

CRC-13/4: Phorate

The Chemical Review Committee,

Recalling Article 5 of the Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade,

Recalling also the conclusion by the Chemical Review Committee, adopted at its fifth meeting, that the notification of final regulatory action for phorate submitted by Canada met the criteria set out in Annex II to the Convention,¹

1. *Concludes* that the notification of final regulatory action for phorate submitted by Brazil² meets the criteria set out in Annex II to the Convention;
2. *Adopts* the rationale for the Committee's conclusion set out in the annex to the present decision;
3. *Recommends*, in accordance with paragraph 6 of Article 5 of the Convention, that the Conference of the Parties should list phorate in Annex III to the Convention as a pesticide;
4. *Decides*, in accordance with paragraph 1 of Article 7 of the Convention, to prepare a draft decision guidance document for phorate;
5. *Also decides*, in accordance with the process for drafting decision guidance documents set out in decision RC-2/2 and amended by decision RC-6/3, that the composition of the intersessional drafting group to prepare the draft decision guidance document for phorate and the workplan of the group shall be as set out in annexes II and III, respectively, to the report of the Committee on the work of its thirteenth meeting.

Annex to decision CRC-13/4

Rationale for the conclusion by the Chemical Review Committee that the notification of final regulatory action submitted by Brazil in respect of phorate in the pesticide category meets the criteria of Annex II to the Rotterdam Convention

1. In reviewing the notifications of final regulatory action by Brazil to ban the use of phorate as a pesticide, together with the supporting documentation provided by the Party, the Committee confirmed that the action had been taken to protect human health. The notification was found to meet the information requirements of Annex I and the criteria set forth in Annex II to the Rotterdam Convention.
 2. The notification and supporting documentation were made available to the Chemical Review Committee for its consideration (UNEP/FAO/RC/CRC.13/13, UNEP/FAO/RC/CRC.13/INF/29).
 3. In reviewing the notification of final regulatory action by Brazil, together with the supporting documentation provided by the Party, the Committee was able to confirm that the action had been taken in order to protect human health.
- (a) **Scope of the notified regulatory action**
4. The notified regulatory action relates to phorate (CAS No. 298-02-2) used as a pesticide.
 5. As a result of the toxicological re-evaluation of the active ingredient phorate, on 13 March 2015 the National Health Surveillance Agency (ANVISA) issued Resolution RDC No. 12. Pursuant

¹ UNEP/FAO/RC/CRC.5/16, annex III, section B.

² See UNEP/FAO/RC/CRC.13/13.

to that resolution, all technical and formulated products based on the active ingredient phorate are prohibited. Consequently, the production, use, trade, import and export of phorate are banned.

6. Prior to the final regulatory action, the use of phorate was allowed in Brazil as an insecticide authorized exclusively for agricultural use.

7. The notification was found to meet the information requirements of Annex I.

(b) Annex II paragraph (a) criterion

(a) Confirm that the final regulatory action has been taken in order to protect human health or the environment;

8. As stated in the notification, the final regulatory action taken by Brazil in relation to phorate prohibited all technical and formulated products based on the active ingredient phorate and banned the production, use, trade, import and export of the active substance (sects. 2.2.1 and 2.3.3 of the notification). Prior to the adoption of the final regulatory action, phorate had been used in Brazil as an insecticide authorized exclusively for agricultural use for the following crops: cotton, potato, coffee, beans and corn (UNEP/FAO/RC/CRC.13/13, annex, sect. 2.3.1).

9. The final regulatory action, as the notification states, has been taken for the pesticide category (UNEP/FAO/RC/CRC.13/13, annex, sect. 2.3.2) to protect human health (UNEP/FAO/RC/CRC.13/13, annex, sect. 2.4.2.1).

10. Brazil has undertaken, as part of its toxicological re-evaluation of the active ingredient, an extensive review of relevant data on the hazards and risks associated with phorate using reviewed documents, published reports and literature.

11. On the basis of the available data, phorate and its metabolites were identified 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 in acetic acid and choline acid. Thus, they 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.

12. Phorate is considered one of the most toxic organophosphate AChE inhibitors, with mean oral LD50 for mice ranging from 1.4 to 10 mg/kg body weight (UNEP/FAO/RC/CRC.13/13, annex, sect. 2.4.2.1). The experimental and epidemiological studies involving the respiratory tract demonstrate that phorate has high toxicity for this system (UNEP/FAO/RC/CRC.13/INF/29, p. 21).

13. Data confirm that phorate can cause complex neurological clinical manifestations in humans, such as encephalopathy, intermediate syndrome and delayed polyneuropathy, described by various authors (Young, Jung, Ayer, 1979; Kashyap et al., 1984; WHO/FAO, 1988; Kusic et al., 1991; Dobozy, 1998; Das and Jena, 2000; Thanal, 2001; Jayakumar, 2002; Mission, 2006; Peter, Prabhakar, Pichamuthu, 2008a; 2008b). However, in laboratory animals that received phorate, there were no cases of intermediate syndrome or late polyneuropathy, which shows this pesticide as more toxic to humans than is demonstrated in tests with laboratory animals.

14. Besides its neurotoxic effects, phorate was found to demonstrate the 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) (UNEP/FAO/RC/CRC.13/13, annex, sect. 2.4.2.1; UNEP/FAO/RC/CRC.13/INF/29).

15. Several studies, analysed by Brazil, also showed that agricultural workers exposed to phorate have been the victims of poisonings and deaths related to the toxicity characteristics of the active ingredient. The exposure becomes even more dangerous due to the difficulties related to the lack of availability and/or inefficiency of personal protective equipment (UNEP/FAO/RC/CRC.13/13, annex, sect. 2.4.2.1; UNEP/FAO/RC/CRC.13/INF/29, p.21).

16. From the Brazilian perspective, there is a comprehensive study on the conditions of pesticide use carried out by Waichman (2008) in Brazilian municipalities of the state of Amazonas (Manaus, Iranduba, Careiro da Várzea and Manacapuru). It 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 are contributing to incorrect handling during the preparation, application and disposal of empty containers. In these conditions the exposure of farmers, their families, consumers and the environment is high.

17. The Committee noted that “Brazilian law predicts that pesticides may have their registrations cancelled in the country when they fall under the following conditions related to human health: when they have no antidote or effective treatment in Brazil; if found teratogenic, mutagenic or carcinogenic; if they cause hormonal disturbances and damage to the reproductive system or if they are more dangerous to humans than demonstrated in tests with laboratory animals” (UNEP/FAO/RC/CRC.13/13, annex, sect. 2.4.2.1).

18. The toxicological re-evaluation undertaken by Brazil led to the conclusion that, considering all the toxicological effects associated with the active ingredient phorate and its characteristics, it was found to be more toxic to humans than animals. The use of the active ingredient phorate thus must be prohibited in Brazil, in order to protect the health of exposed workers, consumers and the general population (UNEP/FAO/RC/CRC.13/13, annex, sect. 2.4.2.1).

19. After analysis of the notification of the final regulatory action (UNEP/FAO/RC/CRC.13/13, annex, sect. 2.4.2) and the supporting documentation provided by Brazil (UNEP/FAO/RC/CRC.13/INF/29), the Committee confirms that the regulatory action was taken to protect human health.

20. Therefore the Committee confirms that the criterion in paragraph (a) is met.

(c) Annex II paragraph (b) criteria

(b) Establish that the final regulatory action has been taken as a consequence of a risk evaluation. This evaluation shall be based on a review of scientific data in the context of the conditions prevailing in the Party in question. For this purpose, the documentation provided shall demonstrate that:

- (i) Data have been generated according to scientifically recognized methods;*
- (ii) Data reviews have been performed and documented according to generally recognized scientific principles and procedures;*

21. In January 2012, ANVISA, together with experts from Oswaldo Cruz Foundation (FIOCRUZ), prepared a technical note on the toxicological re-evaluation of the active ingredient phorate (UNEP/FAO/RC/CRC.13/INF/29, p.27), representing an extensive review of relevant data on the hazards and risks associated with phorate using reviewed documents, published reports and literature, including reports from international agencies or institutes, such as the United States EPA and the International Programme on Chemical Safety (IPCS), as well as the studies submitted to the Brazilian Health Surveillance Agency (ANVISA) in the toxicological dossier to support the registration of technical and formulated products. The key studies submitted to ANVISA in the toxicological dossier are related to acute, sub-chronic and chronic toxicity (22 studies), carcinogenicity and genotoxicity (9 studies), endocrine system and reproductive toxicity (2 studies) and embryofetal development (5 studies) (UNEP/FAO/RC/CRC.13/INF/29, p.20).

22. After analysing the notification and supporting documentation, the Committee concludes that the data referred to and provided in those documents have been generated according to scientifically recognized methods and the reviews have been performed and documented according to generally recognized scientific principles and procedures.

23. Consequently, the Committee confirms that the criteria in paragraph (b) (i) and (ii) are met.

(iii) *The final regulatory action was based on a risk evaluation involving prevailing conditions within the Party taking the action;*

24. The notification, in its section 2.4, states that the final regulatory action was based on a risk or hazard evaluation. In accordance with 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 the environment. In order to carry out such a 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 National System of Toxic-Pharmacological Intoxications and Poisonings (SINITOX), Pesticide Residues in Food Analysis Programme or pesticide holder companies.

25. The technical notes in the re-evaluation process assess the potential exposures, the hazard, in accordance with parameters and methodologies adopted internationally, especially by the World Health Organization (WHO); the Food and Agriculture Organization (FAO); Organisation for Economic Co-operation and Development (OECD); the United States EPA 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 the cancellation of the registration, if a criterion of prohibition of registration is fulfilled (UNEP/FAO/RC/CRC.13/INF/29).

26. Brazil's risk evaluation of phorate took into account toxicology and public health; occupational health and safety, environmental impact and availability of lower-risk alternatives (UNEP/FAO/RC/CRC.13/INF/29). An extensive review of relevant data on the hazards and risks associated with phorate using reviewed documents, published reports and literature was undertaken.

27. The re-evaluation took into account, among other things, a comprehensive Brazilian study carried out by Waichman (2008) on the conditions of pesticide use in municipalities of the state of Amazonas (Manaus, Iranduba, Careiro da Várzea and Manacapuru). The 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 was not used because it was expensive, uncomfortable and unsuitable for the hot climate of the region. Lack of training and poor knowledge of the hazards of pesticides were contributing to incorrect handling during the preparation, application and disposal of empty containers. In these conditions the exposure of farmers, their families, consumers and the environment was high. To summarize, comprehensive information is available on the prevailing conditions of use of pesticides in Brazil; and Brazil used this information in its risk evaluation.

28. The Committee noted that in its notification Brazil underlined that the final regulatory action was, among other things, based on the observation of the higher toxicity of phorate to humans than animals, that the substance is an endocrine-disrupting chemical and that it "fulfilled criteria which are prohibitive for registration for pesticide in Brazil."

29. Furthermore, the second paragraph of section III, 1 (b) of "2.5 Working paper on the application of criteria (b) (iii) of Annex II" of the Handbook of Working Procedures and Policy Guidance for the Chemical Review Committee states: "for acutely toxic pesticides or industrial chemicals, the description of the prevailing conditions in the notifying country could include information on the availability and common use of protective equipment or poisoning scenarios (if relevant and available)".

30. Considering that phorate is an acutely toxic pesticide, the results of the study on common practices in the use of pesticides in Brazil which highlighted problems associated with the use of personal protective equipment, as well as the human intoxication incidents in India, the Committee is of the opinion that the prevailing conditions in Brazil were taken into account in the risk evaluation performed by Brazil.

31. Consequently, the Committee confirms that the criterion in paragraph (b) (iii) is met.

32. The Committee confirms that the criteria in paragraph (b) are met.

(d) Annex II paragraph (c) criteria

(c) Consider whether the final regulatory action provides a sufficiently broad basis to merit listing of the chemical in Annex III, by taking into account:

(i) Whether the final regulatory action led, or would be expected to lead, to a significant decrease in the quantity of the chemical used or the number of its uses;

33. On the basis of the data presented in section 2.5.1 of the notification and in supporting documentation (UNEP/FAO/RC/CRC.13/INF/29, p. 22), the production, import and export of phorate has ceased in Brazil, as illustrated by the table below.

34. The final regulatory action taken by Brazil in 2015 would prevent any further production, import, export and use.

	<i>Quantity per year (metric tonnes)</i>	<i>Year</i>
Produced	Formulated product (final product): 153,9 t	2009
Imported	Active ingredient : 17,15 t	2009
Exported	Active ingredient : 35,96 t	2011
Used	Active ingredient sales : 26,49 t	2009
	Formulated product (final product) sales: 272,58 t	2009
	Formulated product (final product) sales: 6,72 t	2010
	Formulated product (final product) sales: 0,01 t	2011
	No production, import, export and sales.	2012, 2013, 2014, 2015

35. Therefore the Committee confirms that the criterion in paragraph (c) (i) is met.

(ii) Whether the final regulatory action led to an actual reduction of risk or would be expected to result in a significant reduction of risk for human health or the environment of the Party that submitted the notification;

36. The final regulatory action bans the production, use, trade, import and export of phorate. Information presented in section 2.5.1 of the notification and in the supporting documentation confirms the decrease of phorate produced and placed on the market in Brazil to zero. Accordingly, the risks to human health resulting from phorate decreased significantly.

37. Therefore the Committee confirms that the criterion in paragraph (c) (ii) is met.

(iii) Whether the considerations that led to the final regulatory action being taken are applicable only in a limited geographical area or in other limited circumstances;

38. Section 2.5.2 of the notification states that similar health and environmental problems are likely to be encountered in other countries where the substance is used.

39. In the supporting documentation (UNEP/FAO/RC/CRC.13/INF/29, p. 22), it is stated that restriction of the use of phorate should be considered by all States because of the high risk associated with all uses and considering all the toxicological effects associated with the active ingredient, especially for “having characteristics more toxic to humans than laboratory animal tests have been able to demonstrate”; the potential for causing endocrine disruption and the absence of antidote or effective treatment in cases of late polyneuropathy.

40. The considerations that led Brazil to ban the production, use, sale, export and import of phorate can be adequate for all States where that active ingredient is still used as a pesticide.

41. Therefore the Committee confirms that the criterion in paragraph (c) (iv) is met.

(iv) Whether there is evidence of ongoing international trade in the chemical;

42. In document UNEP/FAO/RC/CRC.13/INF/5, which contains responses to a request made by the Secretariat in accordance with paragraph (c) (iv) of Annex II to the Convention regarding trade, information from CropLife International confirms the ongoing trade of phorate.

43. Ongoing trade can be also confirmed by the presence of online offers of phorate for sale (<https://www.tradeindia.com/suppliers/phorate.html>).

44. Therefore the Committee confirms that the criterion in paragraph (c) (iv) is met.

(e) Annex II paragraph (d) criterion

(d) Take into account that intentional misuse is not in itself an adequate reason to list a chemical in Annex III.

45. There is no indication in the notification or supporting documentation that concerns over the intentional misuse of phorate prompted the regulatory action.

46. Based on the above point the Committee confirms that the criterion in paragraph (d) is met.

(f) Conclusion

47. Therefore the Committee concludes that the notification of final regulatory action for phorate in the pesticide category submitted by Brazil meets all the criteria set out in Annex II to the Convention. Taking into account the conclusion by the Committee that the notification of final regulatory action for phorate submitted by Canada also met the criteria in Annex II,³ the Committee concludes that the final regulatory actions taken by Brazil and Canada provide a sufficient basis to merit including phorate in Annex III to the Convention in the pesticide category and that a decision guidance document should be drafted on the basis of the notifications.

³ UNEP/FAO/RC/CRC.5/16, annex III, section B.