Amazonas (Manaus, Iranduba, Careiro da Várzea and Manacapuru). This study concluded that farmers were not prepared for the proper use of pesticides, ignoring the risks of these products to human health and the environment. Personal protective equipment is not used because it is expensive, uncomfortable and unsuitable for the hot climate of the region. Lack of training and poor knowledge of the hazards of pesticides contribute to the incorrect handling during their preparation and application, as well as the disposal of empty containers. In these conditions, the exposure of farmers, their families, consumers and the environment is high. Considering all the toxicological effects associated with the active ingredient phorate, especially its characteristics to be more toxic to humans than animal tests are able to demonstrate, and although no poisoning incidents with phorate have been reported from Brazil, the decision to ban phorate was taken on the basis of the evaluation of its hazardous properties as well as the expected exposure of

		agricultural workers to phorate under conditions of use in Brazil. The final regulatory action was taken in order to protect the health of exposed workers, consumers and the general population.
4.2	**Criteria used**	Risks to human health and the environment
	Relevance to other States and Region	Similar concerns to those identified are likely to be encountered in other countries where the substance is used, particularly in developing countries.
5	**Alternatives**	See section 3.3
6	**Waste management**	None reported
7	**Other**	None reported

Country Name: Canada		
1	**Effective date(s) of entry into force of actions**	In December 2004.
	Reference to the regulatory document	Relevant regulatory documents are: – Proposed Acceptability for Continuing Registration (PACR 2003-01), Pest Management Regulatory Agency (PMRA) Re-evaluation of Phorate, January 24 , 2003 – Re-evaluation Decision Document (RRD 2004-11) Phorate, 13 May 2004, – Re-evaluation note, Rev2007-07, Update on the Use of Phorate on Potatoes, 5 June 2007.
2	**Succinct details of the final regulatory action(s)**	The use of phorate and associated end-use products (EP) entails an unacceptable risk of harm to the environment pursuant to Section 20 of the Canadian Pest Control Product (PCP) Regulation. As a result, PMRA determined that all uses of phorate were to be phased out. Due to the lack of alternatives to phorate for control of wireworm on potatoes, the registration of phorate, for this use only, was allowed to be continued, with interim mitigation measures to protect workers (engineering, controls, requirements regarding additional Personal Protective Equipment (PPE)) and the environment (environmental statements on the label).
3	**Reasons for action**	Environment: an unacceptable risk of harm to the environment
4	**Basis for inclusion into Annex III**	The final regulatory action to ban phorate was based on a risk evaluation taking into consideration local conditions in Canada.
4.1	**Risk evaluation**	Phorate is highly toxic to all terrestrial and aquatic species tested. Incident reports of bird and mammal fatalities in Canada, the United States of America, the United Kingdom of Great Britain and Northern Ireland support the conclusion that phorate presents a significant risk to birds and wildlife. Surface broadcast application presents the greatest risk owing to the large number of exposed granules on the surface. Although soil incorporation is expected to lower the risk of terrestrial and aquatic exposure, it nevertheless presents a very high risk owing to unincorporated granules remaining exposed on the surface. The risk to small and moderate-sized birds and small or moderate-sized mammals remains high to very high with either method of application. Owing to its extreme toxicity to all organisms tested, the very high risk to moderate and smaller sized birds and mammals, the incident reports of bird and mammal mortalities (including large raptors in Canada), in addition to the persistence and mobility of the toxic sulfoxide and sulfone transformation products, Canada has concluded that the use of phorate in the country presents a high risk to the environment. Additional information on toxicity for aquatic organisms was also given in the supporting documentation provided by Canada.
4.2	**Criteria used**	Risks to the environment
	Relevance to other States and Region	Similar concerns to those identified are likely to be encountered in other countries where the substance is used, particularly in developing countries.
5	**Alternatives**	See section 3.3
6	**Waste management**	None reported
7	**Other**	None reported

Annex 3 – Addresses of designated national authorities

BRAZIL

Role: DNA CP* Name: Mr. Reinaldo Salgado Job title: Director Department: Department for Environmental Sustainability Institution: Ministry of Foreign Affairs Postal address: Esplanada dos Ministerios Bloco H, Anexo II, Sala 204 70170-900 Brasilia D.F. Brazil	Phone: +55 61 2030 9644 Fax: +55 61 2030 5102 Email: dips@itamaraty.gov.br, delbrasgen@itamaraty.gov.br, gsq@mma.gov.br
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CANADA

Role(s): DNA P* Name: Mr. Jason Flint Job title: Director General Department: Policy, Communications and Regulatory Affairs Institution: Pest Management Regulatory Agency Postal address: 2720 Riverside Drive K1A 0K9 Ottawa Quebec Canada	Phone: +1 613 736 3660 Fax: +1 613 736 3695 Email: jason.flint@canada.ca
Role: DNA C* Name: Ms. Nathalie Morin Job title: Director Department: Chemical Production Division Institution: Environment and Climate Change Canada Postal address: 351 St. Joseph Boulevard K1A OH3 Gatineau Québec Canada	Phone: +1 819 420 8047 Fax: +1 819 938 4218 Email: nathalie.morin4@canada.ca

***C** Industrial chemicals
CP Pesticides and industrial chemicals
P Pesticides

Annex 4 – References

Regulatory actions

Brazil:

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