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Re-evaluation Decision

RVD2018-38

Thiram and Its Associated End-use Products

Final Decision

(publié aussi en français)

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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.

Thiram is a contact fungicide registered for use as seed treatment (cereals, oilseeds, vegetables and feed/forage), foliar application on tree fruits (apple, peach and plum), strawberry and celery (plant beds), root dip of sweet potato sprouts, and as an animal repellent to protect dormant outdoor ornamentals and young fruit trees. Currently registered products containing thiram are listed in Appendix I.

The regulatory approach for the re-evaluation of thiram was first presented in the Proposed Re-evaluation Decision PRVD2016-07, *Thiram*.¹ PRVD2016-07 proposed the cancellation of all registered uses and the revocation of all MRLs as health and environmental risks were not found to be acceptable. Health Canada received comments relating to the health, environmental 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), and subsequently, in changes to the proposed regulatory decision as described in PRVD2016-07. A reference list of data used as the basis for the proposed re-evaluation decision is included in PRVD2016-07, and further data used in the re-evaluation decision is listed in this document.

This document presents the final re-evaluation decision² for thiram, including the required risk mitigation measures to protect human health and the environment. All products containing thiram that are registered in Canada are subject to this re-evaluation decision.

Outcome of Science Evaluation

Following the consultation on the proposed re-evaluation decision, Health Canada revised the dietary, occupational and environmental risk assessments based on new data/information received. As a result, registration of animal repellent uses and seed treatment uses, except for seed treatment of grasses, dry bulb onion, and alfalfa grown for forage, are acceptable for continued registration with the implementation of new mitigation measures and label amendments. Mitigation includes cancellation of commercial seed treatment of some seed types; however, on-farm treatment of these seeds is permitted. Health risks have not been shown to be acceptable for all other uses when these products are used according to current label directions, or when additional mitigation measures are considered. The environmental risks associated with the use of thiram and associated end-use products are acceptable when thiram products are used according to the revised label directions.

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*.

Regulatory Decision for Thiram

Health Canada has completed the re-evaluation of thiram. Under the authority of the *Pest Control Products Act*, Health Canada has determined that continued registration of some uses of thiram is acceptable. An evaluation of available scientific information found that these uses of thiram meet current standards for protection of human health and the environment when used according to the revised label directions, which include new mitigation measures: animal repellent uses and seed treatment uses, except for the seed treatment of grasses, dry bulb onion, and alfalfa grown for forage. The following uses of thiram are cancelled since health risks have not been found to be acceptable: all foliar uses on apple, peach, plum, strawberry, celery; sweet potato (sprout root dip); and seed treatment in Canada of grasses, dry bulb onion, and alfalfa grown for forage, as well as importation of these treated seeds into Canada. Label amendments, as summarized below and listed in Appendix III, are required. No additional data are required.

Risk Mitigation Measures

Registered pesticide product labels include specific directions for use. Directions include risk mitigation measures to protect human health and the environment and must be followed by law. The key risk-reduction measures required, as a result of the re-evaluation of thiram, are summarized below. Refer to Appendix III for details.

Human Health

- The following uses are acceptable with the implementation of mitigation measures:
 - Commercial-class ornamental animal repellent: Add Personal Protective Equipment (PPE) and limit the amount handled when applying by paint brush.
 - Domestic-class ornamental animal repellent: Remove paintbrush application.
 - Seeds treated in Canada and imported into Canada (except those that are cancelled and listed below) including on-farm treatment of wheat, barley, oats, canola, mustard, rapeseed, rye, triticale, and corn: add increased PPE and engineering controls.
- Cancellation of the following uses:
 - All foliar uses (apple, peach, plum, strawberry, celery)
 - Sweet potato (sprout root dip)
 - Seed treatment in Canada of grasses, dry bulb onion, and alfalfa grown for forage, and importation of these treated seeds into Canada
 - Commercial seed treatment of wheat, barley, oats, canola, mustard, rapeseed, rye, triticale, and corn
 - On-farm liquid hopperbox/seed drill treatment for all crops.
- Revocation of all MRLs of thiram, including those established for imports. Consultation on the revocation of all thiram MRLs will be conducted via a Proposed Maximum Residue Limit (PMRL) document.

Environment

- Precautionary label statements to protect birds and mammals from treated seeds.

Next Steps

To comply with this decision, the required mitigation measures must be implemented on all product labels sold by registrants no later than 24 months after the publication date of this decision document. In addition, products that are cancelled will be phased-out following the implementation timeline outlined below.

- 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 objection³ regarding this decision on thiram 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 Thiram

Comments received during the consultation period covered a range of issues pertaining to the toxicology assessment including the choice of cancer risk assessment method for thyroid c-cell and liver tumours, the choice of studies supporting dietary reference values, and the magnitude of applied uncertainty factors. New data submitted for thiram included genotoxicity studies, historical control data for the noted tumours, and a supplemental developmental neurotoxicity (DNT) study. In addition, the most recent United States Environmental Protection Agency (USEPA) assessments and scientific rationales addressing the issues noted above were provided. Based on this information, the toxicology reference values outlined in PRVD2016-07, and the cancer risk assessment approach were updated.

Detailed responses to the comments received, including details for the basis of the reference value revisions, are provided in Appendix II. Revised reference values are provided in Appendix IV.

1.2 Dietary Exposure and Risk Assessment

In PRVD2016-07, Health Canada had proposed the cancellation of all food and feed uses and the revocation of all Canadian maximum residue limits (MRLs), as dietary risks were not found to be acceptable. Comments were received primarily from the registrants of thiram. Health Canada responses to these and other stakeholder comments are summarized in Appendix II. No new studies were received during the public consultation period.

The dietary risk conclusions from PRVD2016-07, which considered the currently registered use pattern, have not changed, as the acute reference dose (ARfD) and the acceptable daily intake (ADI) remain the same (see Appendix IV), and no new studies were submitted to address dietary risks. Since risks from drinking water alone were identified in PRVD2016-07, refinement of the drinking water exposures for all the scenarios, except the animal repellent use, was considered. Only seed treatment uses resulted in acceptable risk from drinking water exposure, provided that the high application rate for dry bulb onion treatment is removed. Therefore, the dietary assessment considered food exposure and drinking water exposure from seed treatment uses only (excluding dry bulb onion), which resulted in acceptable dietary risk. The animal repellent use is not expected to result in drinking water exposure and therefore was not included in the dietary assessment.

The revised dietary exposure and risk assessment showed that acute and chronic risks from exposure to thiram through food and drinking water are acceptable when only seed treatment uses (excluding dry bulb onion) were considered. The chronic dietary exposure is approximately 38% of the ADI and the acute dietary exposure is approximately 90% of the ARfD. Drinking water contribution accounted for approximately 80% of the total exposure for the most exposed subpopulation (infants). Details on this revised assessment are provided in Appendix V.

1.2.1 Maximum Residue Limits for Thiram on Food

Currently, Canadian MRLs for thiram are specified for a number of commodities on the basis of a residue definition expressed as tetramethylthioperoxydicarbonic diamide. Potential residues on/in other crops with registered uses, including seed treatment uses, are regulated under subsection B.15.002(1) of the Food and Drug Regulations.

The present risk assessment of thiram indicated that the dietary risks associated with the registered seed treatment uses (excluding dry bulb onion) are acceptable with implementation of the required mitigation measures. Potential residues from these seed treatment uses will continue to be regulated under subsection B.15.002(1) of the Food and Drug Regulations, which requires that residues not exceed 0.1 ppm. For all other food uses, human health risks were not shown to be acceptable. Therefore, revocation of all maximum residue limits (MRLs) for thiram is required. Consultation on the revocation of all thiram MRLs will be conducted via a Proposed Maximum Residue Limit (PMRL) document.

1.3 Occupational and Residential Exposure and Risk Assessment

In PRVD2016-07, Health Canada had proposed cancellation of all uses of thiram, as risks were not shown to be acceptable for the assessed human health scenarios. Risks were not shown to be acceptable for workers handling thiram products during mixing/loading and application, as well as from planting treated seeds and entering treated sites following application. Risks were not shown to be acceptable for handlers of the domestic-class product as well as for individuals coming into contact with treated fruit trees in residential settings.

During the PRVD consultation period, additional information and studies were received from the registrants and other stakeholders. This included dermal absorption, dislodgeable foliar residue, and worker exposure studies, as well as use pattern information. Available Agricultural Handler Exposure Task Force (AHETF) seed treatment data were also used. These data and information were incorporated into the revised assessment and used to refine the risk assessment, to the extent possible. Health Canada's responses to specific comments are in Appendix II.

As discussed in Section 1.2, dietary risks were not shown to be acceptable for food uses of thiram, except for seed treatment uses (excluding dry bulb onion), and thus, these food uses are cancelled. Therefore, the occupational risk assessments for these cancelled uses were not revisited. The uses that were considered in the present occupational and residential risk assessment were the remaining seed treatment and ornamental animal repellent uses. Details and tables regarding the revised occupational and residential risk assessment are presented in Appendix VI.

As a result of the comments and additional data and information submitted, the outcome of the occupational and residential risk assessment proposed in PRVD2016-07 has changed for a number of scenarios.

For some currently registered seed treatment uses, risks have been shown to be acceptable for commercial and/or on-farm treatment and planting in Canada, as well as for planting imported treated seeds. Seed treatment of grasses, dry bulb onion, and alfalfa grown for forage in Canada, including importation of these seeds into Canada, cannot be supported and are cancelled.

Risks have been shown to be acceptable for the following product type/application methods and crops, provided the mitigation measures outlined in Appendix III are implemented:

- Commercial seed treatment using Vitaflo commercial-class products on soybean, pea, bean, flax, and lentil.
- Commercial seed treatment using other commercial-class products on soybean.
- On-farm slurry seed treatment using liquid products on wheat, barley, oat, canola, mustard, rye, triticale, corn, flax, soybean, bean, pea, and lentil.
- On-farm slurry seed treatment using the wettable powder product on corn, safflower, onion, alfalfa (grown for seed production), and vegetable/fruit seeds.
- On-farm slurry seed treatment using the dust product on onion.
- Planting of commercially treated or imported corn (including sweet corn), beans, canola, rapeseed, mustard, soybeans, peas, lentils, flax, and vegetable/fruit seeds.
- Ornamental animal repellent commercial and domestic-class products.

Risks have not been shown to be acceptable for the following product type/application methods and crops; therefore, the following uses are cancelled:

- Commercial seed treatment of wheat, barley, oat, rye, triticale, corn, canola, rapeseed, and mustard.
- On-farm dry application treatment for all crops. These products can be applied as slurry treatment, as supported by the registrants.
- On-farm seed treatment using the wettable powder product for mustard, soybean, bean, pea, alfalfa grown for forage, grasses, and dry bulb onion.
- On-farm liquid hopperbox/seed drill treatment for all crops (soybean, lentil, pea).

1.4 Cumulative Risk Assessment

Thiram is a member of the dithiocarbamate class of pesticides along with ferbam and ziram. Ferbam and ziram also degrade to thiram. Since all agricultural uses of ferbam (RVD2018-37) and ziram (RVD2018-39) are cancelled, there is no requirement for a cumulative assessment of the agricultural uses of thiram, ziram and ferbam.

A cumulative risk assessment for thiram from seed treatment uses and thiram resulting from the material preservative use of ziram, which degrades to thiram, may be required upon completion of the risk assessment for the preservative use of ziram (to be conducted separately as per REV2018-02, Approach for the Re-Evaluation of Pesticides Used as Preservatives in Paints, Coatings and Related Uses).

2.0 Revised Environmental Risk Assessment

The environmental risk assessment in PRVD2016-07 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. The environmental risk assessment has been updated to reflect the revised use pattern and to include additional information and comments received during the consultation period. Detailed responses to the comments received are provided in Appendix II.

2.1 Fate and Behaviour in the Environment

Revised drinking water estimated environmental concentrations (EECs) were modelled (Level 2) for seed treatments on peas and beans, onions, spring and winter wheat, barley and triticale based on the updated residue definition of thiram 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 required as the maximum application rates decreased. The revised risk quotients did not change the overall environmental risk profile or related mitigation measures.

2.2.1 Risks to Terrestrial Organisms

A re-examination of the risks to birds and mammals from consumption of thiram-treated seed was conducted following submission of a new study by the registrant. These data demonstrated that birds are repelled by thiram-treated seeds. In addition, there are no relevant incident reports, and labels require that all treated seed be covered with soil after planting, which further reduces the potential for consumption of treated seed by birds and mammals. Although risks to birds and mammals are expected to be low, a label statement indicating that thiram is toxic to birds and mammals will remain on the label, as this statement is required to indicate 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. It was determined that 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 thiram. Since foliar applications of thiram are cancelled due to human health risks and the uses that remain are for seed treatments, the risk of spray drift into aquatic habitats no longer remains.

3.0 Incident Reports

Since the publication of the PRVD2016-07, no additional human, domestic animal, or environmental incidents involving thiram were submitted to Health Canada. Also, since the publication of PRVD2016-07, no additional human or animal incident data were available in the USEPA regulations.gov website and the California Environmental Protection Agency Pesticide Illness database.

4.0 Value Assessment

Health Canada recognizes the value of thiram to agricultural users, especially its use as a seed treatment for managing seed-borne fungal diseases on cereal, pulse, oilseed, grass, vegetable and forage crops, and for the importation of thiram-treated seeds.

5.0 Conclusion of Science Evaluation

Health risks associated with ornamental animal repellent uses and seed treatment uses (except for seed treatment of grasses, dry bulb onion, and alfalfa grown for forage), of thiram products have been found to be acceptable when used according to the revised label directions, which includes new mitigation measures. However, health risks have not been shown to be acceptable for all other uses when these products are used according to current label directions, or when additional mitigation measures are considered. The environmental risks associated with the use of thiram and associated end-use products are acceptable when used according to revised label directions. Use of thiram as a seed treatment is important for control of seed-borne fungal diseases on many crops.

List of Abbreviations

ADI	Acceptable daily intake
AHETF	Available Agricultural Handler Exposure Task Force
ARfD	Acute reference dose
bw	bodyweight
CBI	Confidential business information
CFIA	Canadian Food Inspection Agency
CAF	Composite assessment factor
CD	Caesarean-derived
DEEM	Dietary Exposure Evaluation Model
DACO	Data code
DMCS	N, N dimethyl carbamosulfonic acid
DNT	Developmental neurotoxicity
EBDC	Ethylene bis(dithiocarbamate) pesticides (mancozeb, metiram)
EFSA	European Food Safety Authority
EEC	Estimated environmental concentration
FCID	Food Commodity Intake Database
FQPA	Food quality protection act
HPRT	Hypoxanthine-guanine phosphoribosyltransferase
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
kg	Kilogram
LOAEL	Lowest observed adverse effect level
mg	Milligram
MOE	Margin of exposure
MRL	Maximum residue limit
MRID	Master record identification
NHANES	National Health and Nutrition Examination Survey
NOAEL	No observed adverse effect level
OECD	The Organisation for economic co-operation and development
OPP	Office of Pesticide Programs (USEPA)
OPPTS	The Office of Prevention, Pesticides and Toxic Substances (USEPA)
PCPA	<i>Pest Control Product Act</i>
PHED	Pesticide Handlers Exposure Database
PMRL	Proposed maximum residue limit
PPE	Personal protective equipment
PRVD	Proposed re-evaluation decision
RBC	Red blood cells
REACH	Registration, evaluation, authorisation, and restriction of chemicals
RED	Reregistration eligibility decision
RVD	Re-evaluation decision
UDS	Unscheduled DNA synthesis
USEPA	United States Environmental Protection Agency
WOE	Weight of evidence
WWEIA	What We Eat in America

Appendix I Registered Thiram Products in Canada¹

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee
18422	Technical	Taminco US LLC	Thiram Technical	Dust or Powder	98.0%
18595	Technical	Arysta LifeScience Canada Inc.	Thiram Tech	Dust or Powder	98.0%
18497	Manufacturing Concentrate	Taminco US LLC	Thiram 80.0% Wettable Powder Concentrate	Wettable Powder	80.0%
7715	Domestic	Premier Tech Ltd.	Skoot Repellent For Rabbits, Mice and Deer	Suspension	THI -120 g/L
10959	Commercial	Arysta LifeScience Canada Inc.	Pro-Gro Systemic Dust Seed Protectant	Dust or Powder	VIT – 30.0%; THI -50%
11423	Commercial	Arysta LifeScience Canada Inc.	Vitaflo-280 Fungicide	Suspension	VIT-15.59%; THI-13.25%
13258	Commercial	Plant Products Inc.	Skoot Repellent For Rabbits, Mice and Deer	Suspension	THI-120 g/L
18788	Commercial	Arysta LifeScience Canada Inc.	Anchor Planter Box	Suspension	VIT-66.7 g/L; THI-66.7 g/L
27174	Commercial	Bayer CropScience Inc.	Gaucha CS FL (Insecticide/Fungicide Seed Treatment)	Suspension	VIT-47.6 g/L; THI-95.3 g/L; IMI-285.7 g/L
27555	Commercial	Arysta LifeScience Canada Inc.	Vitavax 200 Flowable Fungicide	Suspension	VIT-195 g/L; THI-195 g/L
27556	Commercial	Arysta LifeScience Canada Inc.	Thiram 75WP Wettable Powder Fungicide	Wettable powder	THI-75%
27564	Commercial	Bayer CropScience Inc.	Prosper FL Flowable Insecticide and Fungicide Seed Treatment	Suspension	VIT-56 g/L; THI-120 g/L; MTA-4 g/L; COD-120 g/L
27566	Commercial	Bayer CropScience Inc.	Raxil T Flowable Fungicide	Suspension	THI-222 g/L; TEU-6.7 g/L
28220	Commercial	Taminco US LLC	Taminco Thiram 75 WP Wettable Powder Fungicide	Wettable Powder	THI-75%
28525	Commercial	Nippon Soda Co., Ltd.	Nisso Foundation Lite	Suspension	THI-88 g/L; IPD-132 g/L
30380	Commercial	Loveland Products Canada Inc.	Loveland Vitaflo Fungicide	Suspension	VIT-15.59%; THI-13.25%
30381	Commercial	Interprovincial Cooperative Limited	IPCO Vitaflow SP Fungicide	Suspension	VIT-15.59%; THI-13.25%
30547	Commercial	Interprovincial Cooperative Limited	Weed Away Vitaflo SP Fungicide	Suspension	VIT-15.59%; THI-13.25%
30548	Commercial	Taminco US LLC.	Granuflo - T	Water Dispersible Granules	THI-75%

¹as of 17 May2018, excluding discontinued products or products with a submission for discontinuation.

Appendix II Comments and Responses

Following publication of the Proposed Re-evaluation Decision PRVD2016-07, *Thiram*, Health Canada received written comments from the registrants, the public and other stakeholders such as Canadian Horticultural Council, provincial ministries of agriculture and seed associations. The comments and responses were summarized or grouped together based on common scientific themes and are presented below.

1.0 Comments Relating 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 Acute Reference Dose (ARfD)

Some comments did not support the use of the developmental neurotoxicity (DNT) study to set an ARfD for the general population specifically. A new brain morphometry analysis for all dose groups in the DNT study, which was lacking in the original study report, was submitted to support revision of the ARfD.

Response:

The effects noted in the DNT study included altered motor activity counts and habituation levels in young animals starting at a dose level that did not produce maternal toxicity, as discussed in the PRVD2016-07. These findings occurred along with various delays in measures of learning and memory capacity, such as changes in brain morphometric measurements and increased time taken to complete the Morris maze test, which were generally observed in the high-dose group.

The new data submitted in response to PRVD2016-07 addressed deficiencies in the original brain morphometry report only. It did not address the above-noted effects that formed the basis of the point of departure (PoD) for the ARfD.

In addition, OECD Guidance Document 124 states that evidence of neurotoxicity should be considered relevant to setting an ARfD for all/various populations, unless it can be demonstrated that the effects result after repeated dosing only. In the thiram toxicity database, there was insufficient information to determine whether the findings observed in the DNT study resulted from a single or repeated dose. Thus, these effects were considered relevant for setting an ARfD for all populations since the DNT study spans various lifestages. Therefore, the original ARfD was maintained. The effects noted on motor activity, habituation, learning, memory, and as well as the outcome from the Morris maze test are considered relevant to the general population, including the young.

1.1.2 Acceptable Daily Intake (ADI)

It was noted that chronic dietary reference values (ADI) are generally based on NOAEL values from long-term dietary toxicity studies in which test animals are treated with test material for the majority of their lives. However, the ADI in PRVD2016-07 was based on the DNT study. On this basis, it was requested that Health Canada revisit the choice of study used for the ADI.

Response:

The selection of a study to form the basis of the ADI reference value is informed by a number of considerations, including the duration of exposure, the effects noted and how these change with time, sensitive populations, and applicable uncertainty factors. For thiram, several studies were considered relevant; the long-term studies and the DNT study. Thiram is known to cause neurotoxicity as evidenced by findings in the acute, subchronic and the DNT studies. In addition, the neurotoxic effects appeared to progress in severity as evidenced by the findings in a non-guideline study in which chronic feeding of thiram to rats produced ataxia, paralysis and degeneration of axons in some animals. No evidence of neurotoxicity was seen in the guideline chronic studies in rats and mice. However, the two-year rat study did not examine parameters, such as motor activity levels, auditory startle, brain morphometrics, or learning and memory measurements, which were affected in the DNT study. A NOAEL was not determined in the dietary two-year rat study; rather, a LOAEL of 1.2/1.5 mg/kg bw/day was established based on an increased incidence of pancreatic acinar atrophy. However, a NOAEL of 1.86 mg/kg bw/day was established in the DNT study. After consideration of applicable uncertainty factors (for more details see Response to Comment 1.1.3), an ADI based on the LOAEL from the dietary two-year rat study was not protective of the effects noted in the DNT study. Information and comments submitted in response to PRVD2016-07 confirmed the suite of effects and did not alter the previously determined NOAEL/LOAEL values. Thus, the study chosen as the basis for the ADI was not revised.

1.1.3 The Use of Uncertainty Factors and the *Pest Control Products Act* (PCPA) Factor in the Thiram Risk Assessment

It was requested that Health Canada reduce the *Pest Control Products Act* factor and the additional 10-fold uncertainty factor applied to occupational endpoints to 1-fold on the basis that the thiram toxicity database should be considered complete and extensive in assessing the potential sensitivity of the young. Additionally, the effects noted in the DNT study did not, in their opinion, constitute sensitivity of the young because a NOAEL was determined for developmental toxicity. It was further suggested that Health Canada should use the Food quality protection act factor rationale from the United States Environmental Protection Agency documents for reducing the *Pest Control Products Act* factor to onefold.

Response:

Health Canada revisited the applied uncertainty factors and the magnitude of the factors utilized in PRVD2016-07, in light of the submitted comments and new data.

The *Pest Control Products Act* factor not only addresses the completeness and adequacy of the data available to describe effects in the young, but also the nature of the findings which includes a consideration of the presence of sensitivity of the young as well as the seriousness of the observed effects.

As noted in PRVD2016-07, and discussed above in Response to Comment 1.1.1, the effects observed in the young animals in the DNT study were considered serious and were noted at dose levels that did not produce maternal toxicity. Newly submitted data provided additional information on the brain morphometric analysis only. No additional information or explanation was provided to address the other developmental effects noted in this study. The magnitude of the *Pest Control Products Act* factor identified in PRVD2016-07 was determined in accordance with “SPN2008-01 - The Application of Uncertainty Factors and the PCPA Factor in the Human Health Risk Assessment of Pesticides”. Thus, the PCPA factor described in PRVD2016-07 will remain unchanged.

With respect to the additional uncertainty factors applied to occupational risk assessments, SPN2008-01, *The Application of Uncertainty Factors* and the *Pest Control Products Act* Factor in the Human Health Risk Assessment of Pesticides, notes that “The PCP Act does not specifically require the application of the *Pest Control Products Act* factor in occupational risk assessment. Regardless, those exposed occupationally could include pregnant or lactating women; therefore, there is the potential for indirect exposure of their offspring to a pesticide. In keeping with the spirit of the legislation, it is necessary to protect these indirectly exposed young to a similar degree as their counterparts that are afforded protection through the application of the *Pest Control Products Act* factor. Consequently, where warranted, an additional uncertainty factor will be applied to worker exposure scenarios if available data identify concerns for potential effects on the young or if appropriate data are not available to adequately address the concerns.” Accordingly, an uncertainty factor was applied to ensure the protection of a pregnant worker and her unborn fetus or nursing infant.

Health Canada’s interpretation of the DNT study remains as described in PRVD2016-07. Thus, the bases for the magnitude of the *Pest Control Products Act* factor and the additional factor applied to the occupational exposure scenarios remain unchanged.

1.1.4 Cancer Risk Assessment

The registrants stated that a linear, low-dose extrapolation approach for cancer risk assessment was not necessary for the liver and thyroid parafollicular cells (C-cell) tumours because these tumours were benign in nature, fell within the historical control (HC) values, were not consistently observed across species and studies, and that they are a common occurrence in aging rats of the strain used for testing. In addition, no evidence of genotoxicity was observed in the guideline in vivo assays. On this basis, it was requested that Health Canada revise its cancer risk assessment for thiram.

Response:

Health Canada conducted a re-analysis of the previously available and newly submitted information in the context of an overall weight of evidence (WOE) for cancer risk assessment. Newly submitted information not previously considered in PRVD2016-07 included additional

registrant-supplied historical control tumour incidence information (PMRA 2646660, and 2646661), and genotoxicity studies (PMRA 2646658, 2646659, and 2646666). In addition, published evaluations from the European Union and the USEPA (PMRA 2860985, 2860986, 2860987, and 2860991) were considered.

A. Genotoxicity

The newly submitted genotoxicity data did not alter Health Canada's previous conclusions with respect to the genotoxic potential of thiram, either because they were duplicates of previously submitted studies which had been considered in PRVD2016-07, or were considered of limited value for assessing genotoxic potential because of significant limitations and uncertainty in their findings. For example, a mouse germ cell cytogenetic test was provided, however, new toxicokinetic (TK) data that became available after the PRVD was published, indicated that thiram and/or its metabolites do not reach the gonads, thus, making the findings of the mouse germ cell cytogenetic test of limited/uncertain value for hazard assessment.

Following review of all currently available information, including newly available information and recent evaluations from the EU and USEPA, Health Canada reached the following conclusions:

- Regulatory agencies worldwide and the registrants of thiram agree that thiram is mutagenic in the bacterial reverse mutation assay (Ames test) for the strains TA100 and TA1535, with and without metabolic activation.
- In an in vitro gene mutation assay in mammalian cells (V79/HPRT Chinese Hamster cells, PMRA#: 1218749), thiram did not induce forward mutation.
- Available in vitro chromosomal aberration test results were mixed with one positive and one negative assay. In vivo genotoxicity micronucleus studies also produced mixed results with one positive and one negative assay.
- An available unscheduled DNA synthesis (UDS) assay was negative.
- The dominant lethal mutation test, previously considered positive, is now considered inconclusive because TK data indicate that thiram and/or its metabolites do not reach gonads.
- The majority of non-guideline genotoxicity studies were positive; however, these studies were generally conducted with the less pure form of thiram which is not currently marketed. In addition, these studies did not adequately meet their respective OECD test guideline requirements.
- The majority of guideline genotoxicity studies produced a negative result; however, significant limitations were noted in some of these studies.

Overall, while thiram may have some mutagenic and clastogenic activity, there is uncertainty concerning its potential for other types of genotoxicity due to the mixed results obtained in the assays that were considered acceptable and devoid of limitations.

B. Carcinogenicity

As indicated in PRVD2016-07, tumour findings in the liver and thyroid C-cells were the basis for the linear low-dose extrapolation approach for the proposed cancer risk assessment. The incidence of tumours in males and females were increased in a slight, dose-related manner. Although these incidences were not statistically significant in pairwise comparisons, they were statistically significant in a trend analysis and exceeded their respective historical control incidence rates starting at the mid-dose for both groups.

To support the claim that all tumour findings were within the HC range and thus should not be considered treatment-related, thyroid C-cell tumour HC data were re-submitted along with additional details (PMRA#s: 2646660 and 2646661). This HC dataset included 13 studies of a 24-month duration conducted in the same laboratory that conducted the rat thiram carcinogenicity study.

Based on a revised WOE analysis, which utilized all available relevant genotoxicity and animal bioassay data, and the available updated historical control incidence data, Health Canada concluded the following:

- Available genotoxicity data indicate that thiram may have some mutagenic and clastogenic activity; however, there is uncertainty concerning its potential for other types of genotoxicity.
- Following review of additional information associated with the HC data, the incidences of these tumours were found to be within their respective HC ranges for the low- and mid-dose groups.
- The increased incidences of these tumours were considered treatment-related in the high-dose group in the two-year study in rats. However, the tumours were benign and there was no evidence of progression to malignant tumours. The incidence of each tumour type lacked pairwise statistical significance, although there was a statistically significant trend.
- The USEPA did not consider these tumours treatment-related, largely due to a lack of pairwise statistical significance.
- The EFSA considered these tumours treatment-related at high-dose level and on this basis established a carcinogenic NOAEL.
- The ADI provided a margin of about 4000-5000 to the 'NOAEL' of these tumours.
- The ADI provided a margin of about 8000-10000 to the dose at which tumours were observed.

In summary, although the noted tumours were considered treatment-related in the high-dose group, the margin from the ADI to the NOAEL for these tumours was considered sufficiently health protective. A linear, low-dose extrapolation approach for assessing the cancer risk was considered unnecessarily conservative.

1.2 Comments and Responses Related to Dietary Exposure

Further refinement to the dietary risk assessment for the final re-evaluation decision (RVD) was conducted by considering comments and information received as a result of the PRVD consultation.

1.2.1 Comments Concerning Residues of Thiram in Seed Treatment Field Trials

The registrants commented that Health Canada should use the limit of detection rather than 0.1 ppm (the general Canadian MRL) for the residue inputs for crops without seed treatment field trial data, since most of the available seed treatment field trials show that residues of thiram were below the limit of detection (LOD) of 0.03 ppm.

Response:

Health Canada agrees with the registrants' suggested approach. The highest average field trial residue value and the mean residue value were used in the revised acute and chronic assessments, respectively. In calculating the highest average field trial and mean values, half-LOD was assigned to residues below LODs.

1.2.2 Comments Concerning the Percent Crop Treated

The registrants commented on Health Canada's use of the assumption that 100% of imported commodities contained thiram residues. The registrants also commented on the conservative assumptions used to calculate the weighted percent crop treated for blended commodities.

Response:

Health Canada agrees that it is unlikely all imported crops are treated with thiram. However, in the absence of specific information, 100% is assumed outside of North America. The domestic production and import supply data, combined with the North American percent crop treated information, are used to refine dietary exposure assessments. Although some inputs are conservative, in general this approach is considered to be a refinement to the risk assessment. In addition, the weighted percent crop treated information was updated using the most recent domestic/import food supply information, including information for blended commodities.

1.2.3 Comments Concerning Processing Factors for Tomato Puree and Juice

The registrants commented on the default concentration factors from DEEM used by Health Canada in the absence of processing studies. The registrants indicated that the one apple washing and processing study available shows considerable reduction in residues from washing (0.21×), and making juice (0.12×) and puree (0.18×). The same study showed concentration in dried apples. Although these factors cannot be applied directly to a commodity like tomato, the study does show that thiram is likely to wash off of tomatoes, and to not concentrate in juice or puree. In the dietary assessment conducted by the registrants, the processing factors for both tomato juice and puree were set to 1.0 instead of using the default factors of 1.5 and 3.3, respectively, while the default processing factors for tomato paste and dried tomatoes were applied.

Response:

The registrants did not specify which chemical was used in the apple study described above. If it was thiram, this study was not available to Health Canada and the conclusions cannot be verified. It appears that the registrants relied on an apple processing study to justify using different processing factors for tomatoes, rather than the default values in DEEM. However, in general, processing factors are not translated to other crop groups without a strong rationale.

1.2.4 Comments Concerning the Dietary Exposure and Risk Assessments**a) Dietary Exposure Evaluation Model**

The registrants recommended that the most recent Dietary Exposure Evaluation Model (DEEM-FCID™, version 4.02) be used.

Response:

The revised dietary exposure and risk assessments used the latest version of DEEM-FCID™; Version 4.02, 05-10-c program.

b) Animal Commodities

The registrants commented that there was no scientific basis for the inclusion of animal commodities in the dietary risk assessment. They indicated that Health Canada made the extremely conservative assumption, based on the limit of detection from seed treatment studies, that residues were present at 0.03 ppm in all meat, milk, poultry and eggs (even though residues were not detected in the seed treatment studies). The registrants suggested that animal commodities be removed from the dietary risk assessment because treated seeds are not permitted to be fed to livestock.

Response:

Health Canada agrees that animal commodities should be excluded from the dietary exposure and risk assessment. Based on the use pattern, exposure to thiram from animal commodities is expected to be negligible. The present dietary risk assessment was updated to reflect the fact that secondary residues on animal commodities are not expected.

c) Alfalfa

The registrants requested that alfalfa seed be removed from the risk assessment because treated seeds cannot be used for human food.

Response:

Thiram treated alfalfa seeds are not permitted for use as food or feed. However, alfalfa sprouts or other plant parts may be used for human consumption. Therefore, alfalfa was included in the previous and the revised dietary risk assessments. Exposure to thiram from alfalfa use was not a major contributor in either risk assessment.

d) Celery

The registrants commented that Health Canada should not have considered foliar application to celery. According to the label, thiram is used in celery plant beds, and therefore it is not directly applied to celery. Thiram is not systemic; therefore, it was recommended that instead of using the MRL of 7.0 ppm for celery, the half limit of detection for seed treatment (0.015 ppm) be used. Furthermore, it was noted that the foliar use pattern on celery can be cancelled as it is not a commercial use.

Response:

Although celery in plant beds is listed on the product labels, there are no directions prohibiting application on foliage. Therefore, it is interpreted that foliar application is possible. A label change would be required to assess this use otherwise. Regardless, the translation of seed treatment data to celery plant beds is not appropriate, as the application of thiram to celery can be made at a rate of 11,810 g a.i./ha with 6 applications per year, whereas, the seed treatment rate for celery seeds is 0.38 g a.i./ha (a thiram seed treatment rate of 270 g a.i./100 kg seeds, and a seeding rate of 0.14 kg/ha). In addition, the registrants did not provide field trial data to demonstrate that thiram residues in celery, following plant bed application, were below the limit of detection of 0.03 ppm. Since the use of thiram on celery (foliar or plant beds) is cancelled; only celery seed treatment use was included in the present revised dietary risk assessment. Since dietary risks were shown to be acceptable when only seed treatment uses were considered, the seed treatment use on celery will continue to be supported in Canada.

e) Apple

The registrants noted that apple juice is imported into Canada primarily from China. Therefore, a residue value of 5.0 ppm (Chinese MRL) should have been substituted for the 7.0 ppm US tolerance and Canadian MRL that was used in the PRVD2016-07 dietary risk assessment for all apple food forms.

Response:

Since the Canadian MRL for apple commodities is 7 ppm and apple commodities containing thiram residues up to 7 ppm are permitted to enter Canada, this is the most appropriate value to use in the dietary risk assessment. However, regardless of which MRL was used, the overall risk conclusions would remain the same, that is, dietary risks are of concern for all food uses except specific seed treatments.

f) Strawberry

The registrants indicated that three quarters of strawberries in the Canadian market are imported from the US and suggested using newer information to calculate the weighted percent crop treated for strawberries. The registrants also commented on the residue data used in Health Canada's previous assessment which used residue values higher than the US tolerance of 20 ppm for strawberries. The registrants, however, did not provide thiram-specific residue data for strawberries.

Response:

In PRVD2016-07, the percent crop treated information and domestic/import food supply data that were available at the time of the initial assessment were used. The US tolerance for strawberries was not used in the assessment because a refined assessment was required. Health Canada used field trial data with refined values for the acute probabilistic and chronic dietary risk assessments.

g) Acute Dietary Exposure Estimation

The registrants proposed that the acute dietary exposure assessment be conducted using the following inputs: 1) half of the limit of detection for seed treatment crops, residues from field trial data for peach and strawberry, Chinese MRL of 5 ppm for apple, and the Canadian MRL of 7 ppm for plum; 2) processing factors for apple/banana/peach/plum/strawberry, including a washing factor for apple, and default processing factors for corn/onion/tomato; and 3) revised weighted percent crop treated values. The acute probabilistic assessment conducted by the registrants showed that risks from exposure to thiram through food only were still of concern for all subpopulations (ranging from 225 to 1025% of the ARfD at 99.9th percentile). Children 1-2 year old represented the most exposed subpopulation. Apple, strawberry, plum and peach were identified as risk drivers, and accounted for 67, 12, 11 and 7% of exposure, respectively.

Response:

Although the registrants proposed using several different inputs to estimate exposure, the registrants' assessment also resulted in exposure greater than the ARfD and ADI, which is consistent with Health Canada's assessment in PRVD2016-07 (refer also to Health Canada's responses in 1.2.1-1.2.4 regarding these inputs).

1.3 Comments Related to Occupational Exposure**1.3.1 Dermal Absorption**

The registrants commented that the dermal absorption value of 50% selected by Health Canada is conservative. During the comment period, they submitted a triple pack of dermal absorption studies (rat in vivo, rat in vitro, human in vitro) conducted with the Vitaflo 280 commercial-class product, and also submitted four additional human in vitro dermal absorption studies conducted with commercial-class products not currently marketed in Canada.

Response:

For PRVD2016-07, no dermal absorption studies for thiram 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).

To update the dermal absorption value for thiram, Health Canada considered a wide range of information: the dermal absorption studies submitted by the registrants, an additional human in vitro study reviewed by the European Food Safety Authority (EFSA), and rat metabolism data. In addition, a comparison of the dose solution used in the dermal absorption studies with the commercial- and domestic-class thiram products being handled in various exposure scenarios was also considered.

Based on the studies in the triple pack, a value of 1% was determined for workers treating seed (that is, mixing, loading, and applying products to seed) with Vitaflo 280 and related commercial-class products during commercial seed treatment. This 1% dermal absorption value was not considered to be appropriate for other commercial- or domestic-class products, as the composition of these products differs from Vitaflo products and the chemical constituents of a pest control product formulation can greatly impact dermal absorption. In addition, this 1% dermal absorption value was not considered to be appropriate for other activities in commercial seed treatment facilities (e.g., baggers, cleaners) as exposure during these tasks is due to contact with dust and dried residues and the relationship between the dermal dose for these workers ($\mu\text{g}/\text{cm}^2$) and the solution applied to the seed is unknown.

Using all the available information in a weight-of-evidence approach, the dermal absorption value of 5% was selected (based on the high and medium doses in the triple pack studies) for all other revised scenarios: mixing, loading, and applying other commercial- and domestic-class thiram products; on-farm seed treatment; planting treated seeds; and other activities during commercial seed treatment.

1.3.2 Imported Vegetable/Fruit Seeds

During the consultation period for PRVD2016-07, it was noted by a number of stakeholders that thiram-treated vegetable/fruit seeds are currently being imported into Canada. These stakeholders include: registrants, American Seed Trade Association, Vert Nature Inc., Plantum, California Seed Association, Canadian Seed Trade Association, Monsanto Canada Inc., HM Clause Inc, Stokes Seed Ltd., Canadian Horticulture Council, and Veg Pro International Inc. Use pattern information for planting these seeds were also provided by some of these stakeholders.

Response:

These seeds are currently registered for on-farm seed treatment, and an on-farm seed treatment and planting risk assessment was conducted. However, to assess the risk from seeds that are treated outside of Canada and imported, Health Canada conducted a separate planting risk assessment for the imported treated seeds identified by stakeholders (sweet corn, broccoli, Brussels sprouts, snap beans, cabbage, carrots, cauliflower, green peas, onion, beets, cucumber, eggplant, green and wax beans, lettuce, melon, peppers, pumpkin, radish, rutabaga/turnip, spinach, squash, zucchini, tomato, watermelon). As detailed in Appendix VI, risks were shown to be acceptable for the planting these imported seeds, provided that the mitigation as outlined in Appendix III for planting seeds treated in Canada are followed. Specific label language was not added to the Canadian product labels regarding the importation of these seeds, as these seeds are also acceptable for commercial and/or on-farm treatment in Canada.

1.3.3 Conversion from On-farm Dry Seed Treatment to Slurry Treatment

The registrants proposed that the commercial-class wettable powder and dust products be converted from a dry seed treatment application to a slurry application. This action was proposed to reduce worker exposure.

Response:

Health Canada considered both dry and slurry on-farm seed treatment in the risk assessment for these two commercial-class products. As noted by the registrants, worker exposure during slurry seed treatment is lower than that during dry seed treatment. To reduce worker exposure while still allowing treatments for as many crops seeds as possible, Health Canada requires that label directions for dry treatment be removed from wettable powder and dust products and would require the addition of label directions for slurry treatment if this treatment is added. See Appendix III for more information.

1.3.4 Commercial and On-farm Seed Treatment Clarifications

The registrants provided information on the treatment types and crops currently registered for some seed treatment products.

Response:

The information provided by the registrants was used to verify the treatment types included in the PRVD2016-07 risk assessment. In some instances, such as when the current label instructions were unclear or grower information was available, both commercial and on-farm seed treatment were assessed for a crop. Clearer label language and mitigation will be required for a number of these products, as detailed in Appendix III.

1.3.5 Ornamental Animal Repellent

Premier Tech Home and Garden and Plant Products Inc provided use information for the commercial- and domestic-class ornamental animal repellent products. This included information on activities conducted following application, application rates and methods, as well as amount handled per day by applicators.

Response:

In PRVD2016-07, risks were not shown to be acceptable for application of the ornamental animal repellent products. Based on the information received, the risk assessment for mixers/loaders and applicators was refined. Risks were shown to be acceptable for the application equipment used by commercial applicators, provided the mitigation measures outlined in Appendix III are followed. Risks were shown to be acceptable for pump-up and knapsack sprayers used by domestic applicators; however, risks have not been shown to be acceptable for homeowners using paintbrushes. As such, instructions for paintbrush application must be removed from the domestic-class product label.

1.3.6 Use Information for Refining the Foliar and Dip Uses

During the consultation period for PRVD2016-07, the registrants, and the Canadian Horticulture Council provided information on the use pattern (such as, application rates, timing of application) for the foliar and dip uses of thiram. The registrants also submitted dislodgeable foliar residue and worker exposure studies.

Response:

Chemical-specific studies and use pattern information are important in the refinement of occupational risk assessments. However, as discussed in Section 3.2, except for seed treatment uses, dietary risks were not shown to be acceptable for all other food uses of thiram and thus, these other food uses are cancelled. Therefore, the occupational and residential risk assessments for these cancelled uses from PRVD2016-07 were not revisited.

2.0 Comments Relating to the Environmental Assessment

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

Environmental Fate

2.1 Comment: The level of detail provided in the PRVD is insufficient to reproduce the water modelling results in order to properly evaluate the risk assessment.

Response:

The application information, as well as the PRZM/EXAMS files and inputs used for water modelling were provided as requested (PMRA 2835859).

2.2 Comment: OECD Guidelines (OECD106) recommend that soils with <0.3% organic carbon not be used in the determination of K_d values as it may disturb correlation between organic content and adsorption. The percent organic carbon for one of the soils used (sand, Table 1, Annex VIII) was extremely low (0.087). Also, K_d values for a muck soil (Table 1, Annex VIII) with significantly higher organic carbon content (30%) were used and as it was not possible to determine textural composition (percent sand, silt and clay), as per guidance for soil selection. It is noted that muck soil is a soil mainly made up of humus substances from drained swampland.

Response:

Health Canada agrees with the commenter. The K_d values for the two muck soils were removed and drinking water estimated environmental concentrations (EECs) were recalculated. Additionally, the draft EFSA review of thiram (2015, Draft Renewal Assessment Report prepared according to the Regulation (EC) No 1107/2009; PMRA 2781303) was published during the comment period. The EFSA review contained additional information from other environmental fate studies that resulted in Health Canada revisiting its residue definition for drinking water to include not only the parent (thiram) but also the major transformation product N, N dimethyl carbamosulfonic acid (DMCS). Data from the aged soil column leaching study (PMRA 2646665) submitted by the registrant was also used for modelling. The model inputs and application information/model outputs were provided to the commenter.

For the PRVD, Level 1 drinking water modelling was conducted for field sprayer and airblast application methods to celery, strawberries and apples (for Nova Scotia only) resulting in surface water EECs of 53 – 508 µg a.i./L (90th percentile of daily average concentrations) and 0.87 – 12 µg a.i./L (90th percentile of yearly average concentrations) and groundwater concentrations of 0 µg a.i./L. Level 2 water modelling conducted for the PRVD resulted in surface water EECs of 0.24 to 68 µg a.i./L.

For the RVD, the combined residue of thiram and DMCS was modelled at Level 1 using the revisions discussed above. This resulted in EECs of 1.5 to 7.3 µg a.i./L for surface water and 3.3 to 16.5 µg a.i./L for groundwater. Groundwater modelling was refined with Level 2 modelling for seed treatment applications to peas/beans, onions, spring and winter wheat, barley, and triticale only. The resulting groundwater EECs ranged from 2.1 – 8.1 µg a.i./L (90th percentile of both daily and yearly average concentrations).

Environmental Toxicology

2.3 Comment:

The risk assessment for birds and/or mammals in the PRVD overestimated risks as there are no thiram-specific incident reports for these organisms, seed treatment labels require all seed to be covered with soil (minimizing availability for consumption) and thiram acts as a repellent to birds and mammals. A study was submitted to support the claim that thiram acts as a repellent to birds when used as a seed treatment. Based on the available evidence, the commenter concludes that the consumption of treated seed by birds and mammals is not expected. While the chronic avian risk is above the level of concern in the refined assessment, risks may actually be lower if the duration of exposure is short as a result of dissipation processes and birds relying on other food sources in untreated areas. The Health Canada risk assessment is based on the maximum seed treatment application rates and maximum seed planting rates, while not all seeds are treated at the highest application rate nor are all seeds planted at the highest rate.

Response:

Based on the study provided, thiram is unlikely to be consumed by birds. However, given the inherent toxicity of thiram, product labels still require a “toxic to birds and small wild mammals” statement.

The submitted study was found to be reliable and was conducted according to the draft OECD *Test for Avian Avoidance of Pesticide-treated Seeds and Baits* (2003). The study demonstrates that birds will avoid seeds treated with thiram (repellency factor of at least 90%). Although thiram exposure to birds and mammals from ingestion of treated seed may not be continuous or recurring, chronic effects to birds may occur as a result of initial exposure to planted seeds. The following statements are required on thiram labels to protect birds and mammals:

“Do not plant treated seed by broadcasting to the soil surface. Ensure that all planted seed are thoroughly covered with soil, especially in turn areas. Plant wheat, corn and canola seed a minimum of 1 inch deep. If seeds are not thoroughly incorporated by the planter during planting, additional incorporation may be required to reduce exposed seeds. Clean-up, bury or cover all spilled seed with soil.”

“Seeding practices such as precision drilling, can further reduce exposure of birds and small mammals to treated seed.”

3.0 Comments Relating to the Value Assessment

Comments related to value were received from: Premier Tech Home and Garden, Plant Products, Engage Agro Corporation; Ontario Ministry of Agriculture, Food and Rural Affairs; Saskatchewan Flax development Commission, American Seed Trade Association, Vert Nature Inc., Plantum Netherlands, Seed Dynamics Inc., California Seed Association, Loveland Products, the Canadian Seed Trade Association, Monsanto Canada Inc., HM Clause Inc., Saskatchewan Ministry of Agriculture, Stokes Seed Limited, Canadian Horticultural Council and Veg Pro International Inc.

3.1 Thiram is Important for Seed Treatment

A number of stakeholders emphasized the importance of thiram for seed treatment use, particularly for importation of thiram-treated vegetable seeds, since vegetable seeds are not produced in Canada.

Response:

Health Canada acknowledges the importance of thiram for seed treatments.

3.2 Thiram is Important for Control of Foliar Diseases and for Resistance Management on Fruit Crops

Thiram is important for the management of foliar diseases on apples, peaches, strawberries and plums. As a multi-site fungicide, thiram is used for resistance management. The phasing-out of thiram will impact the disease management programs for these crops.

Response:

Health Canada acknowledges the value of thiram for both disease management and resistance management on these fruit crops. While these uses are cancelled, a number of active ingredients, including several multi-site fungicides such as captan, chlorothalonil, folpet, copper and sulphur, are currently registered for the management of the listed diseases on apples, peaches, plums and strawberry.

3.3 Thiram is Important as an Animal Repellent

Thiram is used as a taste repellent applied once on the bark in late fall to control rabbit, mice and deer damage to nursery and ornamental plants. This repellent has an unacceptable taste to birds, which reduces feeding and hence damage to plants. The potential exposure to workers is considered low as there will be less post-application activities in late fall.

Response:

The use of thiram as an animal repellent is supported for continued registration, and users will continue to have access to it for this use.

Appendix III Label Amendments for End-Use Products Containing Thiram

The label amendments presented below do not include all label requirements for individual products, such as first aid statements, disposal statements, precautionary statements and supplementary protective equipment. Information on labels of currently registered products should not be removed unless it contradicts the label statements provided below.

1) Label Amendments for End-Use Products Related to Health Risk Assessment:

- Use instructions for the following crops must be removed from the product labels, as outlined in Appendix III, Table 2. This will result in a cancellation of some products if all currently registered uses for those products are cancelled (as outlined in Appendix III, Table 1). Note: Protective equipment currently required on product labels, such as goggles and respiratory protection, were maintained in the product-specific statements, when present.
 - All foliar uses (apples, peaches, plum, celery, strawberry); and
 - Sweet potato dip (roots of sprouts)
 - Commercial seed treatment using Vitaflo products on wheat, barley, oats, rye, triticale, corn
 - Commercial seed treatment using other products on wheat, barley, oats, canola, rapeseed, mustard
 - On-farm dry seed treatment for all crops
 - On-farm wettable powder slurry seed treatment on mustard, soybean, bean, pea, alfalfa, grasses, dry bulb onion
 - On-farm dust slurry seed treatment on dry bulb onion
 - On-farm liquid hopperbox/seed drill treatment for all crops
- Additional label requirements are outlined in Table 2 for specific product labels.

2) Label Amendments for Commercial-Class Seed Treatment End-use Products Related to Environmental Risk Assessment

- Under ENVIRONMENTAL PRECAUTIONS add the following statements:

“Toxic to birds and small, wild mammals. Any spilled or exposed seeds must be incorporated into the soil or otherwise cleaned-up from the soil surface.”
- Under USE RESTRICTIONS add the following statements:

“Do not plant treated seed by broadcasting to the soil surface. Ensure that all planted seed are thoroughly covered with soil, especially in turn areas. Plant wheat, corn and canola seed a minimum of 1 inch deep. If seeds are not thoroughly incorporated by the planter during planting, additional incorporation may be required to reduce exposed seeds. Clean-up, bury or cover all spilled seed with soil.”

“Seeding practices, such as precision drilling, can further reduce exposure of birds and small mammals to treated seed.”

- All containers or packages containing treated seed for sale or use in Canada must also be labeled or tagged under USE RESTRICTIONS as follows:

“Toxic to birds and small, wild mammals. Any spilled or exposed seeds must be incorporated into the soil or otherwise cleaned-up from the soil surface.”

Appendix III

Table 1 Registered Thiram End-Use Products That Are Cancelled

Reg #	Form	Currently Registered		Required Action/Mitigation
		Scenario	Crop	
18788 ^a	SU	On-farm hopperbox/seed drill seed treatment	Pea, lentil, soybean	Cancel products, as all uses on product labels are cancelled
27174 ^b , 27564 ^c	SU	Commercial seed treatment	Canola, mustard, rapeseed	
28220 ^d	WP	Foliar & dip application	All (apple, peach, plum, strawberry, celery, sweet potato)	
30548 ^e	WDG			

Reg # = product registration #; Form = formulation; SU = suspension; WP = wettable powder; WDG = water dispersible granules;

^a Anchor Planter Box Seed Treatment

^b Gaucho CS FL

^c Prosper FL Flowable Insecticide and Fungicide Seed Treatment

^d Taminco Thiram 75 WP. Wettable Powder Fungicide.

^eTaminco. Granuflo T

Appendix III

Table 2 Required Label Modifications for Currently Registered Thiram End-Use Products

Reg #	Form	Currently Registered		Required Action/Mitigation
		Scenario	Crop	
7715 ^a	SU	Ornamental Animal Repellent (domestic-class product) ^b		Under ' PRECAUTIONS '- the product label must be amended as follows: <ul style="list-style-type: none"> • <u>Add:</u> “Do not allow people or pets to enter treated areas until sprays have dried.”
				Under ' Directions for Use '- the product label must be amended as follows: <ul style="list-style-type: none"> • <u>Replace:</u> “SKOOT Repellent for Rabbits, Mice and Deer may be applied undiluted with a paintbrush or diluted with equal parts water and applied with a pump-up or knapsack sprayer.” <u>With</u> “SKOOT Repellent for Rabbits, Mice and Deer may be diluted with equal parts water and applied with a pump-up or knapsack sprayer.”
13258 ^a	SU	Ornamental Animal Repellent (commercial-class product)		Under ' PRECAUTIONS '- the product label must be amended as follows: <ul style="list-style-type: none"> • <u>Add:</u> “Wear long-sleeved shirt, long pants, socks and shoes, and chemical-resistant gloves during mixing/loading, application, clean-up, and repair.” • <u>Add:</u> “Do not enter or allow entry into treated areas until sprays have dried.”
				Under ' Directions of Use '- the product label must be amended as follows: <ul style="list-style-type: none"> • <u>Replace:</u> “SKOOT Repellent for Rabbits, Mice and Deer may be applied undiluted with a paintbrush or diluted with equal parts water and applied with a pump-up or knapsack sprayer.” <u>With:</u> “SKOOT Repellent for Rabbits, Mice and Deer may be applied undiluted with a paintbrush. It may also be diluted with equal parts water and applied by paintbrush, pump-up sprayer or knapsack sprayer.” • <u>Add:</u> “When applying by paintbrush: DO NOT

Reg #	Form	Currently Registered		Required Action/Mitigation
		Scenario	Crop	
				handle more than 44 g a.i. per person per day. These restrictions are in place to minimize exposure to individual applicators. Application may need to be performed over multiple days or using multiple applicators.”
10959 ^c	DU	On-farm seed treatment	Onion seed	<p>Under ‘PRECAUTIONS’- the product label must be amended as follows:</p> <ul style="list-style-type: none"> • <u>Replace</u>: (‘Precautions’ section, item #2) “Wear a mask suitable for protection against PROGRO dust when applying this product to the seed.” (‘Precautions’ section, item #5) “All workers involved in treating seeds, clean-up, repair and maintenance of seed treatment equipment must wear a long-sleeved shirt and long pants, chemical-resistant gloves, shoes and socks. Baggers, sewers and workers involved in handling treated seeds must wear a long-sleeved shirt and long pants, chemical-resistant gloves, shoes and socks, to minimize exposure to dust from treated seeds.” <p><u>With</u>: “When treating seed, handling and planting treated seeds, wear coveralls over a long-sleeved shirt, long pants, socks and shoes, and chemical-resistant gloves. When treating or handling treated seed, work in a well-ventilated area and also wear a NIOSH-approved N95 (minimum) filtering facepiece respirator (dust mask) that is properly fit tested” “Use a closed cab tractor for planting. Chemical-resistant gloves are not required to be worn within the closed cab, but need to be available for exiting the cab during calibration, repair or cleaning of equipment.”</p>
				<p>The front panel of the product label must be amended as follows:</p> <ul style="list-style-type: none"> • <u>Add</u>: “No commercial seed treatment (in facilities or with mobile treaters) is permitted.”
				<p>Under ‘Directions for Use’- the product label must be amended as follows:</p> <ul style="list-style-type: none"> • <u>Add</u>: “For on-farm use only. DO NOT use

Reg #	Form	Currently Registered		Required Action/Mitigation
		Scenario	Crop	
				<p>for commercial seed treatment (in facilities or with mobile treaters).”</p> <ul style="list-style-type: none"> • <u>Add</u> use instructions for treating seed on-farm as a slurry treatment using conventional treating equipment. Remove all use instructions on the label where the treatment method is dry application or using unconventional equipment (e.g. in a pail).
27566 ^d	SU	Commercial & on-farm seed treatment	Wheat, barley, oat	<p>Under ‘PRECAUTIONS’- the product label must be amended as follows:</p> <ul style="list-style-type: none"> • <u>Replace</u> “Applicators and handlers must wear: coveralls over long-sleeved shirt and long pants, chemical-resistant gloves, shoes plus socks, protective eyewear such as goggles or faceshield, NIOSH-approved respirator with any R, P, or HE filter” <p><u>With</u> “When treating seeds, handling and planting treated seeds, wear coveralls over a long-sleeved shirt, long pants, socks and shoes, chemical-resistant gloves, and a respirator with a NIOSH approved organic-vapour-removing cartridge with a prefilter approved for pesticides OR a NIOSH-approved canister approved for pesticides.”</p> <p>“A closed mixing/loading system must be used. Use a closed cab tractor for planting. Respirator and chemical-resistant gloves are not required to be worn within the closed cab, but need to be available for exiting the cab during calibration, repair or cleaning of equipment.”</p> <p>The front panel of the product label must be amended as follows:</p> <ul style="list-style-type: none"> • <u>Add</u>: “No commercial seed treatment (in facilities or with mobile treaters) is permitted.” <p>Under ‘Directions for Use’- the product label must be amended as follows:</p> <ul style="list-style-type: none"> • <u>Replace</u>: “...ready to use formulation for commercial or on-farm treating with conventional seed treating equipment...” <p><u>With</u>: “...ready to use formulation for on-farm treating with conventional seed treating equipment...”</p>

Reg #	Form	Currently Registered		Required Action/Mitigation
		Scenario	Crop	
				<ul style="list-style-type: none"> • <u>Add</u>: “For on-farm use only. DO NOT use for commercial seed treatment (in facilities or with mobile treaters).” <p>Under ‘Use Limitations’-the product label must be amended as follows:</p> <ul style="list-style-type: none"> • Remove entire section, as this relates to the labelling and tagging of treated seed, which is associated with commercial treatment, not on-farm treatment
28525 ^e	SU	Commercial & on-farm seed treatment	Canola, mustard	<p>Under ‘PRECAUTIONS’- the product label must be amended as follows:</p> <ul style="list-style-type: none"> • <u>Replace</u> “Wear chemical resistant gloves and coveralls when handling NISSO FOUNDATION LITE or treated seed. When handling NISSO FOUNDATION LITE and when treating seed or while augering or handling treated seed, work in a well-ventilated area and wear a suitable respirator.” <u>With</u> “When treating seeds, handling and planting treated seeds, wear coveralls over a long-sleeved shirt, long pants, socks and shoes, chemical-resistant gloves, and a respirator with a NIOSH approved organic-vapour-removing cartridge with a prefilter approved for pesticides OR a NIOSH approved canister approved for pesticides.” “A closed mixing/loading system must be used. “Use a closed cab tractor for planting. Respirator and chemical-resistant gloves are not required to be worn within the closed cab, but need to be available for exiting the cab during calibration, repair or cleaning of equipment.” <p>The front panel of the product label must be amended as follows:</p> <ul style="list-style-type: none"> • <u>Add</u>: “No commercial seed treatment (in facilities or with mobile treaters) is permitted.” <p>Under ‘Directions for Use’- the product label must be amended as follows:</p> <ul style="list-style-type: none"> • <u>Add</u>: “For on-farm use only. DO NOT use for commercial seed treatment (in facilities or with mobile treaters).”

Reg #	Form	Currently Registered		Required Action/Mitigation
		Scenario	Crop	
				<p>Under 'Use Limitations' - the product label must be amended as follows:</p> <ul style="list-style-type: none"> Remove (as it relates to labelling and tagging seed, which is associated with commercial treatment, not on-farm treatment): <p>"Treated seed must be labelled as follows: This seed has been treated with NISSO Foundation Lite containing iprodione and thiram. Do not use for feed, food, or oil processing. The date of treatment must also be included."</p>
27555 ^f	SU	Commercial seed treatment	Wheat, barley	Remove use instructions and related label statements from the product label (including the front panel, and Directions for Use section) for wheat and barley crops
			Soybean- export only	<p>Under 'PRECAUTIONS' - the product label must be amended as follows:</p> <ul style="list-style-type: none"> Replace ('Precautions' section, bullet #2) "All workers involved in treating seeds, clean-up, repair and maintenance of seed treatment equipment must wear a long-sleeved shirt and long pants, chemical-resistant gloves, and shoes and socks. Baggers, sewers and workers involved in handling treated seeds must wear a long-sleeved shirt and long pants, chemical-resistant gloves, shoes and socks to minimize exposure to dust from treated seeds." <p>With</p> <p>"Use a closed transfer system for commercial seed treatment (facilities and mobile treaters). Closed transfer includes closed mixing, loading, calibrating and closed treatment equipment. No open transfer is permitted. When treating or handling treated seeds, cleaning seed treatment equipment, wear coveralls over a long-sleeved shirt, long pants, socks and shoes, and chemical-resistant gloves. For cleaning, the coveralls worn must be chemical-resistant. When treating and cleaning seed treatment equipment, also wear a respirator with a NIOSH approved organic-vapour-removing cartridge with a prefilter approved for pesticides OR a NIOSH approved canister approved for</p>

Reg #	Form	Currently Registered		Required Action/Mitigation
		Scenario	Crop	
				pesticides.”
				Under ‘ Directions for Use ’ - the product label must be amended as follows: <ul style="list-style-type: none"> • <u>Replace</u>: “..designed to be used undiluted in commercial seed treaters.” <u>With</u>: “..designed to be used undiluted in commercial seed treaters, for commercial seed treatment only (facilities and mobile treaters).”
				Under ‘ Use Limitations ’ - the product label must be amended as follows: <ul style="list-style-type: none"> • <u>Replace</u>: (‘Use Restrictions’ section, bullet #3) “All bags containing treated seed for sale or use in Canada must be labelled or tagged as follows: This seed has been treated with carbathiin and thiram. Wear a long-sleeved shirt, long pants, shoes and socks, and chemical-resistant gloves when handling treated seeds. DO NOT use treated seed for food, feed or oil processing. Store away from food and feed. Baggers, sewers and workers involved in handling treated seeds must wear a long-sleeved shirt and long pants, chemical-resistant gloves, shoes and socks to minimize exposure to dust from treated seeds.” <u>With</u>: “All containers or packages containing treated seed for sale or use in Canada must be labelled or tagged as follows: This seed has been treated with carbathiin and thiram. DO NOT use treated seed for food, feed or oil processing. Store away from food and feed. For all activities involving handling of treated seeds (including planting), wear a long sleeved-shirt, long pants, socks and shoes, and chemical-resistant gloves. Closed cab tractors must be used for planting treated seeds. Chemical-resistant gloves are not required to be worn within the closed cab, but need to be available for exiting the cab during calibration, repair or cleaning of equipment.”
27556 ^g	WP	Foliar & dip application	All (apple, peach, plum, strawberry, celery, sweet potato)	Remove use instructions and related label statements from the product label for apple, peach, plum, strawberry, celery, and sweet potato crops
		On-farm seed treatment	Soybean, mustard, bean,	Remove use instructions and related label statements from the product label for soybean, mustard, bean, pea,

Reg #	Form	Currently Registered		Required Action/Mitigation
		Scenario	Crop	
			pea, grasses dry bulb onion	grasses, and dry bulb onion crops
			Corn, safflower, onion, alfalfa for seed production, vegetable/fruit seeds (cucumber, cantaloupe, pumpkin, squash, watermelon, beet, broccoli, Brussels sprouts, cabbage, carrot, cauliflower, celery, lettuce, pepper, radish, spinach, sugar beet, turnip, tomato, eggplant, onion)	On the front panel and in all other areas of the label: <ul style="list-style-type: none"> • <u>Replace</u>: “alfalfa” <u>With</u>: “alfalfa for seed production”
				Under ‘ PRECAUTIONS ’- the product label must be amended as follows: <ul style="list-style-type: none"> • <u>Replace</u> (‘Precautions’ section, item #10) “Avoid breathing dust or spray mist. When treating, augering or handling treated seed, work in a well-ventilated area and wear a suitable dust mask, goggles and gloves.”
				<u>With</u> : “Avoid breathing dust or spray mist. “When treating seeds, handling and planting treated seeds, wear a long-sleeved shirt, long pants, socks and shoes, and chemical-resistant gloves. When treating, augering, or handling treated seed, work in a well-ventilated area and also wear goggles and a NIOSH-approved N95 (minimum) filtering facepiece respirator (dust mask) that is properly fit tested”
				The front panel of the product label must be amended as follows: <ul style="list-style-type: none"> • <u>Add</u>: “No commercial seed treatment (in facilities or with mobile treaters) is permitted.”
11423 ^h , 30380 ⁱ , 30381 ^j , 30547 ^k	SU	Commercial on-farm seed treatment	All crops currently registered on the label	Under ‘ Directions for Use ’- the product label must be amended as follows: <ul style="list-style-type: none"> • <u>Add</u>: “For on-farm use only. DO NOT use for commercial seed treatment (in facilities or with mobile treaters).” • Add use instructions for treating seed on-farm as a slurry treatment using conventional treating equipment. Remove all use instructions on the label where the treatment method is a seed dressing, or the treatment method is unspecified.
				On the front panel - the product label must be amended as follows: <ul style="list-style-type: none"> • <u>Replace</u> “Fungicide seed protectant for use on wheat, barley, oats, rye, triticale, flax, corn, dry common beans, snap common beans, peas, lentils and soybeans.” <u>With</u> “Fungicide seed protectant for commercial and on-farm treatment of flax, dry common beans, snap common beans,

Reg #	Form	Currently Registered		Required Action/Mitigation
		Scenario	Crop	
				peas, lentils and soybeans, and on-farm treatment of wheat, barley, oats, rye, triticale, corn”
				<p>Under ‘Directions for Use’- the product label must be amended as follows:</p> <ul style="list-style-type: none"> • <u>Replace</u>: “..designed to be used undiluted in commercial seed treaters.” <u>With</u>: “..designed to be used undiluted in commercial seed treaters, for on-farm and commercial seed treatment (facilities and mobile treaters).”
				<p>Under ‘PRECAUTIONS’- the product label must be amended as follows:</p> <ul style="list-style-type: none"> • <u>Add</u>: “For on-farm seed treatment, use a closed mix/load system. When treating seeds, handling and planting treated seeds, wear coveralls over a long-sleeved shirt, long pants, socks and shoes, and chemical-resistant gloves” <p>“Use a closed cab tractor for planting. Chemical-resistant gloves are not required to be worn within the closed cab, but need to be available for exiting the cab during calibration, repair or cleaning of equipment.”</p>
			Flax, beans, peas, lentil, soybeans	<p>Under ‘PRECAUTIONS’- the product label must be amended as follows:</p> <ul style="list-style-type: none"> • <u>Replace</u>: (‘Precautions’ section, #5) “All workers involved in treating seeds, clean-up, repair and maintenance of seed treatment equipment must wear a long-sleeved shirt and long pants, chemical-resistant gloves, and shoes and socks. Baggers, sewers and workers involved in handling treated seeds must wear a long-sleeved shirt and long pants, chemical-resistant gloves, shoes and socks to minimize exposure to dust from treated seeds.” <u>With</u>: “For commercial seed treatment (facilities and mobile treaters), use a closed transfer system. Closed transfer includes closed mixing, loading, calibrating and closed treatment equipment. No open transfer is permitted. When treating or handling treated

Reg #	Form	Currently Registered		Required Action/Mitigation
		Scenario	Crop	
				<p>seeds, cleaning seed treatment equipment for commercial seed treatment, wear coveralls over a long-sleeved shirt, long pants, shoes plus socks, and chemical-resistant gloves. When cleaning seed treatment equipment also wear a respirator with a NIOSH approved organic-vapour-removing cartridge with a prefilter approved for pesticides OR a NIOSH approved canister approved for pesticides, and coveralls must be chemical-resistant.”</p> <ul style="list-style-type: none"> • <u>Replace:</u> (‘Use Restrictions’ section, bullet #9) “This seed has been treated with carbathiin and thiram. Wear a long-sleeved shirt, long pants, shoes and socks, and chemical-resistant gloves when handling treated seeds. DO NOT use treated seed for food, feed or oil processing. Store away from food and feed. Baggers, sewers and workers involved in handling treated seeds must wear a long-sleeved shirt and long pants, chemical-resistant gloves, shoes and socks to minimize exposure to dust from treated seeds.” <p><u>With:</u> “This seed has been treated with carbathiin and thiram. DO NOT use treated seed for food, feed or oil processing. Store away from food and feed. For all activities involving handling of treated seeds (including planting), wear a long sleeved-shirt, long pants, socks and shoes, and chemical-resistant gloves. Closed cab tractors must be used for planting treated seeds. Chemical-resistant gloves are not required to be worn within the closed cab, but need to be available for exiting the cab during calibration, repair or cleaning of equipment.</p>
			Wheat, barley, oats, rye, triticale, corn	<p>Under ‘Directions for Use’ - the product label must be amended as follows:</p> <ul style="list-style-type: none"> • Wheat, barley, oats, rye, triticale, and corn are permitted for on-farm seed treatment, but not for commercial seed treatment. Therefore, the following statement must be included with the use instructions for these specific seeds: “For on-farm use only. DO NOT use for commercial seed treatment (in facilities or

Reg #	Form	Currently Registered		Required Action/Mitigation
		Scenario	Crop	
				with mobile treaters).”

Reg # = product registration #; Form = formulation; SU = suspension; WP = wettable powder; WDG = water dispersible granules;

^a Skoot

^b Domestic-class product. All other products are commercial-class.

^c Pro-Gro Systemic Dust seed Protectant

^d Raxil T Flowable Fungicide

^e Nisso Founation Lite. Canola and Mustard Seed Treatment

^f Vitacax-200 Flowable Fungicide

^g Thiram 75 WP Wettable Powder Fungicide

^h Vitaflo-280 Fungicide

ⁱ Loveland Vitaflo Fungicide

^j IPCO Vitaflo SP Fungicide

^k WeedAway Vitaflo-SP Fungicide

Appendix IV Revised Toxicology Reference Values for Thiram 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 Act* factors for dietary assessments; MOE refers to a target margin of exposure for occupational assessments

Appendix V 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. It should be noted, however, that ARfD and ADI did not change.
- 2) Since dietary risks from drinking water were shown to be acceptable for seed treatment uses (excluding dry bulb onion), only these uses were included.
- 3) Available seed treatment field trial data were used for both the refined acute and chronic assessments.
- 4) For the chronic assessment, updated percent domestic/import food supply information was used in conjunction with the existing percent crop treated estimates.
- 5) No exposure to thiram from animal commodities is expected from seed treatment uses, and animal commodities were not included.
- 6) Refined drinking water estimated environmental concentrations (EECs) were used. Risks from drinking water exposure have not been shown to be acceptable when using the highest application rate for seed treatment of 2.25 kg a.i./100 kg seeds for dry bulb onions. Therefore, the EECs were based on the highest application rate on pea seeds. No drinking water exposure is expected from the use of thiram as an ornamental animal repellent.
- 7) The acute and chronic dietary assessments for thiram 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.

Thiram may be transformed into nitrosamine *N*-nitrosodimethylamine (NDMA) during water treatment. Residues of NDMA in drinking water resulting from the use of thiram as a seed treatment is expected to be much lower than the maximum acceptable concentration specified in the Health Canada's 2011 Drinking Water Quality Guideline for NDMA.

Appendix V Table 1 Summary of Acute Dietary Exposure and Risk Analyses for Thiram

Subpopulation	Food only ¹ – 95 th Percentile		Food ¹ and Drinking Water ² – 95 th Percentile	
	Exposure (mg/kg bw)	%ARfD ³	Exposure (mg/kg bw)	%ARfD ³
General Population	0.000408	20.4	0.000737	36.9
All Infants (< 1 year old)	0.000657	32.9	0.001798	89.9
Children 1–2 years old	0.000914	45.7	0.001359	67.9
Children 3–5 years old	0.000842	42.1	0.001112	55.6
Children 6–12 years old	0.000565	28.3	0.000803	40.2
Youth 13–19 years old	0.000356	17.8	0.000582	29.1
Adults 20–49 years old	0.000322	16.1	0.000642	32.1
Adults 50+ years old	0.000276	13.8	0.000564	28.2
Females 13–49 years old	0.000312	15.6	0.000632	31.6

Subpopulation	Food only ¹ – 95 th Percentile		Food ¹ and Drinking Water ² – 95 th Percentile	
	Exposure (mg/kg bw)	%ARfD ³	Exposure (mg/kg bw)	%ARfD ³
¹ Seed treatment uses only.				
² Estimated environmental concentrations (EECs) of thiram and <i>N,N</i> dimethyl carbamosulfonic acid (DMCS) in potential drinking water sources (groundwater and surface water) were modelled. The acute EEC used in this estimation is 8.1 µg/L (ground water, 90 th percentile of daily average concentration) modeled using the highest application rate of pea (315 g a.i./ha).				
³ Acute Reference Dose (ARfD) of 0.002 mg/kg bw.				

Appendix V

Table 2 Summary of Chronic Dietary Exposure and Risk Analyses for Thiram

Subpopulation	Food only ¹		Food ¹ and Drinking Water ²	
	Exposure (mg/kg bw/day)	%ADI ³	Exposure (mg/kg bw/day)	%ADI ³
General Population	0.000073	3.6	0.000237	11.8
All Infants (< 1 year old)	0.000141	7.1	0.000753	37.6
Children 1–2 years old	0.000179	9.0	0.000404	20.2
Children 3–5 years old	0.000163	8.1	0.000346	17.3
Children 6–12 years old	0.000106	5.3	0.000242	12.1
Youth 13–19 years old	0.000071	3.5	0.000186	9.3
Adults 20–49 years old	0.000064	3.2	0.000227	11.3
Adults 50+ years old	0.000050	2.5	0.000209	10.4
Females 13–49 years old	0.000060	3.0	0.000220	11.0
¹ Seed treatment uses only.				
² Estimated environmental concentrations (EECs) of thiram and <i>N,N</i> dimethyl carbamosulfonic acid (DMCS) in potential drinking water sources (groundwater and surface water) were modelled. The chronic EEC used in this estimation is 8.1 µg/L (ground water, 90 th percentile of 365-day moving average concentration) modeled using the highest application rate of pea (315 g a.i./ha).				
³ Acceptable daily intake (ADI) of 0.002 mg/kg bw/day.				

Appendix VI Revised Occupational Mixer/Loader/Applicator (MLA) and Postapplication Exposure and Risk Estimates for Thiram

Details and tables for the revised risk assessment are included in this appendix. Please refer to PRVD2016-07 for additional information.

Dermal Absorption

Based on comments and data received during the consultation period for PRVD2016-07, the dermal absorption value was revised to 1% for treaters handling Vitaflo 280 and related products during commercial seed treatment, and 5% for all other scenarios. A specific dermal absorption value for post-application exposure was not required, as discussed below.

Seed Treatment

Most of the surrogate seed treatment studies used in PRVD2016-07 were also used in the revised thiram risk assessment. Where warranted, such as when seed-specific data or higher quality data were available, seed treatment exposure studies from the AHETF were used in the risk assessment. In addition, the throughput values used in PRVD2016-07 were updated to reflect current policies and throughput information from the AHETF. Refer to Tables 1-4 of this Appendix for more information.

For on-farm liquid hopperbox/seed drill treatment, a formulation-specific study was not available to characterize exposure for this scenario. A dry hopperbox seed treatment study was used as surrogate. As the surrogate study was conducted with a dust formulation, it likely overestimates exposure for a liquid formulation; however, it is the best data available for this method of on-farm seed treatment.

Animal Repellent for Ornamentals

The handler risk assessments for commercial applicators using the commercial-class product, and residential applicators using the domestic-class product, were updated based on comments and use information received during the PRVD consultation period. As described in PRVD2016-07, the potential for post-application exposure from animal repellent use was considered to be low.

Appendix VI Table 1 Vitaflo Products Commercial Seed Treatment Exposure and Risk Assessment^a

Crop	Form	Activity ^b	Application Rate (g a.i./100 kg seed)	Throughput ^c (kg seed/day)	MOE (Target =1000)		
					Dermal ^d	ST Inhalation ^d	Combined ^e
2009a ^b : Closed Mix/load, wearing single layer, CR gloves and CR coveralls for cleaners							
Wheat, barley, oat, rye	Liquid	Treater	49	92,000	375,000	206,300	133,000
		Bagger			3740	3710	1860
		Cleaner			3290	4750	1940
		Treater+cleaner			3150	4340	1880

Crop	Form	Activity ^b	Application Rate (g a.i./100 kg seed)	Throughput ^c (kg seed/day)	MOE (Target =1000)		
					Dermal ^d	ST Inhalation ^d	Combined ^e
Triticale		Treater	30	92,000	613,000	337,000	217,000
		Bagger			6100	6060	3040
		Cleaner			5370	7750	3170
		Treater+cleaner			5150	7580	3070
2010 ^h (corn): Closed Mix/load, wearing single layer, CR gloves.							
Corn	Liquid	Treater	111	60,000	870	5990 (resp) ^f	760
		Bagger, sewer, stacker			391	596 (DM) ^f	236
		Cleaner			211	555 (resp) ^f	153
Corn (lower rate)		Treater	42	60,000	2310	15,900 (resp) ^f	2010
		Bagger, sewer, stacker			1040	1580 (DM) ^f	626
		Cleaner			558	1470 (resp) ^f	404
2010 ^h (corn): Closed Mix/load, wearing CR coveralls over single layer, CR gloves.							
Corn	Liquid	Treater	111	60,000	1450	5990 (resp) ^f	1170
		Bagger, sewer, stacker			1050	596 (DM) ^f	380
		Cleaner			333	555 (resp) ^f	208
Corn (lower rate)		Treater	42	60,000	3830	15,900 (resp) ^f	3090
		Bagger, sewer, stacker			2780	1580 (DM) ^f	1010
		Cleaner			884	1470 (resp) ^f	552
2010 ^h (canola): Closed Mix/load, wearing coveralls over single layer, CR gloves							
Flax	Liquid	Treater	78	67,000	5320	2540	1720
		Bagger, sewer, stacker			7770	1900	1525
		Cleaner			679	1500 (resp) ^f	468
Soybean		Treater	39	63,000	11,300	5410	3660
		Bagger, sewer, stacker			16,500	4040	3250
		Cleaner			1360	3000 (resp) ^f	935
Pea (lower rate), bean		Treater	39	73,000	9770	4670	3160
		Bagger, sewer, stacker			14,300	3480	2800
		Cleaner			1360	3000 (resp) ^f	935
Pea, lentil		Treater	49	73,000	7780	3710	2510
		Bagger, sewer, stacker			11,400	2770	2230
		Cleaner			1080	2390 (resp) ^f	744
2000 ^h (canola): CR coveralls over single layer, CR gloves ^g							
Flax	Liquid	Cleaner	78	67,000	7190	5210	6140
Pea, lentil			49	73,000	11,400	8300	10,000
2004 ^h : Closed Mix/Load, wearing single layer, CR gloves. Cleaners also wore CR coveralls ^g							
Flax	Liquid	Bagger, cleaner	78	67,000	4420	3060	1810
Pea, lentil			49	73,000	6450	4470	2640

Crop	Form	Activity ^b	Application Rate (g a.i./100 kg seed)	Throughput ^c (kg seed/day)	MOE (Target =1000)		
					Dermal ^d	ST Inhalation ^d	Combined ^e
2006 ^h : Closed Mix/Load, wearing single layer, CR gloves. Cleaners also wore CR coveralls and face shield ^g							
Flax	Liquid	Treater ,cleaner	78	67,000	1190	9590 (resp) ^f	1060
Pea, lentil			49	73,000	1740	14,000 (resp) ^f	1550
Flax		Bagger, cleaner	78	67,000	4160	4450 (resp) ^f	2150
Pea, lentil			49	73,000	6070	6500 (resp) ^f	3140

Shaded cells indicate where the MOE does not meet or is not in the range of the target MOE and risks are not shown to be acceptable.

Resp= respirator; M/L/A = mixer/loader/applicator; Form = formulation; CR = chemical-resistant; Single layer = long-sleeved shirt, long pants; MOE = margin of exposure.

^a A separate risk assessment was conducted for Vitaflo seed treatment products primarily due to the establishment of a different dermal absorption value from other registered seed treatment products. See Appendix VI, Table 2 for the risk assessment for other commercial seed treatment products.

^b Activities are determined by the tasks performed by workers in each exposure study.

^c Throughput is dependent on seed type.

^d Based on an oral NOAEL of 1.86 mg/kg bw/day from a rat development neurotoxicity study. MOE = NOAEL/exposure. Exposure = [application rate × kg/1000 g × ATPD × unit exposure (Section 3.8) × DA (dermal route only)]/80 kg body weight] A dermal absorption value of 1% was used for activities where the worker would only handle the concentrated product (e.g. treaters). A dermal absorption value of 5% was used for all downstream activities and if the worker treating also performed downstream activities.

^e Combined MOE = NOAEL/ [1/dermal MOE)+(1/inhalation MOE)], as both the dermal and inhalation exposure could contribute to the oral endpoint.

^f When specified, respiratory protection was assumed in the risk assessment. For treaters and cleaners, a respirator ('resp') was assumed to be worn. For other activities (e.g. bagging), a filtering facepiece respirator ('DM') was assumed to be worn. Inhalation exposure was calculated using a protection factor of 80% for a filtering facepiece respirator (dust mask) and 90% for a respirator.

^g Study was considered in the risk assessment to assess chemical-resistant coveralls for cleaners.

^h 2009a= 2009, Fluquinconazole and Prochloraz: Determination of operator exposure during cereal seed treatment with Jockey fungicide in Germany, United Kingdom and France, DACO: 5.4

2010= 2010, Observational study to determine dermal and inhalation exposure to workers in commercial seed treatment facilities: Mixing/treating with a liquid pesticide product and equipment clean-out, DACO: 5.4

2000= 2013, Commercial Seed Treatment Plant Worker Exposure Study with Helix 289FS Seed Treatment on Canola, DACO: 5.3,5.4

2004= 2013, Determination of Operator Exposure to Imidacloprid during Seed Treatment of Oilseed Rape with Chinook FS 200 in the UK, DACO: 5.3,5.4

2006= 2013, Determination of Operator Exposure to Imidacloprid during Seed Treatment of Oilseed Rape with Chinook FS 200 in Germany, DACO: 5.3,5.4

Appendix VI Table 2 Commercial Seed Treatment Exposure and Risk Assessment (products other than Vitaflo 280) ^a

Crop	Form	Activity ^b	Application Rate (g ai/100 kg seed)	Throughput ^c (kg seed/day)	MOE (Target =1000)		
					Dermal ^d	ST Inhalation ^d	Combined ^e
2009a ^b : Closed Mix/load, wearing single layer, CR gloves and CR coveralls for cleaners							
Wheat, barley	Liquid	Treater	63	92,000	58,300	160,000	42,800
		Bagger			2910	2890	1450
		Cleaner			2560	3690	1510
		Treater+cleaner			2480	3630	1470
Oat		Treater	50	92,000	73,500	202,000	53,900

Crop	Form	Activity ^b	Application Rate (g ai/100 kg seed)	Throughput ^c (kg seed/day)	MOE (Target =1000)		
					Dermal ^d	ST Inhalation ^d	Combined ^e
		Bagger			3660	3640	1820
		Cleaner			3220	4650	1900
		Treater+cleaner			3090	4550	1840
2010 ^h (canola): Closed Mix/load, wearing coveralls over single layer, CR gloves							
Canola, rapeseed, mustard	Liquid	Treater	200	67,000	415	9910 (resp) ^f	398
		Bagger, sewer, stacker			3030	3700(DM) ^f	1670
		Cleaner			265	585 (resp) ^f	182
Canola, rapeseed, mustard (lower rate)		Treater	133	67,000	624	14,900 (resp) ^f	599
		Bagger, sewer, stacker			4560	5570 (DM) ^f	2510
		Cleaner			398	881 (resp) ^f	274
Soybean (export only)		Treater	45	63,000	1970	14,200 (resp) ^f	1730
		Bagger, sewer, stacker			14,400	3510	2820
		Cleaner			1180	2610 (resp) ^f	813
2000 ^h (canola): CR coveralls over single layer, CR gloves ^g							
Soybean (export only)	Liquid	Cleaner	45	63,000	12,500	9070	11,000
2004 ^h : Closed Mix/Load, wearing single layer, CR gloves. Cleaners also wore CR coveralls ^g							
Soybean (export only)	Liquid	Bagger, cleaner	45	63,000	7680	5330	3150
2006 ^h : Closed Mix/Load, wearing single layer, CR gloves. Cleaners also wore CR coveralls and face shield ^g							
Soybean (export only)	Liquid	Treater ,cleaner	45	63,000	2080	16,700 (resp) ^f	1846
		Bagger, cleaner			7230	7740 (resp) ^f	3740

Shaded cells indicate where the MOE does not meet or is not in the range of the target MOE and risks are not shown to be acceptable.

Resp= respirator; M/L/A = mixer/loader/applicator; Form = formulation; CR = chemical-resistant; Single layer = long-sleeved shirt, long pants; MOE = margin of exposure

^a This risk assessment applies to commercial seed treatment products, excluding Vitaflo 280 seed treatment products, as different dermal absorption values were determined for these products. See Appendix VI, Table 1 for the risk assessment for Vitaflo 280 and related commercial seed treatment products.

^b Activities are determined by the tasks performed by workers in each exposure study.

^c Throughputs are dependent on seed type.

^d Based on an oral NOAEL of 1.86 mg/kg bw/day from a rat development neurotoxicity study. MOE = NOAEL/exposure. Exposure = [application rate × kg/1000 g × ATPD × unit exposure (Section 3.8) × DA (dermal route only)]/80 kg body weight]. A dermal absorption value of 5% was included for all activities.

^e Combined MOE = NOAEL/ [1/dermal MOE)+(1/inhalation MOE)], as both the dermal and inhalation exposure could contribute to the oral endpoint.

^f When specified, respiratory protection was assumed in the risk assessment. For treaters and cleaners, a respirator ('resp') was assumed to be worn. For other activities (e.g. bagging), a filtering facepiece respirator ('DM') was assumed to be worn. Inhalation exposure was calculated using a protection factor of 80% for a filtering facepiece respirator (dust mask) and 90% for a respirator.

^g Study was considered in the risk assessment to assess chemical-resistant coveralls for cleaners. Only soybean was included in the additional analysis as it did not have risks of concern with other commercial treatment activities.

^h 2009a= 2009, Fluquinconazole and Prochloraz: Determination of operator exposure during cereal seed treatment

with Jockey fungicide in Germany, United Kingdom and France, DACO: 5.4

2010= 2010, Observational study to determine dermal and inhalation exposure to workers in commercial seed treatment facilities: Mixing/treating with a liquid pesticide product and equipment clean-out, DACO: 5.4

2000= 2013, Commercial Seed Treatment Plant Worker Exposure Study with Helix 289FS Seed Treatment on Canola, DACO: 5.3,5.4

2004= 2013, Determination of Operator Exposure to Imidacloprid during Seed Treatment of Oilseed Rape with Chinook FS 200 in the UK, DACO: 5.3,5.4

2006= 2013, Determination of Operator Exposure to Imidacloprid during Seed Treatment of Oilseed Rape with Chinook FS 200 in Germany, DACO: 5.3,5.4

Appendix VI

Table 3 On-Farm Seed Treatment Exposure and Risk Assessment for Mixing/Loading and Planting

Crop	Form	Activity ^a	Application Rate (g ai/100 kg seed)	Throughput ^b (kg seed/day)	MOE (Target = 1000)		
					Dermal ^c	Inhalation ^c	Combined ^d
						No Resp	
Dry application: 2005 ^g : Open loading, Closed cab planter, single layer, CR gloves							
Vegetable/fruit seeds (except carrot, sugar beet, onion)	WP (dust) ^g	Mix/load, plant	150-270	0.7-19.6	5370-150,000	2480-69,500	1700-47,500
Dry application and liquid hopperbox/seed drill application: 2005 ^f : Open loading, Closed cab planter, CR coveralls over single layer, CR gloves							
Corn, sweet	WP (dust) ^g	Mix/load, plant	165	550	861	145	124
Corn, field			90	1260	689	116	99
Mustard			270	900	322	54	46
Safflower			150	1080	482	81	69
Soybean			105	5230	142	24	20
Bean				800	93	16	13
Pea				960	78	13	11
Alfalfa			270	1080	278	47	40
Grasses				1200	241	41	35
Carrot				81	3570	601	514
Sugar beet				96	3020	507	434
Onion (dry bulb)			1875	140	298	50	43
Onion					2250	248	42
			240		2330	391	335
			Dust		1250	447	75
Soybean	Liquid ^h	40	5230	374	63	54	
Lentil			4320	452	76	65	
Pea			9600	204	34	29	
Liquid slurry application: 2007 ^j : Closed mixing/loading, Closed cab planter, coveralls over single layer, CR gloves							
Wheat	Liquid	Mix/load, plant	50	1400	38,000	10,320	8120
Barley				9700	5490	1490	1170
Oat				9150	5820	1580	1240
Rye			49	5380	10,100	2740	2160
Canola			198	640	21,000	5700	4480
Mustard				900	15,000	4050	3190
Triticale			30	16,800	5280	1430	1130
Corn, sweet			111.30	550	43,500	11,800	9280
Corn, field				1260	19,000	5150	4050
Flax			78	1660	20,600	5580	4390

Crop	Form	Activity ^a	Application Rate (g ai/100 kg seed)	Throughput ^b (kg seed/day)	MOE (Target = 1000)		
					Dermal ^c	Inhalation ^c	Combined ^d
						No Resp	
Bean			39	8000	8530	2320	1820
Soybean				5230	13,000	3540	2790
Lentil			49	4320	12,600	3410	2680
Pea				9600	5660	1540	1210
Liquid slurry application: 2006 ^{fj} : Open mixing/loading, Closed cab planter, single layer, CR gloves							
Corn, sweet	WP ⁱ	Mix/load, plant	165	550	4850	2570	1680
Corn, field			90	1260	3880	2060	1340
Mustard			270	900	1810	960	627
Safflower			150	1080	2720	1440	941
Soybean			105	5230	801	425	278
Bean				800	524	278	181
Pea				960	436	231	151
Alfalfa			270	1080	1570	830	543
Grasses				1200	1360	720	470
Vegetable/Fruit seeds			150-270	0.7-19.6	17,000-3,320,000	9000-1,230,000	5880-806,000
Onion (dry bulb)			1875	140	1680	888	581
Onion			2250		1400	740	484
			240		13,100	6940	4540
	Dust ⁱ	1250		2510	1330	871	
Liquid slurry application: 2006 ^{fj} : Open mixing/loading, Closed cab planter, coveralls over single layer, CR gloves							
Onion	Dust ⁱ	Mix/load, plant	1250	140	3580	1330	970
Liquid slurry application: 2006 ^{fj} : Open mixing/loading, Closed cab planter, CR coveralls over single layer, CR gloves							
Mustard	WP ⁱ	Mix/load, plant	270	900	2820	960	716
Soybean			105	5230	1450	425	320
Bean				800	814	278	207
Pea				960	679	231	173
Alfalfa			270	1080	2440	830	619
Grasses				1200	2111	720	537
Onion (dry bulb)			1875	140	2610	888	663
			2250		2170	740	552

Shaded cells indicate where the MOE does not meet or is not in the range of the target MOE and risks are not shown to be acceptable.

Resp = respirator; Form = formulation; CR = chemical-resistant; Single layer = long-sleeved shirt, long pants; WP = wettable powder; MOE = margin of exposure

^a Activities are determined by the tasks performed by workers in each exposure study.

^b Throughput is dependent on seed type, seeding rate and area planted.

^c Based on an oral NOAEL of 1.86 mg/kg bw/day from a rat development neurotoxicity study. MOE = NOAEL/exposure. Exposure = [application rate × kg/1000 g × ATPD × unit exposure (Section 3.8) × DA (dermal route only)]/80 kg body weight. A dermal absorption value of 5% was included for all activities.

^d Combined MOE = NOAEL/ [1/dermal MOE)+(1/inhalation MOE)], as both the dermal and inhalation exposure could contribute to the oral endpoint.

^e Respiratory protection was not considered feasible with a closed cab. As planting inhalation was not monitored separately from mixer/loader exposure, a respirator or dust mask protection factor could not be applied to the inhalation exposure.

^f The PPE in this study was open mix/load, closed cab, single layer and gloves. Protection factors were used to estimate exposure with higher levels of PPE. A protection factor of 75% was used for coveralls and 90% was used for chemical-resistant coveralls.

^g Wettable powder applied as a dust.

^h No data are available to assess hopper box treatment using a liquid. This study was used as surrogate and may overestimate exposure.

ⁱ No acceptable on-farm slurry seed treatment exposure studies were conducted with wettable powders or dusts. To estimate exposure, PHED mixer/loader unit exposure values for wettable powders were added to the liquid mixer/loader/planter unit exposure values.

^j 2005= 2005, Determination of Dermal and Inhalation Exposure to Workers During On-Farm Application of a Dry Hopper Box Pesticide Treatment to Seed, and Planing of Treated Seed, DACO: 5.4

2007= 2007, Dermal and Inhalation Exposure to Handlers of a Liquid Seed Treatment Fungicide During On-Farm Treatment of Cereal Grain, DACO: 5.4

2006= 2013, GAUCHO 480 SC - Worker Exposure During On-farm and Commercial Seed Treatment of Cereals, DACO: 5.3,5.4

Appendix VI

Table 4 Planting Exposure and Risk Assessment for Commercially Treated Seed and Imported Seed^a

Crop	Form	Application Rate (g ai/100 kg seed) ^b	Throughput ^b (kg/day)	MOE (Target = 1000)		
				Dermal ^c	Inhalation ^c	Combined ^d
					No Resp ^e	No Resp ^e
1990 ^k : Open loading, closed cab planting, single layer, CR gloves						
Bean	Liquid and imported ^j	39	8000	2250	43,000	2140
Canola, rapeseed		200	640	5480	105,000	5210
Mustard			896	3920	74,800	3720
	WP	270		2900	55,400	2760
Soybean	Liquid	39	8720	2060	39,400	1960
Pea		49	9600	1490	28,500	1420
Lentil			4320	3310	63,300	3150
Flax		78	1600	5620	107,000	5340
2007 ^k : Open loading, closed cab planting, single layer, CR gloves						
Corn, sweet (imported seeds)	Imported ^f	165 ^g	547	2180	1990	1040
	Liquid and imported ^j	111 (head smut) ^h		3230	2950	1540
		Corn, other types ⁱ		1260	1400	1280
Corn, other types ⁱ			83	1880	1720	897
		43	3710	3400	1770	
Cucumber, cantaloupe, pumpkin, squash, watermelon	Imported ^f	150 ^g	2-14	93,500-668,000	85,500-611,000	44,500-319,000
Beet, broccoli, Brussels sprouts, cabbage, cauliflower, celery, lettuce, pepper, radish, spinach, sugar beet, turnip, rutabaga		270 ^g	1-96	7580-606,000	6930-554,000	3620-290,000
Onion, tomato, eggplant		240 ^g	2-140	5850-390,000	5350-356,000	2790-186,000
Dry bulb onion		1875 ^g	140	748	684	357
		2250 ^g		624	570	298
2007 ^k : Open loading, closed cab planting, jacket over single layer, CR gloves						
Corn, field (corn smut)	Liquid and imported ^j	112	1260	1830	1270	750
Corn, field		83		2470	1720	1010
2013 ^k : Open loading, closed cab planting, single layer, jacket, CR gloves						
Wheat	Liquid and imported ^j	64	14,000	285	46	40
Wheat (lower rate)		34		536	87	75
Barley		64	9700	412	67	57
Barley (lower rate)		34		775	125	108

Crop	Form	Application Rate (g ai/100 kg seed) ^b	Throughput ^b (kg/day)	MOE (Target = 1000)		
				Dermal ^c	Inhalation ^c	Combined ^d
					No Resp ^e	No Resp ^e
Oat		50	9150	558	90	78
Rye		50	5380	949	153	132
Rye (lower rate)		34		1400	226	194
Triticale		30	16,800	506	82	71
Alfalfa	Imported ^f	270 ^g	1040	909	147	126
Grasses			1200	788	127	110

Shaded cells indicate where the MOE does not meet or is not in the range of the target MOE and risks are not shown to be acceptable.

Resp = respirator; WP = wettable powder; Form = formulation; CR = chemical-resistant; Single layer = long-sleeved shirt, long pants ; MOE = margin of exposure

^a Planting on-farm treated seed was addressed in the on-farm exposure studies.

^b Throughputs are dependent on seed type, seeding rate and area planted.

^c Based on an oral NOAEL of 1.86 mg/kg bw/day from a rat development neurotoxicity study. MOE = NOAEL/exposure. Exposure = [application rate × kg/1000 g × ATPD × unit exposure (Section 3.8) × DA (dermal route only)]/80 kg body weight. A dermal absorption value of 5% was included for all activities.

^d Combined MOE = NOAEL/ [1/dermal MOE)+(1/inhalation MOE)], as both the dermal and inhalation exposure could contribute to the oral endpoint.

^e Respiratory protection was not considered feasible with a closed cab; as planting inhalation was not monitored separately from mixer/loader exposure, a respirator or dust mask could not be applied to the inhalation exposure.

^f As the seed is imported, the formulation of the product used on the seeds would be unknown. However, this is not expected to have a significant impact on planter exposure.

^g Rates for imported seeds are from an on-farm dry application product label. It is unknown if these rates are reflective of the rates used on imported seeds.

^h The application rate for head smut is the highest rate on the commercial-class product labels for corn. Therefore, it was assessed separately from the other rates for corn also included on the commercial-class product labels.

ⁱ As a specific seeding rate was provided by RUAS for sweet corn, the term 'other type' of corn was used to capture the non-sweet corn varieties of corn, such as field corn.

^j As the risk assessment did not show that risks were acceptable for commercial treatment of these seeds, the planting of imported seeds was also assessed.

^k 1990= 1990, Exposures of Workers to Isfenphos during Planting of Oftanol Treated Canola Seed, DACO: 5.4
2007 = 2008, Determination of operator exposure to imidacloprid during loading/sowing of Gaucho treated maize seeds under realistic field conditions in Germany and Italy, DACO: 5.6
2013 = 2013, Determination of Dermal and Inhalation Exposure to Operators During Loading and Sowing Seed Treated with Austral Plus Net Using Conventional or Pneumatic Sowing Machines, DACO: 5.3,5.4

References

A. Information Considered in the Updated Health Assessment

Toxicology

List Studies/Information Submitted by Registrant

PMRA Document Number	Reference
2646650	2016, Registrant comments for the consultation on thiram, proposed re-evaluation decision, PRVD2016-07
2646660	2016, 104-week dietary combined chronic toxicity and carcinogenicity study with thiram in rats supplementary information on thyroid historical control data, DACO 4.4.4.
2646661	2016, Historical control data used in the support of Covance study no.6111-113, performed at Covance Laboratories Inc., DACO 4.4.4
2646662	2010, Thiram: morphometric examination of brains derived from a developmental neurotoxicity study in the CD Rat, DACO 4.4.14
2646658	1990, Mouse germ-cell cytogenetic assay with thiram, DACO 4.5.5
2646659	1991, Mutation assay in somatic cells of the mouse (mouse spot test) with thiram, DACO 4.5.5
2646666	1987, Micronucleus cytogenetic assay in mice, DACO 4.5.7

Additional Information Considered

Published Information

PMRA Document Number	Reference
2860984	2010, OECD (Organisation for Economic Co-operation and Development). Series on testing and assessment No. 124. Guidance for the derivation of an acute reference dose.
2860985	2016, EC (European Commission). Draft renewal assessment report prepared according to the commission regulation (EC) N 1107/2009. Thiram - volume 3 – B.6 (AS), DACO 12.5.4
2860986	2016, EC (European Commission). Draft renewal assessment report prepared according to the commission regulation (EC) N 1107/2009. Thiram - volume 1, DACO 12.5.4
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2860991	2003, USEPA (U.S. Environmental Protection Agency). Thiram – revised HED chapter of the reregistration eligibility decision document (RED), DACO 12.5
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List of Studies/Information Submitted by Registrant

PMRA Document Number	Reference
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1167575	Fungicides: Iprodione, Thiram: Insecticides: Lindane: Cercan ST Residue Studies in Mustard, Canada, 1995. (Ref:96-019.Dc). March 1996. Submitted: April 9, 1996.
1173746	Distribution and Metabolism of [14C]Thiram in Plants from Treated Sugarbeet Seed. D. Liu & R. Robinson. Study Completed on November 1, 1994. Date of Submission: November 20, 1997. Date Stamped-"Received Health Evaluation Division Nov 20 1997". (THT18595-003; 92252; XBL93031; RPT00202).
1173747	Uptake and Translocation of [14C]Thiram in Plants from Treated Wheat Seed. D. Liu & R. Robinson. Study Completed on November 4, 1994. Date of Submission: November 20, 1997. Date Stamped-"Received Health Evaluation Division Nov 20 1997". (THT18595-002; 91181; XBL92031; RPT00203).
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1209008	Crop Residue Data
1224385	Determination of Thiram and its 2 Metabolites in Soybeans (HLA 6111-126C)
1224386	Summary

1224387	Determination of Thiram and its Two Metabolites in Succulent Bean (HLA 6111-126E)
1224388	Determination of Thiram and its Two Metabolism in Dried Bean (HLA 6111-126F)
1224389	Determination of Thiram and its Two Metabolism in Cotton (HLA 6111-126J)
1224429	Summaries
1227500	Residues of Thiram and its Dithioglucoside & Monothioglucoside in Wheat (01492)
1227501	Residues of Thiram and its Dithioglucoside & Monothioglucoside in Field Corn (01486)
1227502	Residues of Thiram and its Dithioglucoside & Monothioglucoside in Sweet Corn (01487)
1227503	Residues of Thiram and its Dithioglucoside & Monothioglucoside in Soybeans (01494)
1227504	Residues of Thiram and its Dithioglucoside & Monothioglucoside in Succulent Beans (01484)
1227505	Residues of Thiram and its Dithioglucoside & Monothioglucoside in Cotton (01483) (Cont'd on Roll #791)
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Additional Information Considered

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2906737	Gerecke, A.C. and Sedlak D.L. 2003. Precursors of <i>N</i> -Nitrosodimethylamine in Natural Waters. <i>Environmental Science & Technology</i> . 37, 1331-1336.
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