Re-evaluation Decision RVD2018-37

Ferbam and Its Associated End-use Products

Final Decision

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Re-evaluation Decision

Under the authority of the *Pest Control Products Act,* all registered pesticides must be regularly re-evaluated by Health Canada's Pest Management Regulatory Agency (PMRA) to ensure that they continue to meet current health and environmental safety standards and continue to have value. The re-evaluation considers data and information from pesticide manufacturers, published scientific reports and other regulatory agencies. Health Canada applies internationally accepted risk assessment methods as well as current risk management approaches and policies.

Ferbam is a protectant fungicide registered to control various fungal diseases on: pome and stone fruits, greenhouse vegetables, grapes, berries, tobacco (seed bed), and spruce cones. Currently registered products containing ferbam are listed in Appendix I.

The regulatory approach for the re-evaluation of ferbam was first presented in the Proposed Re-evaluation Decision PRVD2016-05, *Ferbam*.[1] PRVD2016-05 proposed the cancellation of all registered uses and the revocation of all maximum residue limits (MRLs) as health and environmental risks were not found to be acceptable . Health Canada received comments relating to the health and value assessments. These comments are summarized in Appendix II along with the responses by Health Canada. These comments and new data/information resulted in revisions to the risk assessments (see Science Evaluation Update), but did not result in changes to the proposed re-evaluation decision as described in PRVD2016-05. A reference list of data used as the basis for the proposed re-evaluation decision is included in PRVD2016-05, and further data used in the re-evaluation decision are listed in this document.

This document presents the final re-evaluation decision[2] for ferbam, including the cancellation of products containing ferbam to protect human health. All products containing ferbam that are registered in Canada are subject to this re-evaluation decision.

1 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act.*

2 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

Outcome of Science Evaluation

Health risks from ferbam and its associated end use products have not been shown to be acceptable for any use, when used according to current label directions, or when additional mitigation measures are considered. From an environmental perspective, the risks from ferbam and its associated end-use products are acceptable when used according to revised label directions. Health Canada recognises the value of ferbam to agricultural users, including the need to manage specific diseases and for resistance management in orchard fruit, grape and berry production

Regulatory Decision for Ferbam

Health Canada has completed the re-evaluation of ferbam. Under the authority of the *Pest Control Products Act*, Health Canada is cancelling the registration of products containing ferbam for sale and use in Canada. An evaluation of available scientific information found that all uses of ferbam products have not been shown to have acceptable health risks when used according to the current label directions, or when additional mitigation measures are considered. No additional data are required.

All ferbam MRLs will be revoked as all currently registered food uses are cancelled. Consultation on the revocation of all ferbam MRLs will be conducted via a Proposed Maximum Residue Limit (PMRL) document.

Next Steps

To comply with this decision, all ferbam products are to be phased out following the implementation timeline outlined below. Appendix I lists the products containing ferbam that are registered under the authority of the *Pest Control Products Act*.

- One (1) year of sale by registrant from the publication date of this decision document, followed by;
- One (1) year of sale by retailer from the last date of sale by registrant, followed by;
- One (1) year of permitted use from the last date of sale by retailer.

Other Information

Any person may file a notice of objection[3] regarding this decision on ferbam within 60 days from the date of publication of this Re-evaluation Decision. For more information regarding the basis for objecting (which must be based on scientific grounds), please refer to the Pesticides section of Canada.ca or contact the PMRA's Pest Management Information Service.

[3] As per subsection 35(1) of the *Pest Control Products Act*

Science Evaluation Update

1.0 Impact on Human and Animal Health

1.1 Toxicology Assessment for Ferbam

As indicated in PRVD2016-05, the toxicology database for ferbam is incomplete. Based on similarities in the chemical structure, toxicity and metabolism of ferbam and thiram, the thiram toxicology database was bridged to ferbam. Thus, toxicology reference values established for thiram were utilized for the risk assessment of ferbam. In response to the publication of PRVD2016-05, the same comments were submitted by the registrants for thiram and ferbam. Thus, Health Canada responses to the submitted comments for thiram also apply to ferbam. No new toxicology data specific to ferbam were provided. Please refer to the thiram re-evaluation decision document for detailed responses. Revised reference values are provided in Appendix III.

1.2 Dietary Exposure and Risk Assessment

In PRVD2016-05, Health Canada had proposed the cancellation of all food uses and the revocation of all Canadian maximum residue limits (MRLs) as dietary risks were not found to be acceptable. The registrant did not submit specific comments for ferbam, but cited comments on PRVD2016-07, *Thiram*. Thus, Health Canada responses to the submitted comments for thiram also apply to ferbam. No new studies were received during the public consultation period.

When all uses were included in the revised dietary assessment, acute and chronic risks were not shown to be acceptable. Despite the refinements considered, including assessing each use separately, and the high level of mitigation applied in the revised dietary assessment, risks from drinking water alone were not shown to be acceptable, except for certain greenhouse vegetables. Details on this revised assessment are provided in Appendix IV.

1.2.1 Maximum Residue Limits for Ferbam on food

Currently, Canadian MRLs for ferbam are specified for a number of commodities on the basis of a residue definition expressed as (*OC*-6-11)-tris(dimethylcarbamodithioato-κS,κS′)iron (calculated as zineb). All ferbam MRLs will be revoked as all currently registered food uses are cancelled. Consultation on the revocation of all ferbam MRLs will be conducted via a Proposed Maximum Residue Limit (PMRL) document.

1.3 Occupational and Residential Exposure and Risk Assessment

The occupational and non-occupational assessments for ferbam were previously conducted and published in PRVD2016-05.

In PRVD2016-05, Health Canada had proposed cancellation of all uses of ferbam. Risks were not shown to be acceptable for workers handling ferbam products during mixing/loading and application, as well as when entering treated sites following application. Risks were also not

shown to be acceptable for non-occupational exposure following application of ferbam to fruit trees in residential settings.

During the PRVD consultation period, comments regarding occupational exposure were received. Health Canada responses to specific comments are in Appendix II. As discussed in Appendix IV, dietary risks were not shown to be acceptable for all food uses of ferbam, except certain greenhouse vegetables. As these uses are cancelled, the occupational risk assessments for these uses were not revisited. Therefore, the use considered in the present occupational risk assessment was greenhouse vegetables.

The information submitted during the PRVD consultation period was insufficient to refine the use pattern (such as application rate, area treated per day) assessed for greenhouse vegetables. No chemical-specific studies were submitted or were available in the public literature. Dermal absorption and exposure inputs (such as peak dislodgeable foliar residues, and transfer coefficients) cannot be further refined in the absence of additional data. Therefore, the occupational non-cancer risk assessments could not be refined from what were reported in PRVD2016-05, as the non-cancer toxicological reference values, use pattern, and exposure inputs remained the same. Risks were not shown to be acceptable, for greenhouse vegetables after a single application. These risks could not be addressed with further mitigation, therefore; use on these crops is cancelled.

The risks of concern identified in PRVD2016-05 remain for greenhouse tobacco seedlings and spruce cones, as the occupational non-cancer risk assessments could not be refined in the absence of additional data, as discussed above. These risks could not be addressed with further mitigation; therefore, use on these crops is cancelled.

1.4 Cumulative Risk Assessment

Ferbam is a member of the dithiocarbamate class of pesticides along with thiram and ziram. Ferbam and ziram also degrade to thiram. Since all agricultural uses of ferbam and ziram (RVD2018-39) will be cancelled, there is no requirement for a cumulative assessment of the agricultural uses of thiram, ziram and ferbam.

2.0 Revised Environmental Risk Assessment

The environmental risk assessment in PRVD2016-05 considered the registered use pattern at the time as well as mitigation in the form of spray buffer zones and label statements highlighting the risk of runoff. At that time, it was determined that risks to birds and aquatic organisms could not be fully mitigated. However, the risk assessments conducted for the PRVD have since been re-examined by Health Canada. During the public consultation period, no comments were received regarding the environmental assessment conducted for ferbam. As ferbam degrades rapidly in the environment to thiram, a study received during consultation demonstrating that birds are repelled from thiram treated seed was used as evidence that birds would likely also be repelled from potential food treated with ferbam.

2.1 Fate and Behaviour in the Environment

Revised drinking water estimated environmental concentrations (EECs) were modelled (Level 2) for dormant spray application on peaches based on the updated residue definition of ferbam plus *N*,*N* dimethyl carbamosulfonic acid (DMCS). These Level 2 scenarios are refined to the extent possible given current information.

2.2 Environmental Risk Characterization

Revisions to the risk quotients were not required and therefore did not change the overall environmental risk profile.

2.2.1 Risks to Terrestrial Organisms

Ferbam quickly transforms in the environment to thiram, which is expected to repel birds and mammals. A label statement indicating that ferbam is toxic to birds and mammals will remain on the label as this statement is required to indicate the inherent toxicity to these organisms.

2.2.2 Risks to Aquatic Organisms

With respect to risk to aquatic organisms, risk assessments conducted for the PRVD were re-examined. The risks associated with spray drift into aquatic habitats at the time of application could be mitigated with spray buffer zones. Risks associated with runoff from agricultural fields were based on conservative modelled EECs (Level 1) and no monitoring information is available for ferbam. Although the level of concern is exceeded slightly for certain aquatic organisms based on the modelled EECs at the highest registered application rate, most Risk Quotients (RQ) were less than 5 with the exception of amphibians (RQ = 5). Due to the conservative modelling scenarios, risks are not expected to have an impact at the population level for aquatic organisms under conditions of use.

3.0 Incident Reports

Since the publication of the PRVD2016-05, no additional human, domestic animal, or environmental incidents involving ferbam were submitted to Health Canada. Also, since the publication of PRVD2016-05, no additional human or domestic animal incident data were available in the USEPA regulations.gov website and the California EPA Pesticide Illness database. No environmental incidents involving ferbam were located in the USEPA's Ecological Incident Information System (EIIS) database.

4.0 Value Assessment

Health Canada recognizes the value of ferbam to agricultural users, including the need to manage specific diseases and for resistance management in orchard fruit, grape and berry production.

5.0 Conclusion of Science Evaluation

Health risks from ferbam and its associated end use products have not been shown to be acceptable for any use, when used according to current label directions, or when additional mitigation measures are considered. From an environmental perspective, the risks from ferbam and its associated end-use products are acceptable when used according to revised label directions. Use of ferbam is important for control of fungal diseases and resistance management on many crops.

List of Abbreviations

ADI	Acceptable daily intake
ARfD	Acute reference dose
bw	bodyweight
CAF	composite assessment factor
CD	caesarean-derived
CFIA	Canadian Food Inspection Agency
DEEM	Dietary Exposure Evaluation Model
DMCS	N, N dimethyl carbamosulfonic acid
EBDC	Ethylene bis(dithiocarbamate) pesticides (mancozeb, metiram)
EEC	Estimated environmental concentration
EFSA	European Food Safety Authority
FCID	Food Commodity Intake Database
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
kg	Kilogram
mg	Milligram
MOE	Margin of exposure
MRL	Maximum residue limit
NHANES	National Health and Nutrition Examination Survey
NOAEL	No observed adverse effect level
OPP	Office of Pesticide Programs (USEPA)
PCPA	*Pest Control Product Act*
PMRA	Pest Management Regulatory Agency
PMRL	Proposed maximum residue limit
PRVD	Proposed re-evaluation decision
RED	Reregistration eligibility decision
RQ	Risk Quotient
RVD	Re-evaluation decision
USEPA	United States Environmental Protection Agency
WWEIA	What We Eat in America

Appendix I Registered Ferbam Products in Canada[1]

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee
20144	Technical	Taminco US LLC	Ferbam Technical	Dust or Powder	87.5%
20136	Commercial	Loveland Products Canada Inc.	Ferbam 76WDG Fungicide	Dry Flowable	76%
20536	Commercial	Taminco US LLC	Ferbam 76WDG Agricultural Fungicide	Wettable Granules	76%

[1] as of 17 May 2018, excluding discontinued products

Appendix II Comments and Responses

Following publication of the Proposed Re-evaluation Decision PRVD2016-05, *Ferbam*, Health Canada received written comments from the registrant, the public and other stakeholders such as Canadian Horticultural Council. The comments and Health Canada responses were summarized or grouped together based on common scientific themes and presented below.

1.0 Comment(s) Related to the Health Risk Assessment

1.1 Comments and Responses Related to Toxicology

Comments related to the toxicology assessment were received from the registrants.

1.1.1 Comment

The registrant referenced the comments provided for PRVD2016-07 on thiram as being applicable to ferbam.

Response

Since no new data specific to ferbam were provided during the consultation period, Health Canada responses to submitted comments are the same for thiram and ferbam. For further details, refer to the thiram RVD.

1.2 Comments and Responses Related to Dietary Exposure

The registrant did not provide specific comments on the dietary risk assessment for ferbam presented in PRVD2016-05, but cited their comments on the dietary risk assessment for thiram presented in PRVD2016-07. Thus, Health Canada responses to the submitted comments for thiram also apply to ferbam. However, certain comments specific to ferbam are provided below. Please refer to the thiram RVD for other comments and responses.

1.2.1 Comment Concerning the Dietary Exposure and Risk Assessments

a) Acute Dietary Exposure Estimation

The registrant did not propose detailed refinements for the dietary exposure assessment for ferbam, but stated that the dietary assessment they had conducted for thiram would be applicable for ferbam. It was noted that the registrant's assessment for thiram exceeded the acute reference dose for thiram.

Response:

Health Canada's 2016 assessment used Canadian maximum residue limits (MRLs) of ferbam and field trial data of ziram and/or thiram as residue inputs for the exposure estimation. Therefore, further refinements were considered in the revised dietary assessment for food and drinking water. However, acute and chronic dietary risks were not shown to be acceptable. See Appendix IV for further information on the dietary assessment.

1.3 Comments and Responses Related to Occupational Exposure

1.3.1 Dermal Absorption

The registrant suggested that the submitted dermal absorption data for thiram be considered to refine the dermal absorption value for ferbam.

Response:

For PRVD2016-05, no dermal absorption data for ferbam were available; therefore, a dermal absorption value of 50% was established based on the physical/chemical properties of the active ingredient (solubility, physical state, molecular size).

No chemical-specific data for ferbam were submitted to Health Canada during the PRVD consultation period or were available in the public literature. Data for thiram were submitted to Health Canada; however, as minor changes to chemical structures and differences in product formulation can have an impact on dermal absorption, the thiram dermal absorption data was not considered appropriate to refine the current dermal absorption value for ferbam. Therefore, the dermal absorption value of 50% was maintained for ferbam.

1.3.2 Use Pattern Information

During the PRVD2016-05 consultation period, the registrant and the Canadian Horticulture Council provided information on the foliar use pattern of ferbam for a number of crops (such as, application rates, timing of application, post-application activities).

Response:

Use pattern information is important in the refinement of occupational risk assessments. The information provided during the PRVD consultation period for greenhouse vegetables was limited and was insufficient to refine the occupational risk assessment for greenhouse crops.

2.0 Comments Relating to the Value Assessment

Comments related to value were received from: the Ontario Highbush Growers Association, Ontario Ministry of Agriculture, Food and Rural Affairs; Loveland Products Canada Inc., and The Canadian Horticultural Council.

2.1 Comment: Ferbam is Important for Resistance Management

Ferbam is an inexpensive, broad-spectrum fungicide that is extremely important for resistance management as a rotational fungicide. The multi-site mode of action of ferbam is important for the control of pathogen populations of certain fungal diseases that may develop resistance to single-site mode of action fungicides.

Response

Health Canada agrees that ferbam is important for disease resistance management. There are a number of other active ingredients, including some multi-site fungicides, registered for most of

the crop-disease combinations that were identified by stakeholders as important uses. As part of their resistance management programs, growers have the option to rotate these alternatives with fungicides from different mode of action groups.

2.2 Comment: Ferbam is Important for the Management of Fungal Diseases on Fruit and Vegetable Crops

Ferbam is important for the management of leaf curl on peaches and nectarines, spur blight on caneberries; botrytis fruit rot, shoot blight and blossom blight on blueberries; botrytis gray mold on greenhouse vegetables, brown rot in apricots, cherries and plums; and scab, rust, bitter rot, black rot, Brook's spot, calyx-end rot, fly speck, frogeye leaf spot and sooty blotch on apples.

Response

Health Canada acknowledges the importance of ferbam for disease management on a number of fruit and greenhouse vegetable crops. However, a number of other active ingredients including some multi-site fungicides such as copper, sulphur (lime sulphur or calcium polysulphide), chlorothalonil, captan, folpet and two co-formulated products containing famoxadone and cyprodinil, and boscalid and pyraclostrobin, are registered to manage the diseases listed on the identified fruits and vegetable crops.

Appendix III Revised Toxicology Reference Values for Ferbam Health Risk Assessment

Exposure Scenario	Point of Departure and Endpoint	Study	CAF or MOE[1]
ARfD (all populations)	NOAEL =1.86 mg/kg bw/day Effects on motor activity & learning (Altered motor activity, decreased motor activity habituation, increased time to complete the Morris Maze)	Developmental neurotoxicity study in rats	1000
	ARfD = 0.002 mg/kg bw		
Chronic Dietary (all population)	NOAEL =1.86 mg/kg bw/day Reduced body weight, effects on motor activity & learning (Altered motor activity, decreased motor activity habituation, increased time to complete the Morris Maze)	Developmental neurotoxicity study in rats	1000
	ADI = 0.002 mg/kg bw/day		
Residential and Occupational (all routes and durations)	NOAEL =1.86 mg/kg bw/day Reduced body weight, effects on motor activity & learning (Altered motor activity, decreased motor activity habituation, increased time to complete the Morris Maze)	Developmental neurotoxicity study in rats	1000
Cancer	Threshold approach for liver and thyroid C-cell tumours in rats		

[1] CAF (composite assessment factor) refers to a total of uncertainty and Pest Control Products Actfactors for dietary assessments; MOE refers to a target MOE for occupational assessments

Appendix IV Revised Dietary Exposure and Risk Estimates

The dietary exposure and health risk assessment was revised as follows:

1) The new toxicological information resulted in the removal of the cancer potency factor (q_1*) for thiram (and also applied to ferbam). It should be noted, however, that ARfD and ADI did not change.
2) In addition to an assessment that included all currently registered food uses, each food use was also assessed separately.
3) Monitoring data from the Canadian Food Inspection Agency (CFIA) were used to refine the dietary exposure and risk assessment.
4) For both the acute and chronic assessments, updated percent crop treated estimates and percent domestic/import food supply information were used to adjust the available residue data.
5) Refined drinking water estimated environmental concentrations (EECs) were used in the risk assessment.
6) The acute and chronic dietary assessments for ferbam were conducted using the latest version of the Dietary Exposure Evaluation Model – Food Commodity Intake Database™ (DEEM-FCID™; Version 4.02, 05-10-c) program, which incorporates food consumption data from the National Health and Nutrition Examination Survey/What We Eat in America (NHANES/WWEIA) dietary survey for the years 2005-2010 available through Centers for Disease Control and Prevention's National Center for Health Statistics.

When all uses were included in the dietary assessment, acute and chronic dietary risks were not shown to be acceptable. Therefore, each use was assessed separately in the dietary assessment.

- Risks were not shown to be acceptable from exposure through residues in drinking water alone resulting from application of ferbam to pome and stone fruits, grapes and berries.
- For greenhouse uses, when only cucumber and lettuce were included in the dietary assessment, risks were shown to be acceptable. However, occupational risks were not shown to be acceptable (see details in Science Evaluation Update Section 1.3 *Occupational and Residential Exposure and Risk Assessment*).

Despite the refinements considered and the high level of mitigation applied in the revised dietary assessment, risks were not shown to be acceptable. Therefore, cancellation of all registered food uses and revocation of all MRLs for ferbam are required.

References

A. Information Considered for the Toxicological Risk Assessment

List Studies/Information Submitted by Registrant

PMRA Document Number	Reference
2646693	2016, Registrant comments for the consultation on ferbam, proposed re-evaluation decision, PRVD2016-05
For a list of other studies/information used, refer to thiram RVD.	

B. Information Considered in the Dietary Assessment

Studies/Information Submitted by Registrant

PMRA Document Number	Reference
1173817	Ferbam: Nature Of The Residue In Livestock-Lactating Goats. Final Report. (Hla6231-102).
2646650	Registrant Comments for the Consultation on Thiram, Proposed Re-Evaluation Decision PRVD2016-07.
2646693	Registrant Comments for the Consultation on Ferbam, Proposed Re-Evaluation Decision PRVD2016-05.

Additional Information Considered

Published Information

PMRA Document Number	Reference
2906734	CFIA. 2014. National Chemical Residue Monitoring Program 2012-2013 Report.
2907047	European Commission. 1995. Commission Decision of 13 July 1995 concerning the withdrawal of authorizations for plant protection products containing ferbam or azinphos-ethyl as active substances (95/276/EC). http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:31995D0276&from=EN
2906735	EFSA. 2015. Draft Renewal Assessment Report Prepared According to Regulation (EC) NO 1107/2009: Thiram.
2907051	Hunter, L.W.M. and Gilbert, B.N. 1976. Metabolism and Residues of ^{3}H- and ^{35}S-Labeled Ferbam in Sheep. Journal and Agricultural Food Chemistry. 24 (3): 670 – 672.
2907052	JMPR. 1996. Ferbam (FER 4.14_105 T R).
2907053	USEPA. 2005a. Reregistration Eligibility Decision (RED) Document for Ferbam.
2907054	USEPA. 2005b. Revised Ferbam Residue Chemistry Considerations for Reregistration Eligibility Decision. Dated 03/03/05. EPA-HQ-OPP-2004-0337-0007.
2907055	USEPA. 2005c. EPA Memorandum: Default Processing Factors For Commodities Which Appear in DEEM. August 4, 2005. (DEEM 7)

PMRA Document Number	Reference
2906743	USEPA. 2016. Ferbam and Thiram Final Work Plan. EPA-HQ-OPP-2015-0567-0011.