Re-evaluation Decision RVD2020-12

Mancozeb and Its Associated End-use Products

Final Decision

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Re-evaluation decision for mancozeb and associated end-use products

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

Mancozeb is a multi-site contact fungicide. It is currently registered for the management of a large number of diseases on a variety of fruits and vegetable crops, outdoor ornamentals, forestry uses, greenhouse vegetables, greenhouse tobacco transplants, and seed treatments (including potato seed piece treatment). Mancozeb products are applied as a foliar treatment by ground and aerial application, as an in-furrow application and as a seed treatment. Mancozeb belongs to the group of fungicides commonly known as ethylene bis (dithiocarbamates) (EBDCs), along with the active ingredients metiram, maneb and nabam. In Canada, nabam has no registered food uses and maneb is not registered in Canada, which leave only mancozeb and metiram with food uses (metiram is registered for use on potato only). These EBDCs decompose to ethylene thiourea (ETU), whose cumulative risk profile is also taken into account in this re-evalution. Currently registered products containing mancozeb can be found in the Pesticide Label Search and in Appendix I. The Proposed Re-evaluation Decision PRVD2018-17, *Mancozeb and its Associated End-use Products*,[1] containing the evaluation of mancozeb and proposed decision, underwent a 90 day consultation period ending on 3 January 2019. PRVD2018-17 proposed the cancellation of all uses of mancozeb, except greenhouse tobacco, due to risks to human health and the environment that were not found to be acceptable.

Health Canada received comments and information relating to the health, environmental and value assessments. Commenters are listed in Appendix III. These comments are summarized in Appendix IV along with the responses by Health Canada. These comments and new data/information resulted in revisions to the toxicology, dietary, occupational and environmental risk assessments (see Science evaluation update), and resulted in changes to the proposed re-evaluation decision as described in PRVD2018-17.

A reference list of information used as the basis for the proposed re-evaluation decision is included in PRVD2018-17, and further information used in the re-evaluation decision is listed in Appendix XI of this RVD. Therefore, the complete reference list of all information used in this final re-evaluation decision includes both the information set out in PRVD2018-17 and the information set out in Appendix XI herein.

This document presents the final re-evaluation decision[2] for the re-evaluation of mancozeb, including the required amendments (risk mitigation measures) to protect human health and the

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*.

environment, and any label amendments required to bring labels to current standards. All products containing mancozeb that are registered in Canada are subject to this re-evaluation decision.

Re-evaluation decision for mancozeb

Health Canada has completed the re-evaluation of mancozeb. Under the authority of the *Pest Control Products Act*, Health Canada has determined that continued registration of products containing mancozeb is acceptable with additional risk mitigation measures. An evaluation of available scientific information found that the registrant supported uses of mancozeb products (ground and aerial foliar application to potatoes; ground foliar application on apples, onions, sugar beets, ginseng, field cucumbers, field tomatoes, grapes, pumpkin, squash, and melon (including cantaloupe but excluding watermelon and in-furrow application to onions) meet current standards for protection of human health and the environment and have value when used according to the revised conditions of registration which includes new mitigation measures. Label amendments, as summarized below and listed in Appendix X, 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 required amendments, including any revised/updated label statements and mitigation measures, as a result of the re-evaluation of mancozeb, are summarized below. Refer to Appendix X for details.

Uses not supported by manufacturers for re-evaluation will be removed from all product labels:

The following uses, formulations and application methods of mancozeb are cancelled due to lack of support from the manufacturers and were therefore not included in the updated assessments:

- All seed treatments (including potato seed piece treatment), greenhouse uses (in other words, tobacco, tomatoes), use on pears, carrots, celery, lettuce, watermelon, lentils, wheat, alfalfa grown for seed, as well as ornamentals and forestry uses.
- All applications using any hand held equipment.
- All end-use (commercial class) wettable powder or dust formulations.

Human health

Risk mitigation:

To protect workers, those entering treated areas, bystanders and the general public from occupational, residential, and dietary exposure, the following risk-reduction measures are required for continued registration of mancozeb in Canada:

The following uses are acceptable with the mitigation measures outlined below:

- Foliar application to potatoes, apples, onions, sugar beets, ginseng, field cucumbers, field tomatoes, grapes, pumpkin, squash, and melons, including cantaloupe but excluding watermelon.
- In-furrow application to onions.

Required mitigation measures:

- Applications to the above crops must occur at the reduced use pattern (lower application rate and/or maximum number of applications per year; new or longer preharvest intervals (PHIs) and application intervals) as proposed by the registrant(s).
- Engineering controls and personal protective equipment (PPE).
- Prohibition of use by handheld equipment.
- Prohibition of application by hand.
- Requirement for longer restricted-entry intervals (REIs) for certain crops and postapplication activities.
- Prohibition of use in residential areas.
- Revision of the residue definition for mancozeb to "mancozeb expressed as carbon disulfide (CS_2)".
- Revision of MRLs for crops supported by manufacturers to reflect the new residue definition and the reduced use pattern (lower application rate and/or maximum number of applications per year, new or longer PHIs and application intervals).
- Revocation of all other MRLs for mancozeb (that is, EBDC MRLs).

To reduce potential exposure to ethylene thiourea (ETU) from use of multiple ethylenebisdithiocarbamate (EBDC) pesticides:

- Requirement for a label statement limiting applications of both mancozeb and metiram so that the total quantity of active ingredients does not exceed the specified maximum seasonal rate for either active ingredient.

To protect bystanders from spray drift:

- Requirement for a label statement to promote best management practices to minimize human exposure from spray drift or spray residues resulting from drift.

Environment

Risk mitigation:

To protect the environment, the following risk-reduction measures are required:

- Standard label statements are required to minimize potential risks resulting from runoff.
- Standard label statements to inform users of the potential toxic effects to sensitive biota.
- Buffer zones are required to mitigate risks from spray drift.
- Hazard statements are required on product labels warning of the potential for leaching and groundwater contamination.
- Updated discharge of effluent statements.
- Updated storage statements.

Value

Label improvements to meet current standards:

- Update labels according to Regulatory Directive DIR2013-04, *Pesticide Resistance Management Labelling Based on Target Site/Mode of Action*, including updating the fungicide group code to M3.
- Tank mix partners must be clearly indicated, by product name, on mancozeb product labels. Specific directions regarding use of the tank mix, or a reference to the tank mix partner label, must be included. A general reference that "this product can be tank mixed with other products" is not acceptable. Therefore, remove any vague or non-specific claims that the product can be tank mixed with another pesticide.

Risk mitigation:

- Remove any vague reference to “apply as needed”, or “apply as required”. Directions for Use should reflect the use-specific re-application interval.

Next steps

To comply with this decision, the required amendments (mitigation measures and label updates) must be implemented on all product labels no later than 24 months after the publication date of this decision document. Accordingly, both registrants and retailers will have up to 24 months from the date of this decision document to transition to selling the product with the newly amended labels. Similarly, users will also have the same 24-month period from the date of this decision document to transition to using the newly amended labels, which will be available on the Public Registry.

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.

Refer to Appendix I for details on specific products impacted by this decision.

Other information

Any person may file a notice of objection[3] regarding this decision on mancozeb and its associated end-use products 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 the Canada.ca website (Request a Reconsideration of Decision) or contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (hc.pmra-info-arla.sc@canada.ca).

The relevant confidential test data on which the decision is based (as referenced in PRVD2018-17 and in Appendix XI of this document) are available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa). For more information, please 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 Introduction

Health Canada received comments and information relating to the health, environmental and value assessments of products containing mancozeb. These comments and new data/information resulted in revisions to the toxicology, dietary, occupational and environmental risk assessments and resulted in changes to the proposed re-evaluation decision as described in PRVD2018-17, *Mancozeb and Its Associated End-use Products*.

In addition, the following uses, formulations and application methods of mancozeb are cancelled due to lack of support from the manufacturers and were not included in the updated assessments:

- All seed treatments (including potato seed piece treatment), greenhouse uses (in other words, tobacco, tomatoes) use on pears, carrots, celery, lettuce, watermelon, lentils, wheat, alfalfa grown for seed, as well as ornamentals and forestry uses.
- All applications using any hand held equipment.
- Any end-use (commercial class) wettable powder or dust formulations.

The revised use pattern proposed and supported by manufacturers, which formed the basis for the updates to the risk assessments is outlined in Appendix II.

2.0 Revised health risk assessment

2.1 Toxicology assessment for mancozeb

Comments and new toxicology information were received from the registrants in response to the consultation document on mancozeb, PRVD2018-17. Comments addressed a range of issues and included the significance of retinopathy in rats, the outcomes of developmental inhalation toxicity study in rats and dog studies to derive reference values, as well as interpretation of available genotoxicity studies for cancer risk assessment. Scientific data submitted to address deficiencies noted in PRVD2018-17 included a developmental neurotoxicity (DNT) study for mancozeb with a discussion on the statistical analysis, an extended one generation reproduction toxicity study (EOGRTS) on its metabolite ethylene thiourea (ETU), recent (2015) developmental toxicity studies and immunotoxicity studies for mancozeb and its metabolite ETU, respectively. In addition, available scientific literature studies were evaluated and reviews from other regulatory agencies (European Food Safety Authority (EFSA), United States Environmental Protection Agency (USEPA)) were consulted. As a result of the assessment of the new information submitted, Health Canada has revised the *Pest Control Products Act* factor (PCPA factor) and consequently updated the toxicology reference values for mancozeb and its metabolite ETU. Detailed responses to the comments received are provided in Appendix IV. The evaluation of new studies and information is reflected in Appendix V, Tables 1a and 1b. Updates to toxicology reference values for risk assessment are reflected in Appendix V, Tables 2a and 2b.

Following the evaluation of new data on mancozeb, the outcomes of the dietary DNT study in rats were used to derive the acute reference dose (ARfD) for females 13–49 years of age, and the

short- and intermediate-dermal endpoint. In this study, mancozeb dietary exposure at 5, 15, and 30 mg/kg bw/day from gestational day (GD)-6 to post-natal day (PND)-72 demonstrated maternal treatment-related effects on thyroid weight and thyroid histopathology at the highest dose tested. In addition, a decrease in maternal body weight gain during gestation, and thyroid hormonal changes during gestation and lactation periods also occurred in a concurrently conducted dose range-finding study. A maternal no observed adverse effect level (NOAEL) of 15 mg/kg bw/day was determined. Offspring post-weaning body weights and overall (PND 28-72) body weight gains were similar to controls at all dose levels. However, a slight decrease (not statistically significant) in pup body weight gain was observed during PND 0-4 period. It should be noted that a decrease in pup body weight (11–22%) was observed from PND 7-21 in the concurrently reviewed dose range-finding study at a dose level ≥ 30 mg/kg bw/day.

In the main study, no treatment-related effects on viability/survival, litter parameters, or sexual maturation were observed in the F1 pups. The functional observational battery (FOB) parameters, locomotor activity, brain weight or brain morphometric measurements, and gross or microscopic lesions, were not affected by mancozeb exposure in the F1 pups.

Learning assessment in a Biel water maze on PND 22 demonstrated statistically significant treatment-related effects (elevated level of errors and time to escape for trails 11–12) for the high-dose group females. Therefore, an offspring NOAEL of 15 mg/kg bw/day was identified for this DNT study based on the memory effects of PND-22 females and body weight decrease in the concurrently reviewed dose range-finding study. No sensitivity of the young was evident in the main study, as the developmental effects occurred at a dose level where some maternal thyroid toxicity occurred.

In the EOGRT study for ETU, which included a developmental neurotoxicity component and characterization of thyroid effects at multiple life stages, the animals were exposed to the ETU level of 0.2, 2, 10 mg/kg bw/day. The EOGRT study confirmed that the thyroid is the most sensitive target organ for ETU-induced toxicity. Thyroid treatment-related effects included significant changes in the thyroid hormone profile, thyroid weights, and thyroid histopathology (follicular cell hypertrophy/hyperplasia) at dose levels ≥ 2 mg/kg bw/day ETU in both males and females at multiple life stages. At 0.2 mg ETU/kg bw/day, the lowest dose level in the study, there was a change in thyroid histopathology (follicular cell hypertrophy) in P1 males (20 of 27 animals affected) and F1 Cohort 1A males (15 of 26 animals affected), which was accompanied by pituitary gland hypertrophy (very slight 9/26), demonstrating a perturbation of the hypothalamus-pituitary-thyroid (HPT) axis at this dose level. Therefore, an offspring lowest observed adverse effect level (LOAEL) for males of 0.2 mg/kg bw/day was selected.

Reproductive parameters were not affected in the P generation, however, a reproduction NOAEL of 2 mg/kg bw/day was identified based on the increased proportion of abnormal sperm and increased ovarian follicle count for the F1 generation in high dose males and females, respectively.

Results from the neurotoxicity cohort of the EOGRT study suggested that brain weight decrease and decreases in gross brain measurements in all ETU high dose level males and females were treatment related and consistent with findings in the Cohort 1 A males and parental female animals. Habituation of the auditory startle reflex (ASR) in the high dose level animals was also

affected. However, the power of the study was low (40%), thus, no conclusion could be made on whether the statistically significant effects in the high dose group were real. In addition, there were statistically significant brain linear measurement changes affecting all dose levels, but without a clear dose response relationship in some parameters. The potential relationship of these changes with the possible structural defects caused by hypothyroidism remains a concern and also remains unclear for the mid- and low-dose level animals. Therefore, the neurotoxicity cohort of EOGRT study is considered a screening level assessment and a NOAEL for developmental neurotoxicity was identified at a dose level of 2 mg/kg bw/day.

Newly submitted adult immuno-toxicity studies for both mancozeb and ETU were negative for treatment-related effects on the primary immune response to sheep red blood cells in male rats. In both studies, the NOAEL for immuno-toxicity was at the highest dose level tested.

The most recent developmental toxicity study for mancozeb (2015) confirmed that ETU was transferred in utero from dams to pups, with a plasma ratio of 1. A maternal NOAEL of 40 mg/kg bw/day was identified for mancozeb based on body weight and food consumption decrease. No sensitivity of the young was observed and a developmental NOAEL of 160 mg/kg bw/day for mancozeb was selected.

There were no maternal treatment related effects in a newly submitted ETU developmental toxicity study in rats at any of the dose levels tested (5, 15 or 30 mg/kg bw/day) on GD 6-19. However, at the highest dose level, numerous fetal head and skeletal developmental malformations were observed. The developmental NOAEL of 5 mg/kg bw/day was based on the increased incidence of hydrocephalus. As previously noted, fetal effects were observed in the absence of maternal toxicity.

In a newly submitted rabbit developmental toxicity study, ETU was administered to female rabbits by gavage on GD 7-29 at dose levels of 0, 5, 15, or 50 mg/kg bw/day. Maternal body weight gains and food consumption were reduced for the duration of the study in the mid- and high-dose groups. Thyroid weight increase seen in the top dose level females was associated with discoloration and enlarged gland. An increase in post-implantation loss, as well as in resorption number (litter mean) was noted in mid- and high-dose level dams. Fetal weights were statistically significantly decreased in the mid- and high-dose groups. Two fetuses in separate litters of the high-dose group had domed heads (hydrocephaly), a recognized effect of ETU treatment in rats. No sensitivity of the young was noted in the study. The NOAEL for maternal and developmental toxicity was identified at 5 mg/kg/day dose level.

The evaluation of the above additional studies led to the reassessment of developmental and reproductive toxicity and the applied *Pest Control Products Act* uncertainty factor for mancozeb and ETU. For mancozeb, no sensitivity of the young was noted in the developmental rat and rabbit toxicity studies via gavage, or in a developmental study in rats via inhalation exposure. In rats and rabbits, the primary maternal effect after oral exposure was decreased body weight and body-weight gain, and, at the highest dose tested, there were abortions and resorptions, and increased mortality. High dose pups in the rat developmental studies at a dose level $\geq$ 360 mg/kg bw/day had increased incidences of brain malformations, forelimb flexure, and decreased fetal body weight. These effects in rats are consistent with rat developmental effects evident after ETU administration. In a published rat developmental inhalation study, dams at the highest dose

tested had decreased body-weight gain, hindlimb weakness, slower righting reflexes. The hindlimb weakness correlates with the effects observed in the short-term neurotoxicity study, and with the maternal findings (mild hind leg paralysis) in a published DNT study. The developmental neurotoxicity potential was characterized by the evaluation of the new DNT study in rats. The neurotoxic effect of mancozeb (memory effects in female rats in Biel water maze) were considered serious endpoints, since the concern is for a dose-effect occurring at a particular sensitive window or point in development. However, the level of concern was tempered by the presence of maternal toxicity. The PCPA factor was reduced to threefold when using the rat (oral or inhalation) or rabbit developmental toxicity studies, or the rat DNT study to establish a point of departure (POD) for risk assessment.

For ETU, with respect to pre- and postnatal toxicity, sensitivity of the young was observed in numerous rat developmental studies. Multiple and serious head, central nervous system and skeletal malformations were noted after 1–2 doses via either the dermal or oral route of exposure. These effects occur at non-maternally toxic doses. The new developmental toxicity study in rat confirmed a NOAEL of 5 mg/kg bw/day for serious developmental malformations in the absence of maternal toxicity. ETU was also developmentally toxic to the rabbit, but no sensitivity of young was observed. A published cat study demonstrated less severe developmental toxicity at doses similar to the rat, but these dose levels were also maternally toxic. Although sensitivity of the young was identified in developmental toxicity studies, no sensitivity of the young was noted in the EOGRT study, which characterized potential reproductive and developmental neurologic effects. The PCPA factor of 10-fold was retained where the new rat developmental toxicity study was used to establish the POD for ETU for risk assessment. The use of thyroid toxicity-based NOAEL values derived from the EOGRT study as a POD for various exposure scenarios is protective of the developmental toxicity noted in the new rat developmental toxicity study. Therefore, the PCPA factor was reduced to onefold when the EOGRT study is used to define the POD for risk assessment.

2.2 Dietary exposure and risk assessment

In PRVD2018-17, dietary risks were shown to be acceptable for mancozeb. However, for ETU, dietary risk, specifically the lifetime cancer risk, was not shown to be acceptable. Therefore, all food uses or uses contributing to the diet through drinking water were proposed for cancellation.

In response to PRVD2018-17, the Mancozeb Task Force (MTF) provided extensive comments, including a list of prioritized uses and crops supported with a reduced use pattern (in other words, lower application rate and/or maximum number of applications per year; new or longer PHIs and application intervals). In addition, new data were submitted. The comments relevant to the dietary exposure assessment and Health Canada's responses, including how the new data were considered, are summarized in Appendix IV.

The dietary assessments for mancozeb and ETU were updated by including only those crops identified in the list of prioritized crops provided by the MTF. These crops are apples, cucumbers, ginseng, grapes, melons (including cantaloupe, but excluding watermelon), onions, potatoes, pumpkin, squash, sugar beets and field tomatoes. Potential residues from all other crops, including imported commodities, were assumed to be zero. In addition, the dietary assessments were updated using the revised toxicology reference values, available monitoring

data from the Canadian Food Inspection Agency (CFIA) for the years 2013–2017, revised experimental processing factors, and updated percent crop treated data and domestic production and import statistics. For drinking water, a new, lower estimated environmental concentration from a water monitoring study was used for the ETU cancer assessment.

As mancozeb is not expected to occur in drinking water, the dietary assessment for mancozeb was based on exposure from food only. For ETU, the dietary assessment was based on exposure from both food and drinking water. A quantitative cancer risk assessment was not conducted for mancozeb as it was considered to be addressed by the cancer risk assessment of ETU. The results of the updated dietary assessments are as follows:

- For mancozeb, acute and chronic (non-cancer) risks from exposure through food only were shown to be acceptable for all subpopulations.
- For ETU, acute and chronic (non-cancer) risks from exposure through food and drinking water were shown to be acceptable for all subpopulations.
- For ETU, the lifetime cancer risk from exposure through food and drinking water was shown to be acceptable at 1×10^{-6}.

The detailed results of the dietary assessment are presented in Appendix VI. Details of the drinking water estimated environmental concentrations are provided in Appendix IX.

Maximum residue limits (MRLs) and residue definition

Currently, Canadian MRLs for EBDC fungicides, including mancozeb and metiram, are specified for a number of commodities on the basis of a residue definition expressed as manganese and zinc ethylenebis (dithiocarbamate) (polymeric). Residues on other crops with registered uses are regulated under the general MRL (GMRL) of 0.1 ppm. As noted in PRVD2018-17, chemical-specific enforcement methods for the EBDC fungicides, including mancozeb, are not currently available. Therefore, Health Canada had proposed to revise the residue definition for mancozeb to residues of "mancozeb expressed as carbon disulfide (CS_2)."

As a result of the re-evaluation of mancozeb, the following MRL actions are required:

- Revision of the residue definition for mancozeb to "mancozeb expressed as carbon disulfide (CS_2)", as proposed in PRVD2018-17.
- Revision of MRLs for crops supported by the MTF to reflect the new residue definition and the reduced use pattern (lower application rate and/or maximum number of applications per year, new or longer PHIs and application intervals). These crops are apples, cucumbers, ginseng, grapes, melons (including cantaloupe, but excluding watermelon), onions, potatoes, pumpkin, squash, sugar beets and field tomatoes.
- Revocation of all other MRLs for mancozeb (that is, EBDC MRLs).

Changes to MRLs for the EBDC fungicides will be published as a Proposed Maximum Residue Limit (PMRL) document for consultation.

There are no MRLs established for ETU under the *Pest Control Products Act*. However, ETU is regulated as a contaminant in foods from all sources under Division 15 of the Food and Drug

Regulations. ETU is in Part 1 of the List of Contaminants and Other Adulterating Substances in Foods, which stipulates that no amount of ETU is considered acceptable in foods, with some exceptions when included in Part 2 of the List. In Part 2 of the List, a maximum level of 0.05 ppm is specified for ETU in fruits, vegetables and cereals. As noted above, the lifetime cancer risk from dietary exposure to ETU was shown to be acceptable when all crops supported by the MTF were considered and when residues from other crops, including imported commodities were assumed to be zero. Imports are a major source of exposure, which would normally require risk-based MRLs to reflect the dietary assessment conducted for ETU. However, the current maximum level of 0.05 ppm is close to the highest limit of quantification (LOQ) of 0.04 ppm of the enforcement methods used by the CFIA. Therefore, the current regulations for ETU as a contaminant in foods is sufficiently protective. The establishment of a health risk-based MRL for ETU from pesticide sources under the *Pest Control Products Act* is not required.

2.3 Occupational and non-occupational risk assessment

In PRVD2018-17, occupational risks were not shown to be acceptable for some application and postapplication scenarios. Calculated restricted-entry intervals (REIs) were not considered to be agronomically feasible for some crops. Since all uses were proposed for cancellation due to dietary risks, mitigation measures for occupational exposure were not proposed at that time.

During the consultation period for PRVD018-17, additional information was received from the registrants and grower groups. A list of prioritized uses/crops that were supported as well as uses/crops/formulation and application methods no longer supported by the registrants were provided. For the supported crops, a reduced use pattern was proposed (in other words, lower application rate and/or maximum number of applications per year; new or longer PHIs and application intervals). Only the supported uses were considered in the updated occupational risk assessment for mancozeb (Appendix II). These uses are apples, cucumbers, ginseng, grapes, melons (including cantaloupe, but excluding watermelon), onions, potatoes, pumpkin, squash, sugar beets and field tomatoes.

Health Canada responses to specific comments are provided in Appendix IV. Details regarding the updated occupational risk assessment are presented in Appendix VII.

The occupational and bystander exposure and risk assessments were updated to incorporate the revised toxicology reference values, additional use information, the reduced use pattern of the supported crops, and to reflect current evaluation standards. Comments were received and considered in the updated health risk assessment (see Appendix IV).

For mixers/loaders and applicators, non-cancer and cancer risks for both mancozeb and ETU were shown to be acceptable, provided that engineering controls and additional PPE are employed. Engineering controls include the requirement of closed cab groundboom application for custom applicators. Additional PPE includes the required use of a respirator when mixing/loading dry flowable formulations, or when applying dry flowable formulations using an open cab groundboom, and to wear a chemical-resistant hat when applying using an open cab airblast. See Appendix X for all specific required mitigation measures.

For postapplication workers, non-cancer and cancer risks were shown to be acceptable for both mancozeb and ETU, provided that the required REIs are followed. See Appendix X for required crop- and activity-specific REIs. These REIs are considered to be agronomically feasible.

For the bystander assessment, which considered exposure from spray drift or volatilization of mancozeb, risks were shown to be acceptable for both mancozeb and ETU. The detailed results of the bystander assessment are presented in Appendix VII (Tables 7–11).

2.4 Aggregate exposure and risk assessment

In PRVD2018-17, separate aggregate risk assessments were conducted for mancozeb and for ETU. Since dietary cancer risks were not shown to be acceptable for ETU, the aggregate risk assessments were limited to exposure from food and drinking water only and did not consider non-occupational sources. For the current assessment, the aggregate assessments were updated to consider non-occupational exposures, since dietary risks in the updated assessments (see Section 2.2) are now shown to be acceptable.

Potential non-occupational exposures to mancozeb and ETU could occur to bystanders from spray drift and/or volatilization. The bystander assessment was updated and risks were shown to be acceptable for both mancozeb and ETU (see Section 2.3). For the aggregate assessment, bystander inhalation exposure from spray drift/volatilization is combined with the dietary exposure. The aggregate risk is shown to be acceptable.

2.5 Cumulative assessment

Mancozeb belongs to a group of pesticides known as the EBDCs fungicides. These pesticides share a common metabolite, ETU. A common mechanism of ETU toxicity on which to base a cumulative assessment is confirmed and is well characterized for mancozeb and metiram. The risk characterization for ETU showed the thyroid-related effects to be the most sensitive endpoint in the EBDCs database. This is consistent with other regulatory authorities (USEPA, EFSA Thyroid Cumulative Risk Assessment).

A cumulative risk assessment for the pesticidal uses of EBDCs based on ETU was considered. Exposure to ETU in food and drinking water may occur from the use of mancozeb or any other EBDC fungicide. Currently, metiram is the only other EBDC fungicide with registered food uses in Canada, while nabam is registered in Canada for industrial uses only. Exposure to ETU in the environment may also occur from non-pesticidal sources of ETU. These sources are regulated under the *Canadian Environmental Protection Act* (1999). The aggregate assessment for ETU, which included bystander exposure, is also considered to reflect a cumulative risk assessment, since food and drinking water were assessed using monitoring data, which likely captures exposure to ETU from all pesticide sources. To limit potential exposure to ETU from the use of multiple EBDC fungicides, the following label statement is required on product labels for mancozeb and metiram:

“The total seasonal application of mancozeb and metiram cannot exceed the maximum seasonal quantity on potatoes of one or the other active ingredient with no more than 3 applications being metiram.”

2.6 Health incident reports

As of 21 April 2020, seven human, one domestic animal, and one human and domestic animal incident report were submitted to Health Canada.

In the human incidents, which included multiple active ingredients, exposure often occurred via the respiratory or ocular routes. Three of the human incidents were considered to be at least possibly associated with the pesticide exposure; reported symptoms included eye or respiratory irritation and vomiting. The remaining incident reports, including the three serious human incidents, did not contain sufficient information to determine an association to the pesticide exposure or were unrelated to the exposure. Overall, given the presence of multiple active ingredients and the lack of exposure information in the serious human incidents, as well as the relatively minor nature of symptoms reported in the minor or moderate cases along with the precautionary statements already included on the product labels, no additional mitigation measures are required based on the review of these incident reports.

Domestic animal incidents involved dogs that experienced seizures, but the exposures involved multiple active ingredients and the reports did not contain sufficient information to determine whether the reported effects were associated with the pesticide exposure. Based on the presence of multiple active ingredients and lack of exposure information in the incidents, as well as the precautionary statements aimed at reducing the likelihood of spray drift that already appear on the product labels, no additional mitigation measures are required based on the review of these incident reports.

3.0 Updated environmental risk assessment

The environmental risk assessment has been updated based on the revised use pattern proposed by the Mancozeb Task Force (MTF) (Appendix II). Additional information submitted by the MTF, comments and information received from grower groups and the public during the consultation period and information from the 2018 European Commission review (PMRA# 3017377–3017383) have been considered. Updated estimated environmental concentrations (EECs) and changes to the risk assessment for both mancozeb and its transformation product ethylenethiourea (ETU) are summarized below.

3.1 Fate and behaviour in the environment

Environmental fate studies reviewed for PRVD2018-17 had deficiencies that made reliable estimation of mancozeb half-lives in soil and water challenging. These deficiencies included lack of study details, poor mass balance, extraction/analytical methods that were not specific to measuring mancozeb and/or chromatographic separation problems (in other words, HPLC – column smearing or peak streaking) and a high percent of applied radioactivity (AR) reported as unextractable residues. As a result, the biotransformation half-lives derived for PRVD 2018-17 were based on total extracted radioactivity. The aerobic DT_{50} values reported in PRVD2018-17 ranged from 2 to 8 days in soil and 19.9 to 62.4 days in aquatic systems. Due to the deficiencies in the available studies, the EECs included mancozeb and transformation products, making them highly conservative.

Revised summaries of the environmental fate and behaviour of mancozeb and ETU are presented in Appendix VIII, Tables 1 and 2. New fate information addressed the deficiencies identified in PRVD2018-17 and provided evidence that hydrolysis is a major route of transformation of mancozeb in the environment. Hydrolysis half-lives for parent mancozeb range from 0.7 (pH 7) to 1.9 days (pH 9) at 25°C. The hydrolytic transformation products identified include ethyleneurea (EU) and ETU as well as the intermediate species ethylenebisisothiocyanide sulfide (EBIS) and hydantoin. Mancozeb does not photolytically degrade on dry soil, however, rapid decomposition would be expected in moist soil due to hydrolysis. Due to its hydrolytic instability, the solubililty of mancozeb is difficult to measure but is considered to range from 6–20 mg/L. Volatilization from water and/or dry/moist soil surfaces is not expected to be an important route of dissipation.

In the terrestrial environment, mancozeb is expected to be non-persistent under aerobic soil conditions (laboratory aerobic DT_{50}<2 days). The short DT_{50} values determined for mancozeb from soil biotransformation studies are thought to be attributable to hydrolysis rather than aerobic soil-biotransformation. Major transformation products (>10%) included ETU, EU, EBIS and M11.

Adsorption studies indicate mancozeb and the suite of transformation products formed from rapid hydrolysis bind strongly to soils, with ETU partitioning mainly into the aqueous phase. These results are consistent with soil column leaching experiments that show the majority of applied radioactivity remained in the uppermost soil layers. Uncharacterized leached radioactivity from the soils ranged from 4–19% of AR. Given the low solubility and rapid hydrolysis of mancozeb, once solubilized it is likely that mancozeb would not be available for leaching. When taking into consideration the criteria of Cohen et al. (1984) and the groundwater ubiquity score (GUS) it was determined that mancozeb is likely a non-leacher. This is consistent with the results of the available field dissipation studies that indicate limited downward movement of mancozeb. Mancozeb, therefore, is not expected to leach and reach groundwater. ETU undergoes rapid aerobic biotransformation, is non-persistent and has the potential to leach.

In the aquatic environment, mancozeb is expected to be non-persistent under aerobic aquatic conditions (laboratory aerobic DT_{50} values range from 0.2–1.0 days). The rapid dissipation of parent mancozeb under aerobic aquatic conditions is thought to be attributable to hydrolysis

rather than biotransformation. Major transformation products identified included EBIS, ETU and EU which were found predominantly in the water phase of test systems.

Acceptable anaerobic biotransformation studies were not available for review. Due to rapid hydrolysis, mancozeb would be expected to break down before anaerobic conditions (in soil and/or water) develop after application.

In addition to the log octanol/water partitioning coefficient (K_{ow} = 1.33), which suggests mancozeb has a low potential for bioaccumulation in aquatic biota, rapid hydrolysis reduces exposure. Bioaccumulation by aquatic organisms is expected to be low.

During the consultation periods, the MTF submitted additional mancozeb residue decline data on crop foliage, grass and insects. The bird and mammal risk assessment was updated with DT_{50} values calculated from this data to derive cumulative EEC values on food items following multiple applications of mancozeb.

3.2 Environmental toxicology

Environmental toxicity data for mancozeb and ETU are summarized in Appendix VIII, Tables 3–6. This information consists of data previously considered (PRVD2018-17); additional toxicity information reported in the 2018 European Commission (EC) review (PMRA# 3017377–3017383), as well as toxicity studies submitted by the MTF during the consultation period for PRVD2018-17.

No environmental toxicity information is available for the transformation products of mancozeb other than ETU. Major transformation products identified in fate studies include EBIS, M11, ETU and EU.

EBIS and M11 are both transient in nature. As short-lived transformation products, they are degraded almost as quickly as they are formed from mancozeb, and as such they are expected to occur only at low levels that do not persist and accumulate in soil, water or biota. Because analytical measurements for mancozeb in toxicity studies were predominantly performed using CS2-liberation methods, any analyses measuring CS2 would also include EBIS because it is also a dithiocarbamate; therefore, the conclusions made for mancozeb would be applicable to EBIS.

M11, an unidentified transformation product observed in aerobic soil, also appears to be transient and formed immediately after mancozeb is applied (in other words, peaking at 16.6–20.3% of applied radioactivity at 1.44 hours but declining to <LOD – 1.7% AR after 24 hours). Due to its rapid formation and short-lived nature observed in soil, M11 is not considered to pose a risk to biota.

EU is produced through transformation of ETU. Because EU is formed from ETU, environmental levels are not expected to exceed those of ETU. Although toxicity endpoints for EU are not considered in the ETU risk assessment, a review of aquatic toxicity data reported in the recent 2018 European Commission review of EDBCs and ETU shows that EU is less toxic than ETU. Health Canada, therefore, considers the aquatic risk assessment for ETU to be inclusive of any potential risks to organisms resulting from the application of mancozeb.

3.3 Environmental risk characterization

The environmental risk assessment was updated to reflect the revised use pattern proposed by the MTF and considers newly available information (environmental fate and toxicology).

3.3.1 Risk to terrestrial organisms from mancozeb

Earthworms

The 14-day LC_{50} for the earthworm *Eisenia foetida* is > 1000 mg a.i./kg soil. At the maximum proposed single application rate for onions (6600 g a.i./ha – granular application in-furrow), the calculated EEC in soil is 2.9 mg a.i./kg soil. The associated risk quotient (RQ) based on the proposed seasonal rate for apples (RQ < 0.003) indicates that mancozeb is not expected to pose an acute risk to earthworms.

On a chronic basis, the lowest chronic NOEC value for mancozeb is 10 mg a.i./kg soil dw based on reduced reproduction potential (in other words, number of juveniles) in *Folsomia candida*. The associated RQ based on the maximum proposed seasonal application rate is 0.3. Mancozeb is not expected to pose a chronic risk to earthworms.

Pollinators

Honey bees can be exposed to mancozeb from direct application or contact with treated plant material, or through ingestion of pollen and nectar that has been directly sprayed. Developing bees could be exposed through consumption of contaminated pollen and nectar brought back by foraging bees. Mancozeb is not systemic, therefore it is not expected to be translocated through plants into pollen and nectar.

Based on the risk assessment presented in PRVD2018-17, a risk to honeybees was not anticipated at the highest single application rate for pears (4.5 kg a.i./ha); however, this initial pollinator risk assessment only considered adult bee acute contact and oral toxicity data. The current pollinator risk assessment considers new information, which includes:

1. An acute honeybee toxicity study submitted by the MTF during the consultation period for PRVD2018-17.

2. Bee toxicity data reported in the 2018 EC review (PMRA# 3017377–3017383), including honey bee acute adult toxicity with technical grade active ingredients and end-use products, larval toxicity, adult chronic toxicity, and a higher tier feeding study to examine larval, adult and colony effects, as well as bumble bee acute toxicity.

Bee EECs for contact and dietary exposure were estimated using the single maximum mancozeb foliar application rate proposed for apples (4.5 kg a.i./ha) and cucumber (2.44 kg a.i./ha).

The screening level risk assessment is presented in Appendix VIII, Tables 7 and 8. The risk to adult bees is below the LOC for all foliar applications of mancozeb based on acute contact exposure. Foliar application of mancozeb pose potential acute and chronic dietary risks to adult bees and a potential chronic risk to brood (RQ values up to 4.4).

Field data, reported in the 2018 EC review (PMRA# 3017377–3017383), demonstrates that mancozeb applied as treated 50% aqueous sugar solutions at two feeding rates (0.266 and 0.445 g a.i./500 g sugar solution) did not adversely affect the survival (adult and pupal mortality) and fitness of honeybee colonies (honeybee behaviour, colony strength, brood development, food storage area development).

Although the risk to bees via dietary exposure is expected to be low, there is some uncertainty given the Tier 1 risk assessment slightly exceeded the level of concern, and there is uncertainty regarding the relevance of the exposure in the higher tier feeding study to Canadian use rates. Therefore, hazard/precautionary statements are required on product labels to warn users of the potential risk to bees and to restrict foliar applications to periods when crops are not in bloom.

Beneficial arthropods

The risk to beneficial arthropods from exposure to direct application of mancozeb was determined based on the most sensitive LR_{50} for the predatory mite *T. pyri,* 107 g a.i./ha (extended lab study). The EECs were determined for both on-field and off-field exposure for the revised use patterns proposed by the MTF for apples, potato and cucumber. The EECs for cumulative application rates were estimated by adjusting the sum of the applications for dissipation between applications using the 90th percentile confidence bound on the mean half-life values for vegetation (8.24 days). The EEC values were refined to consider foliar interception. The exposure estimates assume deposition to a 2-dimensional structure. Therefore, the values can be corrected to take into account the 3-dimensional structure where a certain fraction is intercepted by the crop (for in-field exposure) or the off-field vegetation (for off-field exposure). For the in-field EEC, crop-specific foliar interception factors are applied to the cumulative application rate. For the off-field EEC, a vegetation distribution factor is applied to the cumulative drift rate. Results of the risk assessment are presented in Appendix VIII, Table 9.

The risk quotients exceed the acute LOC for predatory arthropods on field at all proposed application rates (RQ values range from 13 to 68). The LOC is exceeded off-field only for application to apples at both the proposed cumulative and single application rate (RQ = 6.3 and 3.1, respectively).

Higher tier studies investigating the effects of mancozeb on beneficial arthropods under field conditions were not available for review. The 2018 EC review (PMRA# 3017377–3017383) reports summary results for a number of semi-field and field studies. Reduced abundance of arthropod species appears to be limited to within the same season for a single application, however, there is uncertainty as to whether recovery extends beyond a season for multiple applications, particularly at the highest rates. Higher application rates are proposed by the MTF (for example, 2440–4500 g a.i./ha) than those used in the field studies (58–2618 g a.i./ha). In addition, as many as 3–8 applications per season are proposed by the MTF (in other words, for apples and potato, respectively).

Mancozeb poses potential risk to non-target arthropods. A precautionary statement is required on product labels to inform users of the potential hazard to beneficial arthropods.

Terrestrial plants

Non-target plants may be exposed to mancozeb by overspray and spray drift. Suitable data on the toxicity of terrestrial vascular plants for mancozeb were not available at the time of the original risk assessment.

During the consultation period, the MTF submitted vegetative vigour and seedling emergence studies (PMRA# 2363967, 2363969 and 2950689). Dithane M45 was applied at an application rate of 17.4 lbs a.i./acre (equivalent to 19.5 kg a.i./ha) to representative species of terrestrial plants (6 species of dicotyledonous plants: lettuce, cucumber, radish, soybean, oilseed rape and tomato; 4 species of monocotyledonous plants: corn, oat, onion, ryegrass). No adverse effects were noted for any of the test species. The most sensitive NOER and EC_{25} for seedling emergence and vegetative vigour from these studies was 13.5 and >13.5 kg a.i./ha, respectively.

At the maximum seasonal application proposed for apples (18 kg a.i./ha), the screening level risk quotient ($EEC/EC_{25} < 0.9$) does not exceed the PMRA's level of concern (LOC = 1).

Although a few plant incidents are reported in Canada, they are considered minor and involved visible injury or minor effects to plants that were not specified. Collectively, the evidence shows that mancozeb is not expected to pose a risk to terrestrial plants.

Birds and mammals

For the bird and mammal risk assessment, the ingestion of food items contaminated by spray droplets is considered to be the main route of exposure. The risk assessment is thus based on the estimated daily exposure, which takes into account the expected concentration of mancozeb on various food items immediately after the last application and the food ingestion rate of different sizes of birds and mammals. At the screening level, only the most conservative exposure estimates are used, in other words, the cumulative application rate (taking into consideration any decrease between applications due to transformation of mancozeb) for agricultural uses that results in the highest estimated daily exposures (apples 4.5 kg a.i./ha × 4 at 7 day intervals – 9.153 kg a.i./ha). The results of the screening level risk assessment are presented in Appendix VIII, Table 10.

At the screening level, the acute and reproductive LOC is exceeded for all bird sizes and feeding guilds. For mammals, the acute LOC is exceeded for medium and large sized mammals and the reproductive LOC is exceeded for all size classes and feeding guilds.

To further characterize the risk to birds and mammals, the assessment was expanded to include a range of mancozeb residue concentrations on all relevant food items at different application rates using maximum and mean residue values. Results are presented in Appendix VIII, Tables 11–16. The risk associated with the consumption of food items contaminated from spray drift off the treated field was assessed taking into consideration the projected spray drift deposition of spray quality of ASAE medium for ground and aerial application (6 and 23 %, respectively) and early airblast application (74%) at 1 m downwind from the site of application.

The refined acute risk analysis shows that mancozeb may pose a risk to birds and mammals feeding on-field and adjacent to fields where mancozeb is applied. The risk quotients that exceed

the acute LOC are very low for mammals and limited to medium sized mammals feeding on-field on short grass and broadleaf plants based on the highest cumulative application rate for apples only. For birds, the RQ values exceeding the acute LOC are low and, in most cases, no risk is identified for off-field feeding or when mean residue values are used. In several cases, the risk quotients exceed the reproductive LOC for mammals and birds feeding on-field based on both maximum and mean residue values. In some instances, risk is also identified for birds and mammals feeding off-field, particularly at the highest cumulative rate. For mammals, reproductive risks identified based on the NOEL (2.5 mg a.i./kg/day) are, in some instances, also observed based on the LOEL (110 mg a.i./kg bw/day dose level).

Information suggests birds may avoid mancozeb treated food items in the field. During dietary feeding studies birds demonstrated an aversion to eating mancozeb treated feed (palatability and regurgitation issues). As such, the acute LD_{50} value used in the assessment is considered highly conservative. For mammals, mancozeb is shown to have low acute oral toxicity (LD_{50} is >5000 mg a.i./kg in rats).

The risk assessment conservatively assumes dietary intake comprises 100% of each type of food item. In some cases, birds and mammals would need to consume an unrealistically large proportion of a single food item (for example, 83% diet of short grass for medium sized birds feeding on fields treated at the highest cumulative application rate for apples based on maximum residue values).

The risk assessment assumes no precipitation between applications. Given that mancozeb is shown to hydrolyze quickly, residues remaining on food items may be short lived (for example, 1 day or less) due to potential interception of rainfall, ground fog and dew formation.

For the purpose of managing fungicide resistance, fungicides with different modes of action are typically used in rotation. Mancozeb residues on food items are conservatively calculated based on highest cumulative crop application rates and the shortest interval between applications (apples and cucumber), without consideration of application of other fungicides for disease resistance management.

The weight of evidence suggests acute risks for birds and mammals resulting from feeding on-field or off-field after foliar applications of mancozeb are not expected. Reproductive risks to birds and mammals are low and the potential period of exposure is anticipated to be short. Although there are no incident reports involving birds and mammals from the use of mancozeb, none would be expected from adverse chronic exposure. Although the reproductive risk to birds and mammals is considered low, a label statement is required to inform the user of the potential hazard.

3.3.2 Risk to aquatic organisms from mancozeb

The screening level risk assessment for aquatic organisms is summarized in Appendix VIII, Table 17. Risk quotients exceed the level of concern for all organisms.

Spray drift

The risk to aquatic organisms was further characterized by taking into consideration the concentrations of mancozeb that could be deposited through spray drift in off-field aquatic habitats that are downwind and directly adjacent to the treated field (Appendix VIII, Table 18).

The acute and chronic LOC is exceeded for all organisms and all application methods except acute freshwater invertebrates and fish (ground application) and acute marine fish (all application methods). In order to reduce the potential risk to aquatic species, spray buffer zones are required.

Runoff

In PRVD 2018-17, run-off was identified as a potential risk to freshwater and marine organisms. This assessment used conservative biotransformation half-lives based on total extracted radioactivity. This approach invariably includes both mancozeb and transformation products in the EECs.

With additional information from an aerobic soil biotransformation study and the 2018 EC review (PMRA# 3017379), the initial conservative approach used in PRVD 2018-17 is no longer supported. Collectively, the fate information demonstrates that mancozeb is hydrolytically unstable and, therefore, non-persistent in the aquatic environment.

For most fate studies, the data does not allow for an adequate estimation of fate parameters for runoff ecoscenario modelling. A phototransformation half-life in water could not be determined due to the spontaneous hydrolysis of mancozeb in water. Transformation kinetics cannot be calculated for aerobic soil biotransformation studies as mancozeb is only detectable at study initation and the first sampling interval. As mancozeb is expected to have transformed quickly via hydrolysis in adsorption studies, adsorption coefficients were calculated based on total radioactivity and are therefore considered to be very conservative.

Due to the problems associated with estimating appropriate fate parameters for modelling, runoff ecoscenario modelling was not conducted for the current risk assessment. Due to hydrolytic instability, the potential for mancozeb to pose risk to aquatic organisms due to runoff is expected to be low.

Major transformation products identified in fate studies include EBIS, ETU, EU and M11. Whereas EBIS and M11 are transient in nature, the main transformation products ETU and EU (a transformation product of ETU) are slightly persistent and mobile in soil. Health Canada has conducted an ecological aquatic risk assessment for ETU (see section 3.3.3), which is considered to be inclusive of any potential risks posed by mancozeb to aquatic organisms.

3.3.3 Updates to the ETU ecological risk assessment

3.3.3.1 Birds and mammals

Summaries of the risk assessment for birds and mammals are presented in Appendix VIII, Tables 19 and 20. Potential risks were identified for birds and mammals. The risk assessment assumes birds and mammals will consume 100% of their diet from contaminated food sources for an extended period of time, which is unlikely. In addition, for the purpose of managing fungicide resistance, fungicides with different modes of action are typically used in rotation. ETU residues on food items are calculated based on highest cumulative crop application rates and the shortest interval between applications (apples and cucumber), without consideration of application of other fungicides for disease resistance management. The risk assessment, therefore, is conservative relative to exposure to residues on food items based on typical use patterns. Risks to birds and mammals from ETU are acceptable.

3.3.3.2 Aquatic organisms

A summary of the screening level risk assessment is presented in Appendix VIII, Table 21. Risk quotients for invertebrates and amphibians slightly exceed the LOC. Direct over-spray of ETU at a rate equivalent to the highest cumulative application rate for mancozeb (assuming 100% conversion and no dissipation between applications) was used in the assessment. The actual conversion rate of mancozeb to ETU is much less (16.6%) and dissipation between applications would be expected.

ETU is a potential endocrine disruptor at high exposure concentrations (PRVD 2018-17), however, the refined risk assessment indicates amphibians are not expected to be at risk and therefore, effects to the endocrine system are not expected.

Considering the conservative assumptions made in the screening level risk assessment, it is concluded that risks from ETU to aquatic organisms are acceptable.

3.4 Environmental incident reports

Five environmental incidents relating to the active ingredient mancozeb were found in the Health Canada database. Exposure was reported to have occurred as a result of drift in two incidents and as a result of water runoff in one incident. The exposure scenarios in the remaining two incidents were unknown. The organisms affected included honeybees, fish, and herbaceous plants.

In the incident involving fish, death was reported in fish after douse water used to fight a chemical warehouse fire (where a number of pesticides were stored) entered a stream via the storm drain system. Mancozeb was considered unlikely to have caused the mortality based on concentrations found in the water samples and corresponding toxicity values. Three honeybee incidents were reported to the Health Canada in 2014 from three beekeepers who had placed bees to pollinate a single watermelon field. Mancozeb along with other insecticides (chlorothalonil, imidacloprid and pyraclostrobin) were applied to the watermelons. Effects observed in the honeybees included death, abnormal behaviour and reproductive impairment. Because mancozeb toxicity to pollinators is relatively low compared to the three insecticides, it is unlikely that exposure to mancozeb contributed to the effects noted in the honeybees. In the

incident involving herbaceous plants, visible injury was reported as a result of spray drift, however no specific injuries to the plants were noted.

According to the USEPA's Ecological Incident Information System (EIIS) database, there are eleven incidents reported for mancozeb of which four are reported to be the result of registered labelled use, three as the result of a spill, accidental or intentional misuse, and three are reported as undetermined. Of the four incidents that resulted from registered use, three incidents involved damage to terrestrial plants. One of these incident reported crop damage to potatoes and is listed as the possible result of using Maxim MZ, a registered seed treatment product containing mancozeb and fludioxonil; no mention was made of the type of damage that occurred with plants. Another incident reported damage to apple trees (in other words, loss of leaves and blossoms) after receiving a second airblast application of Benlate (benomyl) and Manzate (mancozeb). Damage to a fruit and vegetable garden was also reported after neighbouring birch trees were being sprayed; in this incident, mancozeb is listed as the sole probable cause.

The remaining incident involved a bird kill on an island off the coast of France where 35 birds were found dead and another 31 intoxicated after reportedly drinking dew in a cabbage field the same morning as the application of Lannate 20L (methomyl) and Dithane M-45 (mancozeb). It is unlikely mancozeb was the cause as methomyl is highly toxic to birds.

No wildlife incident reports were reported for ETU in either Canada or the United States and the incident report summary for mancozeb are also applicable to ETU.

4.0 Value assessment

Comments received in response to PRVD2018-17, and from the MTF, emphasized the value of, and need for, mancozeb in various Canadian agricultural production practices. These comments are consistent with the value assessment and conclusions stated in the proposed re-evaluation decision PRVD2018-17.

5.0 Conclusion of science evaluation

Mancozeb is a protectant, contact fungicide used to control a broad spectrum of economically important diseases on a wide variety of food and feed crops, forests and woodlots, outdoor ornamentals, and greenhouse food crops. Mancozeb is valued for its consistent performance, economics of use, and, due to its multi-site mode of action, integration into integrated pest management programs to prevent disease resistance. It is of notable value to producers to manage crop diseases that affect quality (marketability) and quantity where there are few or no registered alternative products, including onion smut, onion neck rot, tomato grey leaf spot, and scab on pumpkin, squash and melons.

An evaluation of available scientific information found that most uses of mancozeb products meet current standards for protection of human health and the environment when used according to the revised conditions of registration, which includes new mitigation measures. Label amendments, listed in Appendix X, are required.

List of abbreviations

%	percent
>	greater than
<	less than
≤	less than or equal to
1/n	exponent for the Freundlich isotherm
°C	degrees Celsius
a.i.	active ingredient
atm	atmosphere
ABR	auditory brain stem
Abs	absolute
AHETF	Agricultural Handler Exposure Task Force
ASR	acoustic startle response
ADI	acceptable daily intake
AGD	anogenital distance
ALT	alanine amino transferase
AR	applied radioactivity
ARTF	Agricultural Re-entry Task Force
ASR	auditory startle reflex
AST	aspartate aminotransferase
ARfD	acute reference dose
ATPD	area treated per day
BAF	bioaccumulation factor
BCF	bioconcentration factor
bw	body weight
bwg	body weight gain
CA	composite assessment factor
CEPA	*Canadian Environmental Protection Act*
cm	centimetre(s)
d	day(s)
DA	dermal absorption
DACO	data code
dB	decibel
DFR	dislodgeable foliar residue
DFOP	double first-order in parallel
DT_{50}	dissipation time 50% (the dose required to observe a 50% decline in concentration)
DT_{90}	dissipation time 90% (the dose required to observe a 50% decline in concentration)
dw	dry weight
DW	drinking water
EBDC	ethylenebisdithiocarbamate
EBIS	ethylenebis-isothiocyanate sulfide
EC	emulsifiable concentrate
EC_{10}	effective concentration on 10% of the population
EC_{25}	effective concentration on 25% of the population
EC_{50}	effective concentration on 50% of the population

EDE	estimated daily exposure
EEC	Estimated environmental concentration
EFSA	European Food Safety Authority
EOGRTS	Extended One Generation Reproductive Toxicity Study
EIIS	USEPA Ecological Incident Information System
EPI	Estimation Program Interface
ER_{50}	Effective rate on 50% of population
EU	Ethyleneurea
ETU	Ethylene thiourea
FDS	field dissipation study
Fc	food consumption
FOB	functional observational battery
fw	fresh weight
g	gram(s)
GD	gestational day
h	hour(s)
ha	hectare(s)
HC_{05}	hazardous concentration to 5% of the species
IORE	indeterminate order rate equation
IR	incident reports
K_d	soil-water partition coefficient
K_F	Freundlich adsorption coefficient
K_{Foc}	Freundlich organic-carbon partition coefficient
kg	kilogram(s)
K_H	Henry's Law Constant
K_{oa}	Octanol-air partition coeffficient
K_{oc}	organic-carbon partition coefficient
K_{ow}	n–octanol-water partition coefficient
L	litre(s)
hr(s)	hour(s)
kg	kilogram
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LD	lactational day
LOAEC	lowest observed adverse effect concentration
LOAEL	lowest observed adverse effect level
LOC	level of concern
LOD	limit of detection
LOEC	low observed effect concentration
LOQ	limit of quantitation
LR_{50}	Lethal rate on 50% of population
m	metre(s)
mg	milligram
MOE	margin of exposure
MLA	mixer/loader/applicator
MTC	maximum tolerated concentration
MTF	Mancozeb Task Force
N	North

NA	not available
ND	not detected
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
nr	not reported
OC	organic carbon
OECD	Organisation for Economic Cooperation and Development
PCPA	*Pest Control Product Act*
pKa	dissociation constant
PMRA	Pest Management Regulatory Agency
PND	postnatal day
POD	point of departure
ppb	parts per billion
PPE	personal protective equipment
PRVD	proposed re-evaluation decision
PTU	propylthiouracil
PWC	Pesticide in Water Calculator
RBC	red blood cell
RED	reregistration eligibility decision
Repro	reproduction
REI	restricted-entry interval
Rel	relative
RVD	re-evaluation decision
SFO	Single first order
SRBC	sheep red blood cells
SSD	species sensitivity distribution
SW	saltwater
$t_{1/2}$	half-life
$t_{1/2\ rep}$	representative half-life
$t_{1/2soil}$	half-life in soil
T_3	triiodothyronine
T_4	thyroxine
TC	transfer coefficient
TFD	terrestrial field dissipation
TSH	thyroid stimulating hormone
TSMP	Toxic Substances Management Policy
µg	micrograms
USEPA	United States Environmental Protection Agency
wt	weight
×	times
yr	year(s)

Appendix I Registered products containing mancozeb in Canada

Table 1 Registered products containing mancozeb in Canada requiring (label) amendments[1]

Registration number	Marketing class	Registrant	Product name	Formulation type	Active ingredient (%)
20552	Commercial	Dow AgroSciences Canada Inc.	Dithane F-45 Fungicide	Solution	Mancozeb-37.0%
20553	Commercial	Dow AgroSciences Canada Inc.	Dithane Rainshield Fungicide	Wettable Granules	Mancozeb-75.0%
21057	Commercial	UPL NA Inc.	Manzate DF Fungicide	Dry Flowable	Mancozeb-75.0%
25397	Commercial	UPL NA Inc.	Penncozeb 75DF Fungicide	Wettable Granules	Mancozeb-75%
26842	Commercial	Gowan Company, L.L.C.	Gavel DF Fungicide	Dry Flowable	Zoxamide-8.3%; Mancozeb-66.7%
28217	Commercial	UPL NA Inc.	Manzate Pro-Stick Fungicide	Wettable Granules	Mancozeb-75%
28893	Commercial	Syngenta Canada Inc.	Ridomil Gold MZ 68WG Fungicide	Wettable Granules	Metalaxyl-M and S-isomer-4.00% Mancozeb-64.0%
29221	Commercial	Dow AgroSciences Canada Inc.	Dithane DG 75 Fungicide	Dry Flowable	Mancozeb-75.0%
30241	Commercial	UPL NA Inc.	Penncozeb 75DF Raincoat Fungicide	Wettable Granules	Mancozeb-75%
31181	Commercial	Belchim Crop Protection Canada Inc.	Agrosolan Liquid Fungicide	Wettable Granules	Mancozeb-37%
33292	Commercial	UPL NA INC.	Manzate Dispress	Dry Flowable	Mancozeb-75%
33299	Commercial	UPL NA Inc.	Manzate Max	Suspension	Mancozeb-480 g/L
33565	Commercial	UPL NA Inc.	Elixir WSB Fungicide	Wettable Granules	Chlorothalonil 12.5%; Mancozeb-62.5%
19788	Technical	UPL NA Inc.	Mancozeb Technical Fungicide	Solid	Mancozeb-93%
20734	Technical	Dow AgroSciences Canada Inc.	Dithane Technical Fungicide	Wettable Powder	Mancozeb-83.2%
25166	Technical	UPL NA Inc.	Penncozeb Technical Fungicide	Dust or Powder	Mancozeb-87%

[1] As of 7 July 2020, excluding discontinued products or products with a submission for discontinuation.

Table 2 Products containing mancozeb cancelled as a result of re-evaluation

Registration number	Marketing class	Registrant	Product name	Formulation type	Active ingredient (%)
31478	Manufacturing Concentrate	Agria S.A.	Fortuna 80 WP MUC Fungicide	Wettable Powder	Mancozeb-80%
8556	Commercial	Dow AgroSciences Canada Inc.	Dithane M-45 Fungicide	Wettable Powder	Mancozeb-80%
10186	Commercial	Dow AgroSciences Canada Inc.	Dithane M-45 8% Dust Potato Seed Piece Fungicide	Dust or Powder	Mancozeb-8%
10526	Commercial	UPL NA Inc.	Manzate 200 WP Fungicide	Wettable Powder	Mancozeb-80%
17042	Commercial	Belchim Crop Protection Canada Inc.	Tuberseal Potato Seed Piece Dust	Dust or Powder	Mancozeb-16.0%
23655	Commercial	Dow AgroSciences Canada Inc.	Dithane 80 Fungicide	Wettable Powder	Mancozeb-80%
24734	Commercial	Wilbur-Ellis Company LLC	Potato ST16	Dust or Powder	Mancozeb-16%
24734.01	Commercial	Loveland Products Canada Inc.	PSPT 16%	Dust or Powder	Mancozeb-16%
25396	Commercial	UPL NA Inc.	Penncozeb 80WP Fungicide	Wettable Powder	Mancozeb-80%
26157	Commercial	Norac Concepts Inc.	Mancoplus Potato Seed Piece Treatment	Dust or Powder	Mancozeb-16%
26158	Commercial	Norac Concepts Inc.	Condor MZ Potato Seed Piece Treatment	Dust or Powder	Mancozeb-16%
27616	Commercial	Dow AgroSciences Canada Inc.	Dithane M-45 Seed Protectant Fungicide	Wettable Powder	Mancozeb80%
27965	Commercial	Syngenta Canada Inc.	Maxim MZ PSP	Dust or Powder	Mancozeb-5.7%, Fludioxonil-0.5%
29377	Commercial	Belchim Crop Protection Canada Inc.	Solan MZ Potato ST Fungicide	Dust or Powder	Mancozeb-16%
29378	Commercial	Belchim Crop Protection Canada Inc.	Tuberseal MZ Potato ST Fungicide	Dust or Powder	Mancozeb-16%

[1] As of 7 July 2020, excluding discontinued products or products with a submission for discontinuation.

Appendix II Revised use pattern proposed and supported by manufacturers and considered in the updated risk assessments of mancozeb

Site/crops	Maximum rate (kg a.i./ha)	Number of applicatons per year	Interval between applications (days)	Pre-harvest interval (days)
potatoes	1.69	8	5–7	3
apple	4.50	4 (4 × 4.50 kg. a.i./ha)	7	77
	4.50	4 (3 × 4.50 kg. a.i./ha + 1 × 2.25 a.i./ha)	7	77
onions foliar	1.69	6	7	14
onions in-furrow	6.60	1	N/A	100
sugar beets	1.69	5	7–10	21
ginseng	3.30	6	14	30
cucumbers	2.44	3	7	14
field tomatoes	2.44	2	7–10	30
grapes	2.25	1	N/A	66
pumpkin	2.44	3	7	14
squash	2.44	3	7	14
Melons (including cantaloupe, excluding watermelon)	2.44	3	7	14

Appendix III

List of commenters to PRVD2018-17

Category	Commenter
Registrant	the Mancozeb Task Force (MTF), representing Dow AgroSciences Canada Inc. and UPLNA Inc.
Agricultural	Canadian Horticultural Council
Agricultural	Grape Growers of Ontario
Government	Ontario Ministry of Agriculture and Rural Affairs
Agricultural	Nova Scotia Fruit Growers Association
Agricultural	Horticulture Nova Scotia
Agricultural	Ontario Sugarbeet Growers' Association
Agricultural	Perennia
Agricultural	Ontario Fruit and Vegetable Growers' Association
Agricultural	The Norfolk Fruit Growers' Association
Government	British Columbia Ministry of Agriculture
Agricultural	Ontario Apple Growers
Agricultural	Bradford Co-operative Storage Ltd
Agricultural	Ontario Ginseng Growers' Association
Non-government organization	University of Guelph (Ridgetown Campus)
Agricultural	Canada Potato Council
Agricultural	L'Union des Producteurs Agricoles
Agricultural	Les Producteurs de pommes du Québec
Agricultural	L'Association des producteurs maraîchers du Québec
Agricultural	Les producteurs d'oignons du Québec
Agricultural	Rockyview Elite Tubers Ltd
Agricultural	commercial apple growers from Nova Scotia (80)
Agricultural	commercial apple and other fruit growers from Ontario (53)

Appendix IV comment(s) and response(s)

Health Canada received 156 written comments during the public consultation for the mancozeb proposed re-evaluation decision. Commenters' affiliations are listed in Appendix III. These comments were considered during the final decision phase of this re-evaluation. Summarized comments and Health Canada's responses to them are provided below.

1.0 Comment(s) related to the health risk assessment

1.1 Toxicology

1.1.1 Comment concerning the applied database uncertainty factor for mancozeb

The MTF requested that the threefold database uncertainty factor applied in the risk assessment for mancozeb be removed based on additional studies submitted following publication of PRVD2018-17. These data included a developmental neurotoxicity study (DNT) for mancozeb, and an extended one-generation reproductive toxicity study (EOGRTS) for ETU. Other new studies related to immunotoxicity and developmental toxicity for both mancozeb and ETU were also submitted.

Health Canada response

Since the data requirements outlined in PRVD2018-17 were satisfied through submission of the requested information, the previously applied threefold database uncertainty factor was removed. This change is reflected in the revised toxicology reference values (Appendix V, Tables 2a and 2b)

1.1.2 Comment concerning immunotoxicity related effects in animal and epidemiology studies.

The MTF acknowledged the mancozeb immunotoxicity related findings in animal studies. However, MTF suggested that the outcomes of epidemiological studies (Colosio et al., 1996 and 2007) have several key limitation and do fall in the range of normality for all the parameters. Furthermore, new immunotoxicity studies were submitted in response to PRVD2018-17 to address potential immunotoxicity.

Health Canada response

Thymus effects (increase in cortical lymphoid depletion, and decreased size) were seen in mancozeb dog toxicity studies as well as in the ETU EOGRT rat study. Based on these observations and considering the outcomes from published epidemiology studies in Italian vine workers (Colosio et al., 1996 and 2007), Health Canada suggested that a guideline immunotoxicity study be submitted to address this concern during the consultation period if PRVD2018-17. Health Canada reviewed the new immunotoxicity study that was submitted by the MTF.

No treatment-related effects on the primary immune response to sheep red blood cells in male rats were observed in newly submitted immunotoxicity studies in adult animals for both mancozeb and ETU. In both studies, the NOAEL for immunotoxicity was the highest dose level

tested. The toxicology reference values established for mancozeb and ETU are protective of potential effects on the immune system.

1.1.3 Comment concerning the significance of mild bilateral retinopathy in the rat chronic/oncogenicity study with mancozeb.

The MTF suggested that the observed bilateral retinal degeneration was not significant at dose levels ≤ 125 ppm, that a study NOAEL of 125 ppm (4.8 mg/kg bw/day) was appropriate, and that treatment-related effects were limited to the high-dose level (750 ppm). To support this conclusion, the MTF submitted the historical control data with a new statistical analysis on bilateral retinal degeneration. Further, the MTF noted that the available epidemiology studies were thought to have deficiencies, and as a result did not support a relationship between mancozeb exposure and human retinal degeneration. In the Kamel et al., (2000) study, PMRA# 1135743, retinal degeneration was associated with fungicide use (odds ratio = 1.8, 95% confidence interval: 1.3–2.6) among 154 cases and 17 804 controls. The analysis was limited to farmer pesticide applicators, for which less than 10% were women. No further analyses specific to mancozeb were reported. Several years later, a related analysis (Kirrane et al., 2005) was reported for the more than 31 000 wives in the study. Self-reported retinal degeneration was associated with thewive's fungicide use (odds ratio = 1.9, 95% confidence interval: 1.2–3.1) after 12 adjustment for age and state of residence. The risk of using maneb and/or mancozeb was not significantly higher in the cases (wives with retinal degeneration, odds ratio = 1.4, 95% CI: 0.6–3.0). The observation of an association of fungicide and retinal degeneration is preliminary at best. However, a critical limitation is that this finding is based upon cross sectional data of a self-reported diagnosis and self-reported ever use of pesticides. Also, there is no evidence that any of the spouses were exposed to mancozeb.

Health Canada response

A statistically significant increase (Fisher's Exact Test) in the incidence of mild bilateral retinopathy was evident in the two highest dose groups in female rats, and in the high-dose group in males of the chronic toxicity study (Stadler, 1990; PMRA# 1135743). Recently submitted historical control data reported the incidence of retinopathy in control males and females from long-term feeding carcinogenicity/toxicity studies (1984–1989). However, only one study that examined this endpoint falls within an acceptable time frame and is considered appropriate for comparison with the mancozeb study (Stadler, 1990). A new statistical analysis conducted by the commenter comparing the historical control values from a single study with the 4.8 mg/kg bw/day dose group (female mid-high dose level) from the mancozeb study is not considered scientifically appropriate. Also, the trend statistics (Yates's Chi-Square pairwise tests and Cochran-Armitage linear trend tests) were calculated after excluding the highest dose female data from analysis. Since a valid rationale to exclude the high dose values from the linear trend test was not evident, the statistical analysis is questionable. Thus, the historical control data and the new statistical analysis submitted do not fully support the claim that bilateral retinal degeneration is increased only at dose levels of more than 4.8 mg/kg bw/day in females.

With respect to the referenced epidemiology studies, limitations of the studies included the use of prevalent cases and self-reported exposure and disease information. In general, however, the reported limitations do not exclude a relationship between fungicide exposure and human retinopathy. Specific compounds of interest included maneb/mancozeb and ziram. Since these chemicals share a common core chemical structure and these epidemiology studies correlate with

the animal data, they were taken into consideration in Health Canada's risk assessment of mancozeb. There is no convincing evidence upon which to revise Health Canada's interpretation of the retinopathy findings in the long-term rat and available epidemiology studies.

1.1.4 Comment concerning the dog study selected to establish the ADI for mancozeb.

The MTF suggested that a second available 1-year dog dietary toxicity study (PMRA# 1132298) has better characterized the mancozeb dose-response curve than the capsule toxicity study selected by Health Canada (NOAEL of 2.3 mg/kg bw/day) from which a POD for the ADI was derived. Thus, for a variety of reasons, the dietary toxicity study with a NOAEL of 7 mg/kg bw/day should be used instead, to derive the ADI.

Health Canada response

In PRVD2018-17, the ADI for mancozeb was based on consideration of all treatment related effects noted in both of the available 1-year dog toxicity studies. In the capsule 1-year dog toxicity study selected to establish the ADI, a NOAEL of 2.3 mg/kg bw/day was identified based on thyroid hormone effects, as well as effects on liver weight, body weight gain and food consumption. This was supported by the NOAEL of 1.75 mg/kg bw/day in the second 1-year dog study. As noted by the MTF, the dose spacing in the selected study was wide, making determination of the real NOAEL less accurate. For this reason, both 1-year dog toxicity studies were considered together as they used different and overlapping doses. The commenter suggests that the use of gelatin capsules as a means to deliver mancozeb to the dogs in the first study compromises the study. However, Health Canada maintains that capsules provide a more accurate dosing compared to dietary exposure, especially considering the high variability in food concentration and consumption noted in the second dog study. In addition, the NOAEL selected from the 1-year dog toxicity study was supported by the ETU dietary 1-year dog toxicity study (PMRA# 1619162). The ETU 1-year dog toxicity study NOAEL of 0.18 mg/kg bw/day, converts to an estimated dose of 2.4 mg/kg bw/day mancozeb equivalents, a value that is consistent with the NOAEL of 2.3 mg/kg bw/day established in the 1-year mancozeb dog toxicity study selected for risk assessment. In the absence of any further information, the NOAEL identified to derive the ADI, the ADI selection rationale including the composite assessment factor (CAF), remains unchanged.

1.1.5 Comment concerning the adequacy of mouse reproductive non-guideline (Bindali and Kaliwal, 2002) study for regulatory use

The adequacy of the published study (Bindali and Kaliwal, 2002), (PMRA# 1852272) was questioned by the MTF due to major deficiencies in study design and data interpretation. In addition, the MTF noted that the toxicological findings by Bindali and Kaliwal (2002) were not supported by the guideline two-generation reproductive toxicity study submitted to Health Canada (Solomon et al., 1988).

Health Canada response

Following assessment of new toxicology studies and in consideration of the submitted comments, the studies selected for risk assessment were reconsidered. A POD from the recently submitted mancozeb rat developmental neurotoxicity study (PMRA# 2047261), was selected for the ARfD (Females 13–49 years of age) and for the occupational short- and intermediate-term

dermal exposure scenarios. This study, submitted to fill the data gap on developmental neurotoxicity supercedes the non-guideline reproductive toxicity study by Bindali and Kaliwal, 2002. This change, including the appropriate selection of CAF, is reflected in the revised Toxicology Reference Values identified in Appendix V, Table 2a.

1.1.6 Comment concerning the interpretation of the rat inhalation developmental toxicity study (PMRA# 1852277) for mancozeb

The MTF stated that increased resorptions in the inhalation developmental toxicity study, as noted by Health Canada, occurred only at doses that exceeded the maximum tolerated concentration (MTC). Further, there was uncertainty that the neurological signs (hind limb weakness) at 55 mg/m^3 were due to a direct effect on the nervous system, given that the large decrease in body weight and body weight gain during gestation at the highest concentration indicated that MTC was exceeded. The MTF suggested that the appropriate maternal and fetal NOEL and MTC is 17 mg/m^3 equivalent to 5.27 mg/kg bw/day.

Health Canada response

With respect to the observed slight increase in "average percent resorbed [foetuses] per litter" at 55 mg/m^3, it is not possible to determine whether the effect is secondary to maternal toxicity or is the result of direct toxicity to the fetus. The maternal effects at this dose level were mild in nature, although body weight and body weight gain were decreased by 11% and 40%, respectively. The maternal effects at this dose level were not considered significant enough to clearly suggest that the resorptions were an effect secondary to maternal toxicity. Higher dose levels in the second part of this study, not discussed in PRVD2018-17 (110, 890 and 1890/500 mg/m^3) caused increasing maternal mortality and led to total litter resorption in all dams of the 890 mg/m^3 group and in all but three dams in the 1890/500 mg/m^3 group. In this context, the slightly increased "average percent resorbed per litter" at 55 mg/m^3 was considered by Health Canada to be a dose- and treatment-related effect. Resorptions were noted in other developmental toxicity studies in this database. This effect on fetal viability is considered by Health Canada to be a serious effect, and was discussed in the *Pest Control Products Act* hazard characterization section of PRVD2018-17. With respect to the neurotoxicity effects, the incidence and severity of the neurological signs (hind limb weakness) was proportionally increased with dose in this study. Although the effect is mild at 55 mg/m^3, Health Canada considers that it may be an early indicator of peripheral neuropathy. This interpretation is supported by the fact that this effect, and other evidence of neurotoxicity, was noted in other developmental and neurotoxicity studies in the toxicology database. Therefore, the outcomes of the study evaluation remained unchanged.

1.1.7 Comment concerning the adequacy of the mancozeb inhalation developmental toxicity study used in risk assessment for inhalation scenarios

The MTF noted that the study chosen by the Health Canada for risk assessment (Lu and Kennedy, 1986; PMRA# 1852277) used a whole body exposure technique. As this technique results in a systemic exposure higher than calculated, it was felt that an available 90-day inhalation toxicity study (PMRA# 1220614), which used a nose-only technique, was more appropriate.

Health Canada response

Health Canada concurs with the fact that the "whole body" exposure technique used in the Lu and Kennedy (1986; PMRA# 1852277) study could result in a higher overall systemic exposure than reported in the study. In addition, Health Canada agrees that the 90-day nose-only inhalation toxicity study (PMRA# 1220614) is considered a relevant study for inhalation exposure risk assessment for short- and intermediate-term scenarios. However, the inhalation developmental toxicity study was chosen for the short- and intermediate-term inhalation risk assessment because the 90-day inhalation toxicity study did not assess effects of concern, namely, the serious effect of resorptions noted in the inhalation developmental toxicity study (Lu and Kennedy, 1986). In addition, resorptions were noted in other rat and rabbit studies, as discussed in PRVD2018-17, Section 3.1.1 *Pest Control Products Act* hazard characterization. Therefore, the study selection for short- and intermediate-term inhalation risk assessment remains unchanged.

For the 90-day inhalation toxicity study, the commenter performed a recalculation of the respirable dose as per MPPD software to be used for inhalation exposure scenarios risk assessment. The recalculated respirable dose was 21 mg/kg bw/day, in contrast to the respirable dose of 9.4 mg/kg bw/day used by Health Canada. In the 90-day inhalation toxicity study, the study authors reported a MMAD of 3.8–4.2 μm with a mean respirable fraction of 42–46%. In a guideline inhalation toxicity study, the acceptable range for the MMAD is 1–3 μm and particles in this range are considered respirable to the lung alveoli. The method used by the commenter to determine respirable dose included components of the dose that deposited in the nasal airways, tracheal/bronchial airways, and alveolar region of the rat, using the rationale that all of this material eventually contributes to total dose through absorption through the lungs or orally for material cleared from the lungs. This method of calculating respirable dose is not used by, or considered acceptable to Health Canada. Therefore, the identified NOAEL of 5.27 mg/kg bw/day from rat inhalation developmental toxicity study will continue to be used for the assessment of mancozeb inhalation exposure scenarios.

1.1.8 Comment concerning the applied PCPA factor for mancozeb

The MTF agrees that high-dose group rats and rabbits in the mancozeb developmental toxicity studies had increased resorptions/abortions, but they were clearly related to maternal toxicity and exceeded the maximum tolerated dose (MTD).

Health Canada response

The *Pest Control Products Act* requires the application of an additional 10-fold factor to threshold effects to take into account completeness of the data with respect to the exposure of, and toxicity to, infants and children, and potential prenatal and postnatal toxicity. A different factor may be determined to be appropriate on the basis of reliable scientific data. Based on these requirements and in light of newly submitted information, the PCPA factor rationale was re-examined.

Overall, for mancozeb, no sensitivity of the young was noted in the oral developmental toxicity studies in rats or rabbits. Rats and rabbits showed increased abortions and resorptions (serious effects) in the presence of maternal toxicity. Resorptions were also noted in the developmental inhalation toxicity study in the presence of maternal toxicity. In addition, the rat developmental toxicity studies demonstrated malformations of the head at the highest dose level tested (360–520 mg kg bw/day, NOAEL values: 60 and 128 mg/kg bw/day) in the presence of maternal toxicity. Further, results from the newly available DNT study revealed memory effects in a water

maze test for PND 22 females in the presence of maternal toxicity. Thus, the PCPA factor was reduced to threefold, consistent with previous assessment, taking into account the potential prenatal and postnatal toxicity when using the rat (oral or inhalation) or rabbit developmental toxicity studies, or the rat DNT study to establish a POD for mancozeb.

1.1.9 Comment concerning the assessment of ETU genotoxicity and cancer classification

The MTF suggested that Health Canada revise its assessment of the genotoxicity of ETU to be consistent with other international regulators, such as the European Union/EFSA 2018 assessment, IARC 2001, and also discussed by Elia et al., 1995, who consider ETU not genotoxic in mammalian systems. In addition, the commenter noted that an ETU mode of action (MOA) study to support a margin of exposure approach for induction of liver tumours in mice is in progress.

Health Canada response

There are approximately 100 ETU genotoxicity studies available in the toxicology database, which showed both positive and negative results. In 1988, the WHO concluded that ETU itself is generally not mutagenic, especially in mammalian test systems. However, a more recent and extensive review by Dearfield (1994) reported that ETU has a weak genotoxic potential (gene mutation and structural chromosomal aberrations). This was contradicted by Elia (1995), who suggested that the thyroid tumours in rats and liver tumours in mice were induced by a non-genotoxic, or threshold, mechanism. The European Union/EFSA 2018 evaluation report concluded that mancozeb is not genotoxic in vivo. However, the USEPA in the 2015 scoping document confirmed the conclusion of RED 2005: ETU has week genotoxic potential.

A quantitative (q_1*) approach for cancer risk assessment was presented in PRVD2018-17. The ETU cancer potency factor (q_1*) of 0.0601 $(mg/kg/day)^{-1}$ is used to quantitate risk.

While the thyroid tumours appear to have a threshold mechanism of action, no such mechanism of action is available for the mouse liver tumours induced by ETU. Although the commenter noted that an MOA study for ETU is underway, it was not available for the current evaluation.

Therefore, Health Canada's position on the cancer assessment remains as noted in PRVD2018-17.

1.1.10 Comment concerning the appropriate NOAEL for the acute neurotoxicity study

The MTF noted that the effect on motor activity was deemed treatment related at dose levels of 1000 and 2000 mg/kg bw/day, but not at 500 mg/kg bw/day. As explained in the study report, the effect at 1000 and 2000 mg/kg bw/day was very slight, within the historical control range, and occurred in the presence of systemic toxicity (in other words, perineal soiling, decreased body weight gain and rectal temperature changes). Neuropathology along with other evidence supports a systemic interpretation of the motor activity effect rather than a neurological one; therefore, the NOAEL for the neurotoxicity is 500 mg/kg bw/day, a dose Health Canada identified as a LOAEL.

Health Canada response

Health Canada did not select a specific NOAEL for neurotoxicity, rather, a study NOAEL incorporating all treatment related effects was selected. With respect to setting an ARfD reference value, all studies available were examined for acute toxicological effects. With respect to the acute neurotoxicity study, the total session motor activity data showed decreased total motor activity compared to the control group on the day of treatment, although a dose response was not clear as there was significant variability in the data. The decrease affected all male and female treated groups. There were histopathological effects in nerve tissue noted at the high-dose level in the study that were similar to lesions observed in the 90-day neurotoxicity study.

In a gavage dose-range finding DNT study, and in a full DNT study (PMRA# 2849986), female rats exposed to mancozeb at much lower doses (150–350 mg/kg bw/day) experienced hind limb paralysis within a few days of dosing, although the raw and summary data were not available for examination. In consideration of the available information, the study LOAEL of 500 mg/kg bw/day based on decreased motor activity remains unchanged.

1.1.11 Comment concerning the appropriate NOAEL and statistical approach for mancozeb DNT study used to derive an ARfD (females 13–49 years of age).

MTF stated that Health Canada analyses (2015) was not consistent with current guidance for DNT statistical analysis (2016). Further to the correspondence on the statistical approach for the DNT data between Health Canada and MTF, Health Canada conducted a statistical analysis (ANOVA) for each intersession trial or interval for learning and memory on PND 22 according to the 2016 guidance document. Evidence showed that the mancozeb male control group was atypical in lacking evidence of learning and the resulting data were considered not valid. Health Canada asked the MTF to provide a statistical analysis for females at PND 22 and PND 66 time points in the water maze learning and memory test. Following a meeting between Health Canada and MTF statistical consultants (BioStat), the latest conducted a repeated measures analysis of variance (RANOVA) including results for both errors and latency in the water maze. An additional three-way interaction term TRT*TRIAL*SEX was included in the model. BioStat concluded that there are no meaningful differences in the findings and conclusions between this and the original analysis. Females were analyzed separately, and again no treatment related effects in learning and memory for PND 22 and 66 were noted. Therefore, the identified NOAEL should be the highest dose tested in the study, 30 mg/kg bw/day.

Health Canada response

Following the commenter's latest conclusion on statistical analysis of water maze test performance, Health Canada is not convinced that the RANOVA approach, as carried out by BioStat, is sensitive enough to appropriately assess the memory effects for PND 22 female rats. The RANOVA statistical approach involves complex modeling of numerous parameters, including covariance parameters. Adequate power for detecting memory effects via effects on learning would require a more adequate number of time points, ideally 5 or more, for comparison, as well as larger sample sizes. In this assessment, memory effects (Path RA) had only two time points for comparison.

Health Canada conducted a direct statistical approach (student T-test) to address the deficiencies of a "learning only assessment" for memory effects in PND 22 females. The analysis for memory

effects resulted in p-values below 0.05 for both escape times and errors in the highest exposure groups only. In the highest exposure groups, both measurements, the escape times and errors, actually increased (on average) in trial 12, Path RA over what they were in trial 2, Path A. Therefore, it was concluded that PND 22 females tested for memory effects were statistically significantly affected at the high dose level of 30 mg/kg bw/day. Health Canada's analysis of memory effects is a direct comparison between an individual animal performance (Path A vs. Path RA) through the same maze at the same time point. The outcome of the direct comparison is a single number (first time score – second time score) for each animal, and can be analysed using a simple and robust T-test that minimizes the need for complex modelling.

1.2 Comments related to dietary exposure

1.2.1 Error corrections for the dietary monograph

a) Mancozeb was first registered in the United States in 1962, not in 1948. Zineb was registered in 1948.

b) Plant Metabolism: EDI (ethylene di-isothiocyanate) should be changed to EBIS (ethylene bisisothiocyanate).

c) Plant Metabolism: Health Canada indicated that the residue of toxicological concern, ETU, has been found in all the matrices. However, of the plant metabolism studies in potatoes, soybean, sugar beet, tomato and wheat, ETU was only found in the ^{14}C metabolism study on potatoes.

d) The statements regarding vulcanizer accelerators apply to ETU and not to EBDCs.

e) PMRA# 1749197 is listed as an apple processing study. In the list of references, this study is listed as a potato processing study.

Health Canada response (a) to (e)

Health Canada has made these corrections.

1.2.2 Comment concerning the use pattern

The (MTF provided a list of prioritized uses and crops supported with a reduced use pattern (lower application rate and/or maximum number of applications per year, new or longer PHIs and application intervals). All other uses are not supported. The following crops are supported: apples, cucumbers, ginseng, grapes, melons (including cantaloupe, but excluding watermelon), onions, potatoes, pumpkin, squash, sugar beets and field-grown tomatoes.

Health Canada response

The dietary assessments for mancozeb and ETU were updated by including only those crops identified in the list of prioritized crops provided by the Mancozeb Task Force. Potential residues from all other crops were assumed to be zero. Dietary risks were shown to be acceptable with this modified use pattern. All non-supported uses will be cancelled and Health Canada will require that these uses be removed from product labels.

1.2.3 Comments concerning the residue definition and maximum residue limits

Comment

The MTF noted that although the American tolerances were previously based on zineb, the tolerances currently listed are based on carbon disulfide (CS_2). Mancozeb tolerances have been recently established for almonds, almond hulls, atemoya, broccoli, cabbage, canistel, cherimoya, cucurbit crop group, custard apple, ginseng, head lettuce, leaf lettuce, peppers, sapodilla, mamey sapote, white sapote, star apple, sugar apple, tangerines (import tolerance only), and walnuts. The American tolerances have been revised to reflect the current listings in 40 CFR 180.176. The current tolerance expression is: "residues of mancozeb (a coordination product of zinc ion and maneb (manganese ethylene bisdithiocarbamate)), including its metabolites and degradates. Compliance with the tolerance levels is to be determined by measuring only those mancozeb residues convertible to and expressed in terms of the degradant, carbon disulfide". The MTF supports Health Canada's proposal to express MRLs as mg CS_2/kg to harmonize with the United States, Codex, and the European Union.

Health Canada response

As noted in Section 2.2, Health Canada will revise the residue definition for mancozeb to residues of "mancozeb expressed as carbon disulfide (CS_2)". Revision of the residue definition and changes to MRLs for the EBDC fungicides will be published in a Proposed Maximum Residue Limit (PMRL) document for consultation.

Comment

The Association des producteurs maraîchers du Québec commented on MRLs, stating that if mancozeb poses a health risk to Canadians, importing commodities should be prohibited and the MRL should be zero.

Health Canada response

The dietary risk assessments for mancozeb and ETU were updated to include only the registrant-supported commodities. Potential residues from all other crops, including imported commodities were assumed to be zero. Dietary risks were shown to be acceptable with this modified use pattern. Health Canada will require that all non-supported uses be cancelled and be removed from product labels. Health Canada also intends to revoke any MRLs for the EBDC fungicides, which includes mancozeb, for crops not included in the dietary risk assessment, such that they would be subject to the GMRL of 0.1 ppm established by B.15.002(1) of the Food and Drug Regulations. The GMRL is sufficiently low to prevent imports of treated crops, which are not included on Canadian labels. For ETU, which is regulated as a contaminant in food under the Food and Drug Regulations. A maximum level of 0.05 ppm is specified in fruits, vegetables and

cereals (see Section 2.2). This Maximum Level is also sufficiently low to prevent imports of treated crops which are not included on Canadian labels.

1.2.4 Comment concerning the sources of residue estimates used for the dietary exposure estimation and risk assessment

The Union des Producteurs Agricoles commented that the National Chemical Residue Monitoring Program (NCRMP) is an annual surveillance program overseen by the Canadian Food Inspection Agency (CFIA), which verifies compliance in foods to Canadian standards and guidelines for chemical residues and contaminants. Pesticide residues of EBDCs (measured as CS_2) and ETU are included in the CFIA's monitoring program. Therefore, Health Canada should use the residue concentrations detected in food described in the CFIA's monitoring program to evaluate the dietary risk of mancozeb.

Health Canada response

Available monitoring data from CFIA for the years (2013–2017) were used in the updated dietary risk assessment.

1.2.5 Comment concerning the residue analysis

The MTF commented that for EBDCs, it is important to avoid latex gloves during the sampling procedures because latex gloves are treated with thiram, another carbon disulfide generator. Thus, artificial residues of EBDCs can be found if latex gloves are used. The MTF added that there is some conversion of EBDCs to ETU during the residue analysis. As described in the Fourth Quarter Interim report of the market basket survey, ETU 8-01, 1 October 1990, 0.22% to 8.5% of the EBDC can be converted to ETU during residue analysis. Therefore, the ETU residue reported can be an over-estimate.

Health Canada response

While Health Canada recognizes that some conversion of EBDC to ETU may occur during residue analysis, it is difficult to determine with certainty how much residues of ETU are converted from EBDC during residue analysis and how much residues are derived from the agricultural use of EBDCs.

1.2.6 Comment concerning the livestock, poultry, egg and milk residue data

The MTF agrees that for dairy cattle, no residues would be found in edible tissues of livestock due to the feeding and grazing restriction and because of the metabolism study results. For that reason, the percent of crop treated for foods derived from animals, including meats and milk, should be zero for Canada in the dietary assessment.

For poultry and eggs, the MTF agrees that no residues would be found in edible tissues of hen due to the feeding and grazing restriction and because of the metabolism study results. For that reason, the percent of crop treated for foods derived from poultry, including meat and eggs, should be zero for Canada in the dietary assessment.

Health Canada response

As stated in PRVD2018-17, it is expected that no secondary residues would be found in edible tissues of livestock and hens; thus, animal commodities were not included in the updated dietary assessment for mancozeb. The updated assessment included food commodities derived from the use of mancozeb on the uses supported by the registrants (apples, cucumbers, ginseng, grapes, melons (including cantaloupe, but excluding watermelon), onions, potatoes, pumpkin, squash, sugar beets and field-grown tomatoes). In addition to the feeding and grazing restrictions, none of these uses represents a significant feed item.

1.2.7 Comments concerning crop field trials

Comment

For a number of crops, Health Canada calculated average mancozeb and ETU residues using a value of ½ LOQ for values <LOQ. However, for others, calculations were performed using the LOQ. For a chronic risk assessment, ½ LOQ is considered to reasonably represent the distribution of residues that may be represented by <LOQ measurements. Therefore, all average residue values used in calculation of the anticipated residue values should be calculated using ½ LOQ for values <LOQ.

Health Canada response

Health Canada agrees with the MTF comment. Typically, anticipated residue values are calculated using ½ LOQ for values <LOQ. For most crops supported by the registrants, monitoring data were available from CFIA and were used in the updated dietary risk assessment. Health Canada calculated average mancozeb and ETU residues using the actual detected levels for values <LOQ and ½ LOD for values <LOD.

Comment

Health Canada discussed a variety of apple residue trials in the risk assessment; average residues for use in the revised risk assessment should be calculated from only the residue trials performed at the supported GAP: 4 applications of 4.8 lb/A (5.38 kg/ha), excluding those at higher rates and higher numbers of applications.

Health Canada response

Health Canada agrees with the MTF comment. Typically, average residues used in the risk assessment are calculated from the residue trials performed at the supported GAP. For apples, monitoring data from CFIA were available and were used in the updated dietary risk assessment.

Comment

For rice, Health Canada used residue values for rice straw in the dietary risk assessment. This is not appropriate, as rice straw is not a commodity consumed by humans. Health Canada described residue trials in seed-treated rice, where residues of both mancozeb and ETU were non-detectable in the harvested grain.

Health Canada response

Health Canada agrees with the MTF and notes that the updated dietary risk assessment does not include rice.

Comment

Health Canada indicated that residue decline studies on file for apple, grape, oat, potato, sugar beet and summer squash were conducted in the United States and might not be representative of the Canadian use conditions. The MTF noted that many of the studies represented Canadian use conditions and submitted, with their comments, residue decline studies on sweet corn, onion, summer squash, winter squash, papaya, pear, field corn, cranberries, cucumber, grape and celery.

Health Canada response

Health Canada acknowledges receipt of the studies submitted by the MTF. For uses that are not supported by the registrants, as per their list of prioritized uses, these studies will not be considered further. For supported crops, these studies may be considered at a later time in consideration of the required changes to the MRLs (see Section 2.2). The registrants are encouraged to communicate with Health Canada on the use of these studies for MRL purposes in relation to the modified use pattern of crops on their list of prioritized uses.

1.2.8 Comment concerning processed food/feed

The MTF commented extensively on the processing factors used in the dietary risk assessment presented in PRVD2018-17. Overall, the MTF noted that Health Canada stated that they followed the OECD recommendations for the Dietary Exposure Assessment. However, the OECD guidelines were not entirely followed. When multiple processing studies were conducted on a crop Health Canada used the maximum processing factor. This practice is not in accordance with OECD guidelines. The MTF considered that use of the highest processing factor would overestimate daily exposures, and recommended using the median processing factor as indicated by OECD Guideline 508 for the Testing of Chemical Magnitude of the Pesticide Residues in Processed Commodities.

Health Canada response

In order not to underestimate risk, Health Canada had previously used the maximum processing factor values due to the large degree of variability when multiple processing studies were conducted on a crop. Health Canada acknowledges that this approach may be considered conservative. For the updated dietary assessment, the available mancozeb processing studies were re-visited based on OECD guideline Test No. 508: *Magnitude of the Pesticide Residues in Processed Commodities* (dated 16 October 2008). Given the limited number of studies for each crop/commodity, the mean values for processing factors were used, as statistically meaningful median values could not be calculated. The USEPA considered EBDC fungicides to behave similarly during food processing, and derived mean processing factor values from the EBDC processing studies. Therefore, both Health Canada and USEPA used mean processing factor values in the dietary assessments for mancozeb and ETU.

Comment

The potato processing study titled *Determination of the Magnitude of the Residue Due to Mancozeb and ETU in Potato Processed Fractions* (PMRA# 1749197) was accepted by USEPA and no additional potato processing studies are required at this time. It has been noted that residues concentrate in processed fractions of grains such as bran as well as in potatoes processed food forms such as flakes and flour. A new potato study was requested by USEPA in 2016 and was submitted to USEPA in August 2018. MRID#50646702. This study is being submitted to Health Canada at the same time the Task Force response to PRVD is submitted. This study does not change the previously applied potato processing factors.

Health Canada response

Health Canada received the 2018 potato processing study (PMRA# 2950649). The results of the study showed that most residues of mancozeb in the raw/pre-processing potatoes and the processed commodities were below the detection limits. Therefore, it was not possible to derive processing factors from the study. In the absence of adequate mancozeb-specific processing studies for potatoes, Health Canada adopted the processing factors used by USEPA for potato-processed commodities. The USEPA considered EBDC fungicides to behave similarly during food processing, and derived mean processing factor values from the EBDC processing studies for use in the mancozeb and ETU dietary assessments.

Comment

In the dietary monograph, Health Canada mentioned a requirement for cotton seed processing studies. However, the foliar application of mancozeb to cotton was cancelled. The MTF also commented on processing factors of cereal crops, spinach, carrots, celery and safflower oil.

Health Canada response

Since the foliar application of mancozeb to cotton was cancelled in the United States, Health Canada agrees that requirements for cottonseed processing studies, referred to in the dietary monograph, are no longer applicable. Since the registrants will cancel cereal crops, spinach, carrots, celery and safflower, the processing factors are no longer required.

1.2.9 Comment concerning the calculation of ETU anticipated residues in processed commodities

The MTF noted that in calculating ETU anticipated residues in processed commodities, Health Canada considered 3 potential sources of ETU residues: 1) residues of ETU in the raw agricultural commodity (RAC), reduced or concentrated during processing; 2) residues of mancozeb, reduced or concentrated during processing, and then converted to ETU in the body after consumption; and 3) residues of mancozeb converted to ETU during processing. In a processing study, measured ETU residues in the processed commodity will reflect ETU residues from both the first and third sources above. Therefore, application of a conversion factor to mancozeb residues and also applying a processing factor for ETU derived from a processing study double counts any ETU residues formed from mancozeb during processing. As an example, the registrants proposed the following equation for the calculation of the anticipated residues for processed commodities:

ETU Residue for Risk Assessment = $(ETU_{RAC} * PF_{ETU}) + (Mancozeb_{RAC} * PF_{Mancozeb} * F_{in\ vivo})$.
Where,
ETURAC = concentration of ETU in the raw agricultural commodity.
PFETU = processing factor of ETU in the transformation process.
MancozebRAC = concentration of mancozeb in the raw agricultural commodity.
PFMancozeb = processing factor of mancozeb in the transformation process.
The transformation factor Fin vivo = 7.5% w/w.

Health Canada response

The equation used by Health Canada in PRVD2018-17 to estimate the conversion of mancozeb to ETU during food processing may overestimate the ETU residues. In the updated dietary assessment, Health Canada re-examined the approach to the calculation of ETU anticipated residues in processed commodities.

The equation used in PRVD2018-17 was:

$$ETU_{Total} = (ETU_{RAC} * PF_{ETU}) + (Mancozeb_{RAC} * PF_{Mancozeb} * F_{invivo}) + (Mancozeb_{RAC} * PF_{Mancozeb} * CF_{Mancozeb-ETU})$$

Where,
ETURAC = concentration of ETU in the raw agricultural commodity.
PFETU = processing factor of ETU in the transformation process.
MancozebRAC = concentration of mancozeb in the raw agricultural commodity.
PFMancozeb = processing factor of mancozeb in the transformation process.
The transformation factor Fin vivo = 7.5% w/w.
CFMancozeb-ETU = conversion factor of mancozeb to ETU in the transformation process = (ETU in the processed commodity - ETURAC)/MancozebRAC.

The MTF comment above refers to the third component of the equation $(Mancozeb_{RAC} * PF_{Mancozeb} * CF_{Mancozeb\text{-}ETU})$, which they state double counts ETU residues formed from mancozeb during processing. For the updated dietary risk assessment, Health Canada modified the equation slightly:

$$ETU_{Total} = (ETU_{RAC} * PF_{ETU}) + (Mancozeb_{RAC} * PF_{Mancozeb} * F_{invivo}) + (Mancozeb_{RAC} * CF_{Mancozeb-ETU})$$

Health Canada agrees that applying the processing factor for mancozeb ($PF_{Mancozeb}$) in the third component of the equation may result in double counting the effect of processing procedures on mancozeb residues, since it is accounted for in the conversion factor (CF) used. Therefore, the mancozeb processing factor from the third component was removed in the updated equation. The available field trials and processing studies showed that ETU concentrations in raw agricultural commodities were generally low or below the limit of detection, as well as that the ETU concentrations in processed commodities did not have a good correlation with its levels in the raw agricultural commodities [JMPR, 1993]. Therefore, relying solely on ETU residue measurements is uncertain and may result in underestimation of exposure. As a result, Health Canada does not agree that the effect of processing on the conversion of mancozeb residues to ETU residues should be removed, and hence it is retained in the third component of the updated equation.

1.2.10 Comment concerning the market basket survey

The MTF noted that an analysis of the American use patterns in place during the market basket survey (MBS) (1989–1990) shows that GAPs were less restrictive than current use patterns, with

similar or higher use rates and number of applications, and similar or shorter application intervals and PHIs. Therefore, residues produced under the current Canadian label should be comparable to or lesser than those observed in the MBS. In general, for the commodities included in the MBS, the production, handling and distribution practices in use today are not meaningfully different from those practices employed in the early 1990s, particularly from a residue perspective. Based on this comparison, the market basket survey data are relevant to and/or protective of the current Canadian label.

Health Canada response

Previously, MBS data were used for refinement purposes because they had lower residues than the CFIA data available at that time. In the recent CFIA monitoring programs, analytical methods with lower detection limits were used and the measured residues were lower than previous programs. Therefore, in the updated dietary risk assessment, the CFIA monitoring data for the years 2013–2017 were used, as they are more relevant to Canadian exposure. The CFIA monitoring data were available for most of the crops supported by the registrants.

1.2.11 Comment concerning the percent crop treated

Regarding the percent crop treated data for countries other than Canada and the United States, Health Canada conservatively assigned 100% crop treated (%CT) for imported commodities. It is highly improbable that all imported crops are treated with mancozeb. Therefore, the dietary contribution of mancozeb and ETU residues from imported crops are most likely over-estimated. It would take a considerable amount of time and resources to determine the actual %CT for the imported crops. Thus, the MTF is not providing any refinements for imports. The MTF wishes to point out that 100% CT for the non-United States imported crops is highly conservative, except in the case for bananas, papayas, and mangoes. It is highly unlikely that all other imports would have been treated with mancozeb.

More recent trade and production statistics should be used to determine for each crop the percent of the Canadian food supply derived from domestically produced crops, the percent imported from the US, and the percent imported from elsewhere. Newer percent crop treated information should be considered.

Health Canada response

While Health Canada recognizes that it is unlikely that all imported crops are treated with mancozeb, it is the policy of Health Canada to use a 100% estimate whenever percent crop treated information is not available. This is generally the case for imported commodities coming from countries other than Canada and the United States. Although this approach may overestimate residues from some imported crops, data are not available to use values that are lower than the default assumption of 100% crop treated.

In the updated dietary risk assessment, the most recent information was considered, where available, including updated percent crop treated data and domestic production and import statistics.

1.2.12 Comment concerning the uncertainties

The MTF noted that Health Canada has stated in PRVD2018-17 that there are a number of uncertainties in the risk assessment that resulted in low confidence of the results. Where uncertainties existed within the dietary risk assessment, Health Canada addressed them by applying conservative, worst-case assumptions.

Health Canada response

The approach to the dietary risk assessment presented in PRVD2018-17 was commiserate with the level of uncertainty associated with the data and inputs used in the assessment. Health Canada acknowledges that this approach may be considered conservative. In the updated dietary risk assessment, more recent and relevant residue data were available (that is, monitoring data from CFIA for the years 2013–2017, compared to the older Market Basket Survey data and field trial data used in PRVD2018–17). In addition, the processing studies were revisited, and revised processing factors, including those applied by the USEPA, were used. More recent percent crop treated data and domestic production and import statistics were also used. The more recent data have resulted in a more robust dietary assessment. However, the major impact on the acceptability of risk was the reduced use pattern proposed by the MTF.

1.2.13 Comment concerning the cancer cut-off

The MTF contends that strict adherence to the 1.00×10^{-6} threshold is not justified because: (a) Uncertainties in the derivation of the q_1* do not allow differentiation between risks $1.00 \times 10^{-6} < 3.16 \times 10^{-6}$. (b) A number of conservative assumptions remain in the risk assessment, resulting in a significant proportion of the overall dietary exposure estimate being derived from less-refined assumptions (in other words, 66% of total exposure based on field trial residues and 56% of total exposure based on 100% CT). (c) Derivation of the q_1* only allows one significant figure of accuracy. Thus, exceedance of the one in a million threshold is not distinguishable within a half order of magnitude, thus 3.16×10^{-6} (in other words, $10^{-5.5}$) is a more apt bright line for decision making, where the protection goal is established at one in a million excess cancer risk.

Health Canada response

Health Canada considers limiting use of a pesticide when dietary exposure exceeds 100% of the reference dose or the lifetime cancer risk estimate exceeds 1×10^{-6} (one-in-a-million). Health Canada's Science Policy Note SPN2003-03, *Assessing Exposure from Pesticides, A User's Guide*, presents detailed acute, chronic and cancer risk assessment procedures.

In terms of acceptability of cancer risks, as noted in the Health Canada Science Policy Notice SPN2000-01, *A Decision Framework for the Risk Assessment and Risk Management in the Pest Management Regulatory Agency*, this is a risk management decision that cannot rely exclusively on a numerical standard, but needs to take into consideration all the factors that influence risk. When the majority of inputs in the cancer risk assessment are conservative or are overestimates, cancer risks above the threshold of 1×10^{-6} (that is, one in a million) may be considered acceptable.

For ETU, in the updated dietary risk assessment, available monitoring data from CFIA (2013–2017), revised experimental processing factors, and updated percent crop treated data and domestic production and import statistics were used. In addition, a refined drinking water residue value derived from a water monitoring study was used for the ETU cancer assessment.

Therefore, Health Canada considers the dietary assessment to be refined overall with some uncertainties. As such, the cancer risk threshold of 1×10^{-6} was applied. It should be noted that the dietary risks were shown to be acceptable for all uses supported by registrants.

1.2.14 Comment concerning the dietary exposure and risk assessments

Health Canada conducted acute, chronic and cancer dietary risk assessments using the Dietary Exposure Evaluation Model (DEEM–FCID™, Version 2.14), which uses updated food consumption data from the United States Department of Agriculture's Continuing Surveys of Food Intakes by Individuals (CSFII), 1994–1996 and 1998. The MTF revisions to the dietary risk assessment were conducted using the current DEEM-FCID Version 3.16, which uses 2003–2008 food consumption data from the United States Department of Agriculture's (USDA's) National Health and Nutrition Examination Survey, What we Eat in America (NHANES/WWEIA).

Health Canada response

Health Canada's updated dietary risk assessments 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 the Centers for Disease Control and Prevention's National Center for Health Statistics.

1.2.15 Comments concerning studies submitted in response to PRVD2018-17

The MTF submitted numerous food residue studies in response to PRVD2018-17.

Health Canada response

The MTF submitted 36 food residue-related studies in response to the PRVD2018-17. Studies that are relevant to the uses supported by the registrants were considered in the updated dietary assessment and are included in the reference list of this document. These include field trial data for squash and ginseng, the 1990 Market Basket Survey reports, and a processing study for potatoes.

A number of studies submitted by the MTF (27 studies food residue-related studies) were not used in the updated dietary risk assessment because they were not relevant to the revised use pattern supported by the registrants and/or they were not conducted according to Health Canada guidelines. These studies were not included in the reference list of this document, but they are listed herein: analytical methods for grass (PMRA# 2959901, 2959902), European field trials of broccoli (PMRA# 2959903, 2959906), carrots (PMRA# 2959907, 2959908), dry peas (PMRA# 2959909, 2959910), courgette (PMRA# 2959911, 2959912), onion (PMRA# 2959913, 2959914), pepper (PMRA# 2959915), lettuce (PMRA# 2959916, 2959917, 2959918), winter wheat (PMRA# 2959919, 2959920), grass (PMRA# 2959921, 2959922, 2959923, 2959924, 2959925, 2959926) and livestock feeding studies (PMRA# 2950650, 2950651, 2950652).

1.3 Comments related to occupational exposure

1.3.1 Potato seed piece treatment mitigation

The BC Ministry of Agriculture provided use information from a survey of BC farmers who treat potato seed pieces with mancozeb. They questioned the need to cancel the use rather than mitigating risk using other means. It was also mentioned that advances in equipment (closed system handling, application, postapplication, etc.) significantly reduces exposure to personnel.

Health Canada response

The occupational risk assessment was updated to include only the uses that were prioritized and supported by the registrant. Potato seed piece treatment was not supported by the registrant and was, therefore, not re-assessed.

1.3.2 Greenhouse tomato mitigation

The BC Ministry of Agriculture provided potential mitigation for the greenhouse tomato use.

Health Canada response

The occupational risk assessment was updated to include only the uses that were prioritized and supported by the registrant. Greenhouse tomato was not supported by the registrant and was, therefore, not re-assessed.

1.3.3 Planting treated vegetable seed

Vegetable growers with small acreages may not be able to comply with the statement “Do not plant treated seed by hand.” These growers often start their seeds as plugs in a polyhouse, which would be planted by hand. If vegetable seeds come treated with mancozeb, the package should specify that the seeds have been treated and list the name of the pesticide(s).

Health Canada response

Mancozeb is not registered for the treatment of vegetable seeds in Canada, nor for imported treated vegetable seeds.

1.3.4 Unique farming practices of holland marsh

Bradford Coop expressed concern that the unique agricultural practices, cropping systems, product usage, and land use characteristics of the Holland Marsh were not taken into account in the occupational risk assessment.

Health Canada response

The exposure data used in the risk assessment was based on the registrant supported use information as well as chemical-specific data for mancozeb. Standard inputs included exposure data from across Canada, as it is necessary to address the various agricultural practices throughout the country.

1.3.5 Consideration of risk mitigation measures and refined use information

Risk mitigation measures and use pattern changes such as reducing the number of applications, limiting the area treated per day, increased PPE and engineering controls were provided by the registrants and grower groups.

Health Canada response

The use pattern was significantly reduced by the registrant and this use information was used to update the occupational risk assessment. As noted in PRVD2018-07, agricultural stakeholders were encouraged to contact the registrants regarding changes to the use pattern that will meet their needs.

The updated occupational risk assessment for mancozeb also involved detailed analyses of chemical-specific use information and the impact of additional PPE and engineering controls.

1.3.6 Postapplication personal protective equipment (PPE)

The Canadian Horticultural Council (CHC), Ontario Apple Growers, and the Ontario Fruit and Vegetable Growers' Association (OFVGA) proposed postapplication PPE to greatly decrease exposure during postapplication activities. They requested clarification regarding Health Canada refusal to consider PPE as a means to effectively reduce exposure to fungicide residues when they have already added such provisions on at least 4 other labelled products (PCP #27876, 26062, 26408, 29306). They also requested that Health Canada acknowledge that the vineyard activities that were conducted in the European vineyard worker study (Thouvenin, 2018), represent a worst case scenario for potential worker exposure, and would be adequate to cover all other activities and crops with lesser potential exposure to residues.

Health Canada Response

Studies that are used currently to estimate postapplication worker exposure are based on workers wearing long-sleeved shirts, long pants, socks, and footwear. It is also understood that many postapplication workers may wear gloves for their own personal comfort or for food safety purposes (to reduce food contamination). However, there are no reliable data to indicate the degree of protection gloves may provide to postapplication workers, or conversely, the extent to which gloves may enhance exposure under certain conditions.

Before Health Canada can estimate risk to workers wearing gloves or other PPE, worker exposure studies comparable to those currently used by Health Canada are required. Studies that are currently used are discussed in the Regulatory Proposal PRO2014-14*, Updated Agricultural Transfer Coefficients for Assessing Occupational Postapplication Exposure to Pesticides*. Most, if not all, studies conducted by the Agricultural Re-entry Task Force (ARTF), submitted by registrants, or available in the scientific literature and used to determine Health Canada's transfer

coefficients did not include gloves as a basis to estimate exposure. Gloves may have been worn in some of the studies, but they functioned as dosimeters to measure hand exposure without gloves, rather than exposure as a result of protection from the glove. Some available studies suggest that exposure actually increases when wearing gloves (Brouwer, 2000; Boman et al., 2005; Garrigou et al., 2011; Graves et al., 1995; Keifer, 2000; Rawson et al., 2005). One very limited study showed significant reduction in hand exposure while wearing gloves during tomato harvesting (Rech et al., 1989).

Health Canada is currently participating in a working group that also includes grower and industry representatives. The purpose of the working group is to investigate:

a) the potential use of PPE (specifically gloves) as a risk mitigation option for postapplication workers in pesticide treated areas, and

b) more efficient ways to gather postapplication worker information to ensure that risk assessments are kept up-to-date in reflecting activities that occur in the field.

The scope of this information gathering includes both agricultural crops and ornamentals. The role of Health Canada on this working group is to provide regulatory advice and direction for any proposals suggested by the working group to meet the project goals. Currently, the working group is considering conducting studies to estimate the degree of protection offered by chemical-resistant gloves while performing activities in various crops for the purpose of determining a default protection factor for gloves for postapplication workers. Based on the outcome of these studies, Health Canada may be able to consider gloves as a mitigation measure for postapplication workers in the future. As noted above, presently, such surrogate data are not available.

Health Canada has reviewed the Thouvenin postapplication worker exposure study that was conducted in 2018 in France. This study was designed to quantify exposure to a pesticide while lifting/positioning and pruning grapevine shoots in mature vineyards following application of the pesticide. Workers wore long-sleeved shirts, long pants and partial nitrile gloves while performing these tasks. The study was not designed to collect information for a direct comparison between exposure with and without the use of gloves, as all workers wore gloves. A major limitation of the study was that study team members, and not the workers themselves, removed the workers' gloves. There is uncertainty as to the potential increase in exposure had they removed their own gloves. This combined with the fact that no exposure data were collected during the study for non-gloved workers, means that the study cannot be used to determine a protection factor for gloves. Furthermore, as the purpose of the study was to measure the exposure to a specific active ingredient when wearing gloves during a specific postapplication activity, it cannot be used in a generic fashion to estimate exposure for another active ingredient, crop, or postapplication activity. Thus, additional data are required for workers wearing gloves and not wearing gloves to potentially determine a protection factor.

Regarding the cited labels reported to include postapplication PPE, it should be noted that, based on RVD2018-12, which was withdrawn, the relevant label statement on PCP #26408 was changed to "DO NOT enter or allow worker entry into treated areas during the restricted-entry interval (REI) on the label. Employers should make every effort to schedule pesticide applications and worker tasks in order to avoid early entry of workers into treated areas. Under exceptional circumstances, certified pesticide applicators may enter treated areas for short-term

tasks not involving hand labour if at least 4 hours have passed since application and a long-sleeved shirt, long pants, rubber boots, socks, goggles, 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 is worn. Time spent in the treated area cannot exceed 1 hour in a 24-hour period or until restricted-entry interval is over."This statement includes PPE to protect workers entering treated areas for short-term tasks **not** involving hand labour activities. The other products cited in the comment also do not have postapplication PPE for the purpose of reducing risk during hand labour activities. All of these label statements are for good hygiene practices or to protect workers entering treated areas for non-hand labour activities.

1.3.7 Reconsider the decision to cancel the potato foliar use

The Canadian Potato Council requests that Health Canada reconsider the proposed decision for mancozeb use in potatoes based on the new information submitted, and continue the use of mancozeb in potatoes with a maximum seasonal use rate of 18 kg product/ha for both ground and aerial application. Such a decision is supported by the grower use information submitted.

Health Canada response

The occupational risk assessment was updated to include only the uses supported and prioritized by the registrant. The potato foliar use was assessed and occupational risks were shown to be acceptable.

1.3.8 Postapplication exposure in orchards

OFVGA, Ontario Apple Growers, and CHC proposed that high-density orchards have less exposure and should have a reduced transfer coefficient similar to Captan and Carbaryl.

Health Canada response

Health Canada acknowledges that high-density orchard structures will have different exposure profiles from standard plantings. Where possible, these differences are considered in the postapplication assessment, but before Health Canada can estimate risk for workers in high-density orchards, worker exposure studies comparable to those currently used by Health Canada are required. In the case of mancozeb, no new chemical-specific data were available to revise the post-application assessment for orchard activities. Studies that are currently used are discussed further in the Regulatory Proposal PRO2014-14*, Updated Agricultural Transfer Coefficients for Assessing Occupational Postapplication Exposure to Pesticides*.

Health Canada is currently exploring this issue, and the means to estimate worker risks in high-density orchard settings. This includes the feasibility of obtaining chemical-specific postapplication exposure studies for workers in high-density orchards, for the purpose of estimating risk under these conditions. Alternatively, transfer coefficients reflective of modern orchard structures could be developed from new worker exposure studies with concurrent dislodgeable foliar residue (DFR) data, should such studies become available. There are some chemical-specific data available; however, more data are required before it can be used in a surrogate capacity for other chemicals.

Based on the updated risk assessment for apples, the use has been shown to be acceptable with mitigation measures such as a reduced application rates and number of applications, and increased REIs.

1.3.9 REI for orchard hand thinning

The BC Ministry of Agriculture stated that REIs for hand thinning in apples of up to 2–3 weeks may be feasible.

Health Canada response

The occupational risk assessment for apples was updated to incorporate the revised toxicological endpoints and the reduced use pattern supported by the registrant. In addition, chemical-specific dislodgeable foliar residue data in apples were available. Risk for workers was shown to be acceptable with an REI of 35 days for hand thinning. This REI is close to what the registrant had proposed (31 days). As much as possible growers should apply mancozeb after thinning, which may be possible with the reduction in the number of applications for apples.

1.3.10 Dermal absorption

The MTF commented that the dermal absorption value used for ETU (45%) was too high based on the amount of transfer/absorption occurring in orchards along with the use of protective equipment. It was suggested that a dermal absorption value of 29% be used for ETU based on the fact that skin bound residues should not be included in the dermal absorption value since it was shown in the dermal absorption study that dermal absorption plateaus by day 2 and is completed by day 7.

Health Canada response

The risk for handlers (mixer/loaders and applicators) and postapplication workers considered exposures to both mancozeb and ETU. Mancozeb was of primary concern for handlers, with the exception of open cab airblast application where exposures to both mancozeb and ETU were of concern. Mancozeb exposure was the risk driver for workers who conduct hand labour activities relatively soon after application, whereas the importance of ETU exposure increases for postapplication workers entering at later time periods after application. This is due to the fact that ETU residues increase over time while mancozeb residues decrease. Therefore, the impact of reducing the dermal absorption of ETU for various scenarios needs to be considered in the context of the risk assessment for both mancozeb and ETU.

The data in the study does indicate that the majority of the applied dose is excreted in the first 3 days. However, the applied dose continues to be excreted, in relatively low, but consistent amounts over the next 7 days. It is unknown whether this amount is coming from the dose that has already been absorbed (for example, in the carcass) or whether it is coming from the residues in the skin. As the skin is reported as a single value (in other words, stratum corneum is included with the remainder of the epidermis and potentially dermis), excluding this matrix may not be appropriate.

In terms of the dermal absorption value for ETU, the scientific evidence available to Health Canada supports a value of 45%.

2.0 Comment(s) related to the environmental risk assessment

2.1 Comments from the Canadian Potato Council

Comment

The potential use of vegetative buffer strips to reduce the risk of pesticide movement off field has been documented by Hoekstra and Hannam (2017) and Carluer et al. (2016). There is opportunity for improvement in the adoption of vegetative strips adjacent to waterways and/or on headlands rather than maintaining those areas through cultivation.

Health Canada response

The updated risk assessment concludes runoff of mancozeb and its transformation products do not pose a risk to aquatic organisms; however, standard label statements for preventing runoff are still required on the label.

Comment

Currently, there are no required buffer zones stated on the Canadian or United States labels for the foliar uses of mancozeb. A risk mitigation measure that should be considered to allow the continued use of mancozeb as a foliar fungicide for potatoes, the implementation of buffer zones between the treated area of a field and sensitive habitats should be considered. We urge the PMRA to develop buffer zones that protect aquatic and terrestrial habitats, while considering the long history of use of mancozeb in Canada.

Health Canada response

For all broadcast foliar applications of mancozeb, spray buffer zones are required as a mitigation measure to reduce the risk to aquatic organisms from spray drift (see Appendix VIII). A precautionary statement is required on mancozeb product labels to inform users of the potential hazard to beneficial arthropods, which includes a recommendation to minimize spray drift to reduce harmful effects on beneficial arthropods in habitats next to the application site such as hedgerows and woodland.

2.2 Comments from the Union des Producteurs Agricoles

Comment

PRVD2018-17 is based on the use pattern of mancozeb in 2013 and does not take into account certain real data from monitoring programs, the results of which were published after 2013. It is imperative that Health Canada take these data into account in evaluating the risks of mancozeb.

Health Canada response

All available mancozeb and ETU water monitoring data was considered in the revised risk assessment.

Comment

Comment on the evaluation of groundwater drinking water risks. Since 1992, Quebec's Ministère de l'Environnement et de la Lutte contre les changements climatiques (MELCC) has been carrying out annual monitoring to document the presence of pesticides and their metabolites in groundwater in wells located in agricultural areas. The most recent report published by MELCC describes the presence of pesticides in groundwater near sectors dominated by market gardening, orchards, vineyards and berry production. According to the results, the metabolite ETU was not detected in the water in the 36 wells where concentrations were analyzed (Giroux 2016).

A previous report published by MELCC described pesticide contamination of groundwater in potato-growing regions during a sampling campaign from 1999 to 2001. According to the results, the metabolite ETU was not detected in the water in the 52 wells where concentrations were analyzed (Giroux 2003).

Health Canada response

All available mancozeb and ETU water monitoring data was considered in the revised risk assessment.

Comment

Additional risk mitigation measures involving labelling could limit the risks associated with the use of mancozeb. Growers tell us that they follow the current precautions appearing on the labels of mancozeb-based products. Implementing additional risk mitigation measures would allow mancozeb to continue to be registered for use on fruit and vegetable crops. Growers say that they are ready to fully implement these measures. Mitigation measures could include, for example, the following indications on the labels of mancozeb-based pesticides: "not to be applied before it rains" or "not to be applied when the wind speed is above a set limit." Other, more restrictive measures could also appear on product labelling, such as a reduced number of applications per season, the elimination of some non-essential uses, and the withdrawal of all types of aerial applications. These additional measures would reduce the risks associated with the use of mancozeb.

Health Canada response

In order to mitigate risks, the MTF proposed changes to the registered use pattern, including supporting only certain uses and reducing the number of applications. Health Canada considered these changes in the revised risk assessment and, as a result, all MTF-supported uses will be retained with mitigation. A precautionary label statement will be required on all product labels recommending users to "Avoid application when heavy rain is forecast." Under "Directions for use" on all product labels, the following wind speed restrictions apply in order to mitigate spray drift:

Field sprayer application: DO NOT apply during periods of dead calm. Avoid application of this product when winds are gusty. DO NOT apply with spray droplets smaller than the American Society of Agricultural Engineers (ASAE S572.1) medium classification. Boom height must be 60 cm or less above the crop or ground.

Aerial application: DO NOT apply during periods of dead calm. Avoid application of this product when winds are gusty. DO NOT apply when wind speed is greater than 16 km/h at flying height at the site of application. DO NOT apply with spray droplets smaller than the American Society of Agricultural Engineers (ASAE S572.1) medium classification. To reduce drift caused by turbulent wingtip vortices, the nozzle distribution along the spray boom length MUST NOT exceed 65% of the wing- or rotorspan.

For all broadcast foliar applications of mancozeb, spray buffer zones are required as a mitigation measure to reduce the risk from spray drift.

2.3 Comment from Corteva Agriscience TM (Agriculture Division of DowDuPont TM)

Based on the "PMRA Proposed Re-Evaluation Decision – consultation document PRVD2018-17" it is evident that due to the low solubility and rapid transformation of parent mancozeb to mancozeb complex through hydrolysis, it is likely that parent mancozeb would not be available for leaching. It was determined that mancozeb complex is likely a non-leacher. Laboratory studies indicate that a significant portion of the mancozeb residues will bind to the soil/sediment particles and that the bound residues are fairly stable or increase in the soil/sediment over time and, therefore, are not releasing from the soil/sediment in order to produce ETU. Mancozeb (parent and complex), therefore, is not expected to pose a risk to groundwater. But, surface runoff assessments indicate that LOC for non-target aquatic organisms has exceeded the acceptable risk level as predicted by an Exposure Analysis Model. It has been suggested by the registrant that the runoff assessment by Health Canada was based on soil hydrological categories C and D, which are of the clay type soils.

Health Canada response
New information received indicates mancozeb hydrolyzes quickly in the environment. The environmental risk assessment has been updated and the revised conclusion is that runoff of mancozeb and its transformation products do not pose a risk to aquatic organisms.

With respect to groundwater, although mancozeb is not expected to leach, the weight of evidence (ETU is highly mobile and has been detected in ground water) suggests ETU has the potential to reach groundwater. A label statement is required to warn users of the potential risk.

2.4 Comments from the Mancozeb Task Force

Comment

A comprehensive ecotoxicological risk assessment was conducted. While there were some LOC exceedances for birds and mammals in some of the application scenarios, rate reductions and label risk mitigation measures are being proposed to mitigate the risk to acceptable levels. The results reflect very conservative models. In addition, further refined avian modelling and discussion is provided which establish that there are no avian concerns with the proposed use patterns. Further refined mammalian modeling and discussion were provided.

Health Canada response

The bird and mammal risk assessment was updated taking into consideration new information as described in Section 3.3.1. The assessment concludes risk to bird and mammals are acceptable. Hazard statements are required on product labels to inform users of the toxicity of mancozeb to birds and mammals.

Comment

The spray drift risk assessment has resulted in proposed buffer zones for the supported crops which are agronomically feasible. Only medium and coarse spray nozzles will be supported going forward.

Health Canada response

Required spray buffer zones have been updated based on new information.

Comment

For the runoff risk assessment, evidence is provided to support using "A" type soils for the potato runoff scenario. Supporting letters from agriculture experts are being provided to support this approach which results in no runoff concern for the proposed use pattern.

Health Canada response

New information received indicates mancozeb hydrolyzes quickly in the environment. The environmental risk assessment has been updated and the revised conclusion is that runoff of mancozeb and its transformation products do not pose a risk to aquatic organisms.

Comment

To address runoff concerns for all crops, environmental label mitigation measures are being proposed such as warnings to avoid: moderate to steep slopes, compacted soil and clay; and not applying the product when heavy rain is forecast.

Health Canada response

The proposed warnings are standard statements for agricultural pesticides and will be required on product labels.

2.5 Comments from the Canadian Horticultural Council

Comment

The Canadian Horticultural Council commented that it is not reasonable to assume that all residual ETU in the Canadian environment is a product of EBDC fungicide application. Considering the volume of ETU used in industrial applications, Health Canada should have taken into consideration these other sources of ETU.

Health Canada response

For the ecological risk assessment, only ETU resulting from the application of mancozeb is considered. The revised environmental risk assessment for ETU is based on the revised use pattern proposed by the MTF and accounts for transformation rates of mancozeb to ETU. For the screening level environmental risk assessment, EEC values are based on the direct overspray of mancozeb to foliage, water and soil. Water monitoring data were not used in the ecological risk assessment, because the screening level risk assessment indicated risk to aquatic biota were acceptable.

With respect to the drinking water risk assessment, EEC values were obtained from water modelling for the acute risk assessment. Water monitoring data measured in areas with a known history of high EBDC agricultural fungicide use was used in the cancer risk assessment and the chronic non-cancer risk assessment. Details of the drinking water EECs are provided in Appendix IX.

Comment

The Canadian Horticultural Council commented that Health Canada's calculation of maximum use rates, frequency and maximum assumptions of ETU formation and minimum degradation significantly overestimate the real life situation. Realistic use-patterns should have been obtained from growers and realistic fate parameters used to estimate drinking water contribution to human consumption.

Health Canada response

Risk assessments examine the full registered use pattern as described on product labels. Risk assessments must be conducted at the maximum potential application rates so that potential risks are identified.

With respect to the drinking water risk assessment, EEC values were obtained from water modelling for the acute risk assessment. Water monitoring data measured in areas with a known history of high EBDC agricultural fungicide use was used in the cancer risk assessment and the chronic non-cancer risk assessment. Details of the drinking water EECs are provided in Appendix IX.

Comment

The Canadian Horticultural Council commented that the generally accepted EBDCs to ETU conversion rate is 3%. They asked that Health Canada reconcile the use of an unprovenanced (sic) number that elevated cancer concerns (from drinking water) when research provides a separate data-based value. There is a demonstrable need for real data, such as those currently being collected through the environmental working group on the neonicotinoid insecticides. The commenter requested that ETU be tested for in the current water monitoring samples and asked that the PMRA do a due diligence search on the provenance of all water monitoring samples from every source prior to their using those results.

Health Canada response

The commenter did not provide any evidence nor specifics (in soil, water or vegetation) for the value of 3% conversion of EBDC fungicides to ETU. Health Canada previously reported that the percentage of ETU formed from mancozeb ranged from 9.6% in aerobic soil to 16.6% in aerobic aquatic biotransformation studies. These values are based on registrant-submitted studies and are data-based empirical evidence.

Foliar dissipation studies reviewed by Health Canada indicate that the maximum percentage of ETU formed after mancozeb applications to tomatoes in Maryland and California and grapes in California were 6.8%, 6.7%, 4.6% and 0.97%. The USEPA chose a value of 1.6% conversion of mancozeb to ETU on foliage, however, that value was obtained after the final application of mancozeb in one of the trials described in the study. Health Canada used this same study to determine conversion of mancozeb to ETU of 6.8% that was determined after the first application of mancozeb. Because the maximum conversion rate was observed after the first application in an empirical study, the PMRA used that conversion rate.

The neonicotinoid monitoring data was collected by a stakeholder working group. Health Canada does not conduct water monitoring and it collects available water monitoring data from contributors. A water monitoring study submitted by the EBDC/ETU Task Force and submitted to the PMRA (PMRA# 1766450) provides data from areas with known high EBDC pesticide use. This information was used in the cancer risk assessment and the chronic non-cancer risk assessment. Cancer risks were shown to be acceptable when using the refined drinking water EEC from this study. Details of the drinking water EECs are provided in Appendix IX.

Comment

The estimated environmental concentration for ETU in drinking water was not obtained from empirically obtained water monitoring data, but instead computer simulated models.

Health Canada response

In PRVD2018-17, cancer risk from drinking water exposure was not shown to be acceptable. Acute and chronic non-cancer risks were shown to be acceptable. While the acute assessment is based on modelled values for drinking water EECs, the cancer assessment is based on EECs derived from a water monitoring study submitted by the EBDC/ETU Task Force to the PMRA (PMRA# 1766450). Cancer risks were shown to be acceptable when using the refined drinking water EEC from this study. Details of the drinking water EECs are provided in Appendix IX.

Comment

The MTF commented that leaching of ETU is unlikely.

Health Canada response

K_{oc} and K_F values indicate that leaching of ETU is possible. Although the presence of ETU is not ubiquitous in all ground water sampling, the fact remains that ETU has been detected in ground water. As such, the weight of evidence leads Health Canada to maintain their conclusion that ETU has the potential to leach. A label statement is required on products to warn users of the potential for leaching.

Comment

The registrant submitted several studies on the fate and toxicity of ETU.

Health Canada response

The submitted studies were screened and assessed to determine if they would result in changes to the risk assessment of ETU. Studies that were highly relevant to a revised risk assessment were fully reviewed and included in the revised risk assessment.

3.0 Comments related to the value assessment

Comments received addressed the importance and value of mancozeb to various industries/sectors.

3.1 General comments

3.1.1 Mancozeb is important for disease control and resistance management.

Many comments highlighted the importance of mancozeb as an effective tool for both disease control and resistance management: notably for the following industries: apple, broccoli, Brussels sprouts, cauliflower, cucumbers, ginseng, grapes, onion, sugar beets, and potato (both foliar and seed piece treatment).

Health Canada response

Health Canada agrees that mancozeb is important for disease control and resistance management. Following consultation, Health Canada received additional information that was used to refine the health assessment. As a result, while there will be mitigation measures required for certain uses, producers will continue to have access to mancozeb to manage labelled diseases, and incorporate into their resistance management practices, specifically for use on apple, potato (foliar), grapes, sugar beets, ginseng, onions and cucumbers.

3.2 Use-specific comments

3.2.1 Use of mancozeb on apples, potato, grapes, sugar beets, ginseng, onions, field tomatoes and field cucumbers.

Mancozeb is very important due to its broad spectrum efficacy and as a tool for resistance management of certain specific diseases, including: scab and rust on apples; early and late blight on potatoes; downy mildew and black rot on grapes; Cercospora leaf spot on sugar beets; Alternaria leaf blight on ginseng; smut and Botrytis neck rot on onion; early and late blight on potatoes and downy mildew on cucumbers.

Health Canada response

Health Canada acknowledges the value of mancozeb for management of the specific diseases associated with the crops listed above. Additional information was received during consultation of PRVD208-17. In addition, after publication of PRVD 2018-17 the Mancozeb Task Force proposed a revised use pattern for these crops, specifically a reduction in the number of applications (except for ginseng), in order to mitigate risks and retain the use of mancozeb. Based on the revised use pattern and additional information received during consultation, Health Canada refined the risk assessment. As a result, risks were mitigated, and the revised use pattern for all these crops was accepted for continued registration, but with some additional mitigation measures. As such, growers will continue to have access to mancozeb to manage the important diseases indicated above. In addition, with the exception of onion smut and Botrytis neck rot, there are number of other active ingredients, including multi-site fungicides, that are registered for these crop-disease combinations, and can be used with mancozeb for season long disease control and resistance management.

3.2.2 Use of mancozeb on broccoli, cauliflower, and Brussels sprouts

Mancozeb is a critical disease management tool for broccoli, cauliflower, and Brussels sprouts production. Mancozeb is one of the few effective fungicides used to treat Alternaria spot and if mancozeb is lost as a management option, these crops will suffer significant losses as there are insufficient tools remaining to manage disease outbreaks.

Health Canada response

Health Canada acknowledges the importance of mancozeb for Alternaria spot management on broccoli, cauliflower, and Brussels sprouts. Following the publication of PRVD2018-17, Mancozeb Task Force prioritised certain crops to be included in the re-evaluation. Only those crops and use patterns supported by the Task Force were considered during the final re-evaluation risk refinement assessment of mancozeb. Broccoli, cauliflower, and Brussels sprouts were not included in the Task Force supported crop list as priority crops. However, growers continue to have access to a number of alternative ingredients, including the multi-site fungicide, chlorothalonil, which are registered for the management of Alternaria spot/blight on broccoli, cauliflower, and Brussels sprouts.

3.2.3 Use of mancozeb on potato seed-piece treatment

Mancozeb as a potato seed piece treatment is important for the management of seed-borne infections of Fusarium causing dry rot. The importance of mancozeb as a seed piece treatment has increased due to concerns about resistance of *Fusarium spp*. to fludioxonil and thiophanate-methyl, and the limited number of actives that are registered for management of diseases on potato seed piece treatment. Mancozeb is commonly used in a premix with more resistant-prone chemistries like fludioxonil. Mancozeb is also very important for the management of *Fusarium* seed piece decay in cut seed due to problems with certain strains of *Fusarium* being resistant to other fungicide modes of action.

Health Canada response

Health Canada acknowledges the importance of mancozeb for potato seed piece treatment for *Fusarium* seed piece decay and *Fusarium* dry rot in seed potatoes in storage. Health Canada also acknowledges that a limited number of alternatives to mancozeb are registered, and that resistance in certain *Fusarium* populations has developed to some of these active ingredients, particularly fludioxonil.

Following the publication of PRVD2018-17, the use of mancozeb as a potato seed piece treatment was no longer supported by the mancozeb Task Force as a prioritised use. Currently a number of other fungicide active ingredients from different mode of action groups remain available to producers to manage potato seed diseases. These include co-formulated products containing penflufen and prothioconazole, and fludioxonil and difenoconazole. The co-formulated product containing penflufen and prothioconazole is now an available option for potato seed piece treatment for the management of resistant *Fusarium* spp. Without mancozeb, if fludioxonil alone or any co-formulated products containing fludioxonil is repetitively used as a potato seed piece treatment, *Fusarium* resistance will have to be closely monitored.

Appendix V Toxicology

Additional toxicity studies

Table 1a Summary of additional toxicity studies for mancozeb submitted in response to PRVD2018-17

NOTE: Effects noted below are known or assumed to occur in both sexes unless otherwise noted; in such cases, sex-specific effects are separated by semi-colons. Effects on organ weights are known or assumed to reflect changes in absolute weight and relative (to body weight) weight unless otherwise noted.

Study Type/Animal/PMRA#	Study Results
Oral (gavage) preliminary developmental toxicity Rat, Sprague Dawley PMRA# 3016507	**Maternal toxicity** **Supplemental (dose range-finding)** **≥ 80 mg/kg bw/day:** ↓ bwg **≥ 120 mg/kg bw/day:** ↓ T4 at 4 hr post dosing **160 mg/kg bw/day:** ↓ bw, ↓ bwg, ↓ fc On GD 19, plasma levels of mancozeb and ETU increased as dosage increased from 80 to 160 mg/kg bw/day. Peak plasma ETU concentrations were reached at 6 hrs post-dosing at all mancozeb dosage levels.
Oral (gavage) developmental toxicity Rat, Sprague Dawley PMRA# 3016509	**Maternal NOAEL = 40 mg/kg bw/day** **Developmental NOAEL=160 mg/kg bw/day** **Maternal toxicity:** **160 mg/kg bw/day:** ↓ bw , ↓ bwg on GD 6-20, ↓ fc, ↑ hair loss (♀) **Developmental toxicity:** **160 mg/kg bw/day:** no treatment-related effects **No evidence of sensitivity of the young** **No evidence of treatment-related malformations**

Study Type/Animal/PMRA#	Study Results
Oral (gavage) developmental toxicity Rat, Sprague Dawley (1988 study) PMRA# 3131868	**Maternal NOAEL = 60 mg/kg bw/day** **Developmental NOAEL = 60 mg/kg bw/day** **Maternal toxicity:** **360 mg/kg bw/day:** 1 animal killed in extremis, 5 animals with hind limb paralysis, ↓ bw (GD10-20), ↓ bwg, ↓ fc (♀) **Developmental toxicity:** **360 mg/kg bw/day:** single incidence of hydrocephaly , ↑ incomplete ossification of interparietal bone and thoracic vertebral centrum **No evidence of sensitivity of the young** **Evidence of treatment-related malformations**
Developmental Neurotoxicity Dietary study Dose-Range Finding SD rats PMRA# 2047262	**Supplemental: Dose-range finding study** **Maternal toxicity:** **≥ 30 mg/kg bw/day:** ↓ bwg GD 6-20, ↓ fc GD 6-20, ↓ T_4 LD 21, ↑ thyroid wt GD-20, ↑ minimal follicular cell hypertrophy (♀) **60 mg/kg bw/day:** ↓ bw GD 6-20, ↓ bw LD 1-17-21, ↑ TSH LD 21 (♀) No treatment related effects were observed on mortality, clinical signs, pregnancy rate, and reproductive parameters. **Offspring toxicity:** **≥ 5 mg/kg bw/day:** ↓ bw PND 7-21(♂/♀) **≥ 30 mg/kg bw/day:** ↓ bwg PND 4-7 and 17-21(♂/♀)
Developmental Neurotoxicity Dietary Study Main Study SD rats PMRA# 2047261	**Maternal NOAEL = 15 mg/kg bw/day** **Offspring NOAEL = 15 mg/kg bw/day** **Maternal Toxicity** **30 mg/kg bw/day:** ↓ bwg on GD 6-9 and 6-12 and on GD 6-20, ↑ absolute and relative thyroid wt, ↑ incidence of thyroid follicular cell hypertrophy. No treatment-related effects were observed on mortality, clinical signs of toxicity, body weight, food consumption, FOB parameters, reproductive parameters, or gross lesions in the dams. **Offspring toxicity** **30 mg/kg bw/day:** ↑ errors and time to escape (memory trial 12, Biel water maze) PND-22 (♀) **No evidence of sensitivity of the young** **Evidence of developmental neurotoxicity** **No sensitivity of the young**

Study Type/Animal/PMRA#	Study Results
Developmental Neurotoxicity Gavage Study Dose Range-Finding Wistar rats (HanTac) PMRA# 2849986 Axelstad et al., 2011	**Supplemental: Dose range-finding study** **Maternal toxicity** All doses were halved on GD 12. **≥200/100 mg/kg bw/day:** ↓ bw, ↑ signs of neurotoxicity (paralysis of the hind limbs within a few days of dosing), 2 dams sacrificed on GD14 (♀). No further signs of toxicity reported in the remaining dams after dose reduction. **≥350 mg/kg bw/day:** ↓ bw, ↑ signs of neurotoxicity (paralysis of the hindlimbs), all animals sacrificed on (GD 14) (♀)
Developmental Neurotoxicity Gavage Study Main Study Wistar rats (HanTac) PMRA# 2849986 Axelstad et al., 2011	**Supplemental** **Maternal toxicity:** **≥50 mg/kg bw/day:** ↓ bwg (GD 7-21) and (GD 7-PND 1), ↓ T_4 level (GD 15) (♀) **150/100 mg/kg bw/day:** ↓ bw (LD 24), 2 dams sacrificed on GD 16 with mild hind leg paralysis (♀). **Dose was reduced to 100 mg/kg bw/day after GD 16** Gestation length, litter size, post-implantation loss, neonatal deathssex ratio, were similar in the four groups **Developmental toxicity:** **≥50 mg/kg bw/day:** ↓ trend in bw on PND 13, 24, and 31(♂/♀) **150/100 mg/kg bw/day:** ↓ bw PND 13 and 45(♂/♀) Levels of T_4 and thyroid weight were not affected in any dose group compared with controls on PND 16. Neonatal deaths, gender distribution, AGD, nipple retention, testosterone levels, reproductive organ weights, and histology on PND 16 were not affected by mancozeb. The adult offspring (3–7 months old) were tested in a battery of behavioral tests. None of the performed behavioral tests showed effects of mancozeb exposure, as neither activity levels in young or adult offspring, performance in the radial arm maze, or acoustic startle response were affected nor were any dose-dependent trends seen (data were not shown). **Limmitations included:** no raw data were provided to verify the study conclusion; the purity of mancozeb was not stated, however it was mentioned that it was a technical grade
Immunotoxicity 28-Day Dietary Study(SD) rats SRBC antibody response test PMRA# 2363852	**NOAEL = 16 mg/kg bw/day** **81 mg/kg bw/day:** ↓ bw, ↓ bwg, ↑ liver weights, ↑ thyroid weight. **No evidence of immuno-disregulation**

Table 1b Summary of additional toxicity studies for etu submitted in response to PRVD2018-17

NOTE: Effects noted below are known or assumed to occur in both sexes unless otherwise noted; in such cases, sex-specific effects are separated by semi-colons. Effects on organ weights are known or assumed to reflect changes in absolute weight and relative (to body weight) weight unless otherwise noted.

Study Type/Animal/PMRA#	Study Results
Oral (gavage) developmental toxicity Rat, Sprague Dawley PMRA# 3016508	**Maternal NOAEL = 30 mg/kg bw/day** **Developmental NOAEL = 5 mg/kg bw/day** **Maternal toxicity:** **30 mg/kg bw/day:** No treatment related effect (♀) **Developmental toxicity:** **≥ 15 mg/kg bw/day:** ↑ incidence of hydrocephaly (7 fetuses/2 litters) **30 mg/kg bw/day:** ↓ bw , ↑ malformations [external (tail short, tail bent, meningocele, domed head, malrotated limb, limb hyperextension)]; visceral (hydrocephaly, subcutaneous hemorrhage, and meningocele) and skeletal (skull anomaly, rib anomaly, interrupted ribs, interrupted ossification of the ribs, vertebral anomaly with or without associated rib anomaly, vertebral centra anomaly, costal cartilage anomaly, only 12 pairs of ribs present, and small, interrupted, detached, or thin ribs)]; ↑ fetal variation [skeletal (27 presacral vertebrae and 14th rudimentary ribs, reduced ossification/unossified bones of the skull, hyoid, sternebra, ribs, vertebral centra/arch, pubis); visceral: renal papilla not fully developed, distended ureter] **Evidence of sensitivity of the young** **Evidence of treatment-related malformations**
Gavage developmental toxicity study Main study (NZW)SPF rabbit PMRA# 2039432	**Maternal NOAEL = 5 mg/kg bw/day** **Developmental NOAEL = 5 mg/kg bw/day** **Maternal toxicity** **≥15 mg/kg bw/day:** ↓ bwg (GD 7-29), ↓ fc (GD 7-29), discolored/darkened thyroids, ↑ early and late resorptions, ↑ post implantation loss **Developmental toxicity:** **≥15 mg/kg bw/day:** ↓ mean fetal wt, ↑ early resorptions, ↑ late resorptions, ↑ post implantation loss **50 mg/kg bw/day:** ↑ domed heads **No evidence of sensitivity of the young** **Evidence of treatment-related malformation**
Dietary EOGRT Study Crl:CD(SD) rat PMRA# 2055156	**Supplemental: Dose range finding study** **Toxicokinetic data collected on dams and pups** **≥2 mg/kg bw/day:** very slight-to-moderate thyroid follicular cell hypertrophy / hyperplasia (♂/♀); ↓ bw, ↓ bwg (during gestation) (♀); ↓ T_3 and T_4 levels, and ↑ TSH levels (♂) **10 mg/kg bw/day:** ↓ bwg premating (♂/♀); ↑ thyroid wt (♂); ↓ T_4 levels, and ↑ TSH levels (♀)

Study Type/Animal/PMRA#	Study Results
	Plasma samples from GD 20 dams, LD 4 dams and pups, LD 21 dams and pups, and adult males showed dose-proportional concentrations of ETU, indicating linear toxicokinetics at all dose levels in all age groups. There were no sex- or lactation-related differences in ETU kinetics. Plasma conc. of ETU in pups was ~ 22% of dam plasma conc. at LD 4, and ~65% of dam plasma conc. at LD 21.
Extended One-generation Reproductive Toxicity Study (EOGRTS) Dietary Crl:CD(SD) rat PMRA# 2313478	**Parental LOAEL = 0.2 mg/kg bw/day(♂)** **Parental NOAEL = 0.2 mg/kg bw/day(♀)** **Parental toxicity :** **≥ 0.2 mg/kg bw/day:** ↓ thyroid wt. (♂/♀); ↑ hypertrophy of individual cells in the pars distalis of the pituitary gland, ↑ diffuse thyroid follicular cell hypertrophy (♂); ↓ bwg premating and LD 1-4, ↓ RBC count (marginal) (♀) (findings in ♀ non-adverse). **≥ 2 mg/kg bw/day:** ↓ thymus weights, ↑ diffuse follicular cell hypertrophy/hyperplasia of the thyroid gland, ↓ serum concentrations of T4 and ↑ in serum TSH levels (♂/♀); ↑ creatinine, ↓ reticulocyte count, ↑ total cholesterol (♂); ↑ reticulocyte count (♀). **10 mg/kg bw/day:** ↓ bw (premating), ↓ fc, ↑ absolute and relative thyroid wt, ↑ single case of nodular hyperplasia (♂/♀); ↓ bwg, ↓ ALT, ↓ abs wt heart, kidneys, adrenal, and epididymides wt, ↑ hepatocyte vacuolization (fatty change) 2 incidences of thyroid adenoma (♂); ↓ bwg GD1-7, ↓ bw LD 4-8, ↑ relative pituitary and liver wt, ↓ brain wt (♀). **Reproductive toxicity**: **Parental reproduction:** **NOAEL= 10 mg/kg bw/day** No significant effect on any of the reproductive indices, including male and female mating, conception, fertility, and gestation indices, or percent post-implantation loss. No significant effect on time to mating or gestation length, or on mean estrous cycle length. **Cohorts 1A and 1B – Reproduction:** **NOAEL = 2 mg/kg bw/day** **LOAEL = 10 mg/kg bw/day** **10 mg/kg bw/day**: ↑ proportion of abnormal sperm (10%) (♂); ↑ ovarian follicle count (♀)
	Offspring: F1 Animals up to PND 21 **NOAEL = 0.2 mg/kg bw/day (thyroid toxicity)** **≥ 2 mg/kg bw/day:** ↓ in T_4 and ↑ TSH serum level PND 22, ↑ very slight diffuse follicular cell hypertrophy of the thyroid gland; **10 mg/kg bw/day:** ↓ bw (by PND 14) and (by PND 21), ↓ in T_4 and ↑ TSH serum level PND 4, ↑ absolute and relative thyroid gland wt, very slight diffuse follicular cell hyperplasia, and slight hypertrophy of the thyroid gland; ↓ absolute and relative thymus wt (♀). No effects on number of live pups born/litter, litter size or survival index on LD 1, 4, 7, 14, or 21. There were no treatment related effects in nipple retention and AGD in ♀/♂

Study Type/Animal/PMRA#	Study Results
	Cohorts 1A and 1B = Systemic/thyroid toxicity **LOAEL = 0.2 mg/kg bw/day (♂)** **NOAEL = 0.2 mg/kg bw/day (♀)** **≥ 0.2 mg/kg bw/day:** ↓ AST, ↓ ALT (♂/♀); ↑ TSH serum level ↓ thyroid wt both Cohorts, ↑ follicular cell hypertrophy of thyroid, ↑ hypertrophy pars distalis/pituitary (♂); **≥ 2 mg/kg bw/day:** ↓ in T_4 serum, ↓ abs and rel thymus both Cohorts; ↓ abs epididymides Cohort 1A/1B, ↑ follicular cell hyperplasia of thyroid (♂). **10 mg/kg bw/day:** ↓ bw/bwg both Cohorts, ↑ cholesterol concentration, ↓ reticulocyte count, ↓ abs and rel kidney wt (♂/♀); ↓ brain wt Cohort 1A, ↑ relative liver wt Cohort 1A, ↓ abs prostate and epididymides Cohort 1A/1B, ↑ proportion of abnormal sperm, ↑ thymus atrophy (♂); ↑ ovarian follicle counts (small, growing, and total) (♀).
	Cohort 2A and 2B - Developmental Neurotoxicity **NOAEL = 2 mg/kg bw/day** **≥ 2 mg/kg bw/day:** hypertrophy of pars distalis pituitary **(♂)** **10 mg/kg bw/day:** ↓ overall brain size, ↓ habituation on ASR, ↓ brain wt (♂/♀); ↓ bw/bwg (PND 21-77), ↓ fc, (♂). This neurotoxicity study was considered a screening level study
Dietary Immunotoxicity Study Crl:CD(SD) rats PMRA# 2363857	**NOAEL = not established** **LOAEL = 1 mg/kg bw/day** **≥1 mg/kg bw/day:** ↓ T_4 serum level **≥4 mg/kg bw/day:** ↓ bw, ↓ bwg , ↓ fc, ↓ thymus wt **19 mg/kg bw/day:** ↓ spleen wt, ↑ thyroid wt, ↑ TSH serum level, moderate to severe follicular hypertrophy/hyperplasia in all males, minimal to slight centrilobular hepatocellular hypertrophy, diffuse fatty changes in liver **No evidence of immuno-disregulation**
Gavage Developmental Neurotoxicity Study **Propylthiouracil (PTU)** Gavage GD 7 to PND 17 Wistar rats Marta Axelstad at al., 2008 PMRA# 2849973	**Supplemental** Study conducted to establish the relationship between transient hypothyroxinemia during development and long-lasting behavioural and functional changes. PTU-induced hypothyroxinemia influenced the developing rat brain in adult offspring. PTU exposure caused motor activity levels to decrease on PND 14, and to increase on PND 23 and in adulthood (two highest dose groups). In the adult offspring, learning and memory was impaired in the radial arm maze (two highest dose groups), and auditory function was impaired (highest dose group). These results were significantly correlated to reductions in T_4 during development. This supports the hypothesis that decreased T_4 may be a relevant predictor for long-lasting developmental neurotoxicity. **Maternal toxicity** **≥1.6 mg/kg bw/day:** ↓ T_4 level (GD 16), ↑ thyroid wt, ↑ thyroid marked hyperplasia. (♀) **≥2.4 mg/kg bw/day:** ↓ bwg (PND 1-17) (♀)

Study Type/Animal/PMRA#	Study Results
	No effects on bw, gestation length, post-implantation loss, and litter size were observed. **Offspring toxicity** **≥0.8 mg/kg bw/day:** ↓ T_4 levels (PND-16), ↑ thyroid weight (PND 16 and 27), ↑ incidence and severity histopathological changes in thyroid (PND16 and PND 64) **≥1.6 mg/kg bw/day:** ↑ incidence and severity histopathological changes in thyroid (PND 27), ↑ total motor activity on PND 64; ↓ bw (PND 23-27), ↑ errors in radial arm maze (♂); ↓ bwg (PND 23-27) (♀) **≥2.4 mg/kg bw/day:** ↓ total motor activity on PND 14, and ↑ on PND 23, ↓ bw (PND23-27), ↑ ABR thresholds by 12–15 dB, ↓ Cubic Distortion Products (hearing) Limitation included: raw data were not provided to verify the study conclusion; the purity of mancozeb was not stated, however it was mentioned that it was a technical grade.
Assessment of developmental effects of hypothyroidism in rats from in utero and lactation exposure to anti-thyroid agents. PTU (0.39, 1.54 mg/kg bw) GD 10-20 and (0.67, 2.2 mg/kg bw/day) PND 1-20 Makoto Shibutani, Gye-Hyeong at al., 2009 (published) PMRA# 2849980	Pregnant rats were administered thyrotoxins, either PTU or methimazole. Pups were dosed until pups were 11 weeks of age. PTU caused clear hypothyroidism-linked effects in dams (increased relative thyroid weights and thyroid follicular cell hypertrophy). Growth retardation of the offspring lasted into adulthood with males beingmore affected. At the end of the study, exposure to the thyrotoxins caused hypothyroidism-related thyroid follicular cell hypertrophy in the adult pups. In addition, mismigration of hippocampal CA1 pyramidal neurons, and a reduction in the area of corpus callosum and oligodendroglial cells in the cerebral deep cortex, reflecting impaired oligodendroglial development, was observed in adult pups.

Toxicology reference values

Table 2a Revised toxicology reference values for mancozeb

Exposure Scenario	Study	Point of Departure and Endpoint	CAF[1] or Target MOE
ARfD Females 13–49 years of age	Rat DNT Study (dietary)	NOAEL = 15 mg/kg bw/day Neurotoxicity (Offspring memory effect)	300
	ARfD Females 13–49 = 0.05 mg/kg bw		
ARfD General Population, excluding Females 13–49 years of age	Rat Acute Neurotoxicity (gavage)	LOAEL = 500 mg/kg bw Decreased motor activity and bwg, perineal soiling, rectal temperature changes	300
	ARfD General Pop (excluding females 13–49 years of age) = 1.7 mg/kg bw		
Chronic Dietary All Populations	1 Year Dog Toxicity Study (capsule)	NOAEL = 2.3 mg/kg bw/day Liver and body weight gain, food	100

Exposure Scenario	Study	Point of Departure and Endpoint	CAF[1] or Target MOE
		consumption, thyroid hormone effects	
	ADI = 0.023 mg/kg bw/day		
Short- and Intermediate-term Dermal[2]	**Occupational (All populations)**		
	Rat DNT Study (dietary)	NOAEL = 15 mg/kg bw/day Neurotoxicity (memory effect)	300
Short- and Intermediate-term Inhalation	**Bystander (Females 13–49 years of age)**		
	Rat Inhalation Developmental Toxicity Study	NOAEL = 5.27 mg/kg bw/day Body weight effects, resorptions, neurological effects	300
	Bystander (General Population, excluding Females 13–49 years of age)		
	Rat Inhalation Developmental Toxicity Study	NOAEL = 5.27 mg/kg bw/day Body weight effects	100*
	Occupational (All populations)		
	Rat Inhalation Developmental Toxicity	NOAEL = 5.27 mg/kg bw/day Body weight effects, resorptions, neurological effects	300
Long-term Dermal[2] and Inhalation[3]	**Occupational (All populations)**		
	1 Year Dog Toxicity Study (capsule)	NOAEL = 2.3 mg/kg bw/day Liver and body weight gain, food consumption, thyroid hormone effects	100
Aggregate (General populations) Short-,intermediate-term Oral/inhalation	Oral: Rat DNT study Inhalation: Rat Inhalation Developmental Toxicity	Common endpoint: bw changes NOAEL= 15 mg/kg bw/day NOAEL= 5.27 mg/kg bw/day	100 100
Aggregate (Females 13–49 years of age) Short-,intermediate-term Oral/inhalation	Oral: Rat DNT study Inhalation: Rat Inhalation Developmental Toxicity	Common endpoint: bw changes NOAEL= 15 mg/kg bw/day NOAEL= 5.27 mg/kg bw/day	300 300
Cancer Risk	q_1* of 0.0601 (mg/kg bw/day)$^{-1}$ Based on incidences of liver tumours in a combined chronic/carcinogenicity/reproduction study on ETU		

[1]CAF (Composite assessment factor) refers to the total of uncertainty and PCPA factors for dietary risk assessments, MOE refers to target MOE for occupational assessments.

[2]Since an oral NOAEL/LOAEL was selected, a dermal absorption factor of 1% is used in a route-to-route extrapolation.

*Resorptions and neurological effects in utero are not applicable to this population; therefore, the *Pest Control Products Act* is reduced to onefold

Table 2b Revised toxicology reference values for ethylene thiourea (ETU)

Exposure Scenario	Study	Point of Departure and Endpoint	CAF[1] or Target MOE
Acute Reference Dose, Females 13–49 years of age	Developmental rat	NOAEL = 5 mg/kg bw/day Malformations in the absence of maternal toxicity	1000
	ARfD Females 13–49 = 0.005 mg/kg bw		
Chronic Dietary	EOGRTS	LOAEL = 0.2 mg/kg bw/day HPT axis perturbation (hypertrophy of thyroid and pituitary in parental animals)	300
	ADI = 0.0007 mg/kg bw/day		
Acute, Short-, and Intermediate-term Dermal[2] and Inhalation[3]	**Occupational**		
	Developmental rat	NOAEL = 5 mg/kg bw/day Malformations	1000
Long-term Dermal[2] and Inhalation[3]	**Occupational** EOGRTS	LOAEL = 0.2 mg/kg bw/day HPT axis perturbation (hypertrophy of thyroid and pituitary in parental animals)	300
Aggregate Short, intermediate-term oral/inhalation	**Aggregate (**All populations)		
	EOGRTS	NOAEL = 0.2 mg/kg bw/day Thyroid effects in parents and PND 21 offspring	100
Cancer Risk	q_1* of 0.0601 (mg/kg bw/day)$^{-1}$ Based on incidences of liver tumours in a combined chronic/carcinogenicity/reproduction study		

[1]CAF (Composite assessment factor) refers to the total of uncertainty and PCPA factors for dietary risk assessments, MOE refers to target MOE for occupational assessments.
[2]Since an oral NOAEL/LOAEL was selected, a dermal absorption factor of 45% is used in a route-to-route extrapolation.
[3] oral NOAEL/LOAEL was selected, an inhalation absorption factor of 100% (default value) is used in route-to-route extrapolation.

Appendix VI Updated dietary exposure and risk estimates

The dietary assessments included only those crops identified in the list of prioritized crops provided by the Mancozeb Task Force. These crops are apples, cucumbers, ginseng, grapes, melons (excluding watermelon), onions, potatoes, pumpkin, squash, sugar beets and field tomatoes. Potential residues from all other crops, including imported commodities were assumed to be zero.

Table 1 Summary of dietary acute and chronic (non-cancer) exposure and risk from mancozeb

Population Subgroup	Food Only			
	Acute (95th percentile)		Chronic	
	Exposure (mg/kg bw/day)	%ARfD[1]	Exposure (mg/kg bw/day)	%ADI[2]
General Population	N/A	N/A	0.000018	0.1
All Infants (< 1 year old)	0.003271	0.2	0.000018	0.1
Children 1−2 years old	0.014478	0.9	0.000090	0.4
Children 3−5 years old	0.011840	0.7	0.000065	0.3
Children 6−12 years old	0.006545	0.4	0.000031	0.1
Youth 13−19 years old	N/A	N/A	0.000015	0.1
Males 13−19 years old	0.003673	0.2	N/A	N/A
Adults 20−49 years old	N/A	N/A	0.000012	0.1
Males 20−49 years old	0.002731	0.2	N/A	N/A
Adults 50+ years old	0.002827	0.2	0.000012	0.1
Females 13−49 years old	0.003044	6.1	0.000012	0.1

[1] Acute Reference Dose (ARfD) for females 13−49 years of 0.05 mg/kg bw; ARfD for the general populations, excluding females 13−49 years, of 1.7 mg/kg bw.
[2] Acceptable daily intake (ADI) of 0.023 mg/kg bw/day.
N/A: Not applicable

Table 2 Summary of dietary acute exposure and risk from ETU

Population Subgroup	Food Only (95th percentile)		Food and Drinking Water[2] (95th percentile)	
	Exposure (mg/kg bw/day)	%ARfD[1]	Exposure (mg/kg bw/day)	%ARfD[1]
Females 13−49 years old	0.000536	10.7	0.001162	23.3

[1] Acute Reference Dose (ARfD) for females 13−49 years of 0.005 mg/kg bw.
[2] Based on estimated environmental concentration (EEC) in drinking water of 16 µg/L.

Table 3 Summary of dietary chronic (non-cancer) exposure and risk from ETU

Population Subgroup	Food Only		Food and Drinking Water[1]	
	Exposure (mg/kg bw/day)	%ADI[2]	Exposure (mg/kg bw/day)	%ADI[2]
General Population	0.000015	2.2	0.000020	2.8
All Infants (< 1 year old)	0.000030	4.2	0.000046	6.5
Children 1−2 years old	0.000070	10.0	0.000076	10.8
Children 3−5 years old	0.000048	6.8	0.000053	7.5
Children 6−12 years old	0.00002	3.3	0.000026	3.8
Youth 13−19 years old	0.000012	1.7	0.000015	2.1
Adults 20−49 years old	0.000011	1.5	0.000015	2.1
Adults 50+ years old	0.000010	1.5	0.000014	2.0
Females 13−49 years old	0.000011	1.5	0.000015	2.1

Population Subgroup	Food Only		Food and Drinking Water[1]	
	Exposure (mg/kg bw/day)	%ADI[2]	Exposure (mg/kg bw/day)	%ADI[2]

[1] Based on estimated environmental concentration (EEC) in drinking water of 0.21 µg/L.
[2] Acceptable daily intake (ADI) of 0.0007 mg/kg bw/day.

Table 4 Summary of dietary cancer exposure and risk from ETU

Population Subgroup	Food Only		Food and Drinking Water[2]	
	Exposure (mg/kg bw/day)	Cancer Risk[1]	Exposure (mg/kg bw/day)	Cancer Risk[1]
General Population	0.000015	0.9×10^{-6}	0.000020	1×10^{-6}

[1] Cancer potency factor (q_1*) of 0.0601 $(mg/kg\ bw/day)^{-1}$
[2] Based on estimated environmental concentration (EEC) in drinking water of 0.21 µg/L.

Appendix VII Revised occupational exposure and risk estimates

Table 1 Mancozeb non-cancer exposure estimates and MOEs for occupational handlers

Crop	Application equipment	Form	PPE [1]	Application rate [2] (kg a.i./ha)	Area treated per day [c]	Dermal exposure [4] (µg/kg bw/day)	Inhalation exposure [5] (µg/kg bwday)	Dermal MOE [6]	Inhalation MOE [7]
Short-, Intermediate-term Exposure									
Potatoes, Onion (foliar), Sugar beets	Open Cab Groundboom (farmer)	DF, WG	MLA – Single layer, CR gloves ML – Respirator	1.69	107	2.48	8.73	6100	600
		SN [8]	MLA – Single layer, CR gloves			1.90	5.22	7900	1000
	Open Cab Groundboom (custom)	DF, WG	MLA – Single layer, CR gloves, respirator		360	8.33	17.86	1800	300
		SN [8]	MLA – Single layer, CR gloves			6.38	17.57	2400	300
	Closed Cab Groundboom (custom)	DF, WG	MLA – Single layer, CR gloves ML – Respirator			7.24	17.04	2100	310
Potatoes	Aerial (mix/load)	DF, WG	ML – Single layer, CR gloves, respirator	1.69	400	7.11	18.42	2100	290
		SN	ML – Single layer, CR gloves			4.94	5.32	3000	990
	Aerial (application)	DF, WG, SN	A – Single layer, CR gloves [9]			0.23	0.08	66000	64000
Apples	Open Cab Airblast	DF, WG	MLA – Single layer, CR gloves ML – Respirator	4.5	20	42.87	12.53	350	420
		SN	MLA – Single layer, CR gloves			42.58	10.80	350	490
Apples	Open Cab Airblast [10]	DF, WG	MLA – Single layer, CR gloves ML – Respirator A – CR hat	4.5	20	5.55	12.53	2700	420
		SN	MLA – Single layer, CR gloves A – CR hat			5.27	10.80	2800	490

Crop	Application equipment	Form	PPE [1]	Application rate [2] (kg a.i./ha)	Area treated per day [c]	Dermal exposure [4] (µg/kg bw/day)	Inhalation exposure [5] (µg/kg bwday)	Dermal MOE [6]	Inhalation MOE [7]
Onion (in-furrow)	Open Cab Groundboom	DF, WG	MLA – Single layer, CR gloves ML – Respirator	6.6	26	2.35	8.28	6400	640
	Open Cab Solid Broadcast Spreader	WG	MLA – Single layer, CR gloves ML – Respirator			2.15	8.11	7000	650
Ginseng	Open Cab Groundboom	DF, WG	MLA – Single layer, CR gloves ML – Respirator	3.3	26	1.17	4.14	13000	1300
		SN	MLA – Single layer, CR gloves			0.90	2.48	17000	2100
Grapes	Airblast	DF, WG	MLA – Single layer, CR gloves	2.25	20	21.68	17.37	690	300
Cucumbers, Tomatoes, Pumpkin, Squash, Melons	Open Cab Groundboom	DF, WG	MLA – Single layer, CR gloves	2.44	26	0.87	18.62	17000	280
		SN				0.67	1.83	23000	2900

ML = mixer/loader; A = applicator; Form = formulation; DF = dry flowable; WG = wettable granule; SN = solution; PPE = personal protective equipment; CR = chemical resistant; MOE = margin of exposure.

[1] Single layer = long pants, long-sleeved shirt

[2] Registrant supported application rate.

[3] Based on default assumptions.

[4] Where dermal exposure µg/kg bw/day = (unit exposure × area treated × application rate × 1% dermal absorption)/80 kg bw.

[5] Where inhalation exposure µg/kg bw/day = (unit exposure × area treated × application rate)/80 kg bw.

[6] Based on the short- to intermediate-term dermal NOAEL of 15 mg/kg bw/day with a target MOE of 300.

[7] Based on the short- to intermediate-term inhalation NOAEL of 5.27 mg/kg bw/day with a target MOE of 300. Shaded cells indicate MOEs below the target.

[8] The registrants did not support a solution formulation for sugar beets.

[9] For closed cab/cockpit scenarios, CR gloves were only worn to perform activities outside of the cab/cockpit.

[10] CR hat is not required mitigation for exposure to mancozeb. However, since it is required mitigation for ETU the exposure while wearing a CR hat was also presented for mancozeb.

Table 2 ETU non-cancer exposure estimates and MOEs for occupational handlers

Crop	Application equipment	Form	PPE [1]	Application rate [2] (kg a.i./ha)	ATPD [3]	Daily exposure (µg/kg bw/day)				Combined MOE [8]
						ETU tank mix [4, 5]		From MCZ [6]	Total ETU [7]	
						Dermal	Inhalation			
Short-, Intermediate-term Exposure										
Potatoes, Onion (foliar), Sugar beets	Open Cab Groundboom (farmer)	DF, WG	MLA – Single layer, CR gloves ML – Respirator	1.69	107	0.14	1.25E-02	0.84	0.99	5100
		SN [9]	MLA – Single layer, CR gloves			0.11	9.02E-03	0.53	0.65	7600
	Open Cab Groundboom (custom)	DF, WG	MLA – Single layer, CR gloves, respirator		360	0.46	1.91E-02	1.96	2.44	2000
		SN [9]	MLA – Single layer, CR gloves			0.37	3.03E-02	1.80	2.20	2300
	Closed Cab Groundboom (custom)	DF, WG	MLA – Single layer, CR gloves ML – Respirator			0.36	1.75E-02	1.82	2.20	2300
Potatoes	Aerial (mix/load)	DF, WG	ML – Single layer, CR gloves, respirator	1.69	400	0.32	1.84E-02	1.91	2.25	2200
		SN	ML – Single layer, CR gloves			0.22	5.32E-03	0.77	1.00	5000
	Aerial (application)	DF, WG, SN	A – Single layer, CR gloves [10]			2.03E-02	1.64E-04	2.31E-02	0.04	110 000
Apples	Open Cab Airblast	DF, WG	MLA – Single layer, CR gloves ML – Respirator	4.5	20	3.82	2.26E-02	4.15	7.99	630
		SN	MLA – Single layer, CR gloves			3.80	2.09E-02	4.00	7.83	640
Apples	Open Cab Airblast	DF, WG	MLA – Single layer, CR gloves ML – Respirator A – CR hat	4.5	20	0.46	2.26E-02	1.36	1.84	2700
		SN	MLA – Single layer, CR gloves A – CR hat			0.44	2.09E-02	1.21	1.67	3000
Onion (in-furrow)	Open Cab Groundboom	DF, WG	MLA – Single layer, CR gloves ML – Respirator	6.6	26	0.13	1.19E-02	0.80	0.94	5300

Crop	Application equipment	Form	PPE [1]	Application rate [2] (kg a.i./ha)	ATPD [3]	Daily exposure (µg/kg bw/day)				Combined MOE [8]
						ETU tank mix [4, 5]		From MCZ [6]	Total ETU [7]	
						Dermal	Inhalation			
	Open Cab Solid Broadcast Spreader	WG	MLA – Single layer, CR gloves ML – Respirator			0.11	1.15E-02	0.77	0.89	5600
Ginseng	Open Cab Groundboom	DF, WG	MLA – Single layer, CR gloves ML – Respirator	3.3	26	6.51E-02	5.94E-03	0.40	0.47	11000
		SN	MLA – Single layer, CR gloves			5.28E-02	4.28E-03	0.25	0.31	16000
Grapes	Airblast	DF, WG	MLA – Single layer, CR gloves	2.25	20	1.93	2.25E-02	2.93	4.88	1000
Cucumbers, Tomatoes, Pumpkin, Squash, Melons	Open Cab Groundboom	DF, WG	MLA – Single layer, CR gloves	2.44	26	4.82E-02	2.00E-02	1.46	1.53	3300
		SN				3.90E-02	3.16E-03	0.19	0.23	22000

ETU = ethylene thiourea; ML = mixer/loader; A = applicator; Form = formulation; DF = dry flowable; WG = wettable granule; SN = solution; PPE = personal protective equipment; CR = chemical resistant; MOE = margin of exposure.

[1] Single layer = long pants, long-sleeved shirt

[2] Registrant supported application rate.

[3] Based on default assumptions.

[4] Where dermal exposure µg/kg bw/day = (unit exposure × area treated × application rate × tank mix conversion factor (0.1% for mixer/loader and 0.2% for applicator) × 45% dermal absorption)/80 kg bw.

[5] Where inhalation exposure µg/kg bw/day = (unit exposure × area treated × tank mix conversion factor (0.1% for mixer/loader and 0.2% for applicator) × application rate)/80 kg bw.

[6] Systemic exposure µg/kg bw/day = total exposure to mancozeb (as expressed in Table 4.1, dermal exposure + inhalation exposure) × metabolic conversion of mancozeb to ETU (7.5%).

[7] Total daily exposure to ETU µg/kg bw/day = Sum of daily exposure to ETU from tank mix (dermal exposure + inhalation exposure) and metabolic conversion to ETU.

[8] Based on the short- to intermediate-term NOAEL of 5 mg/kg bw/day with a target MOE of 1000. Shaded cells indicate MOEs that do not meet the target MOE.

[9] The registrants did not support a solution formulation for sugar beets.

[10] For closed cab/cockpit scenarios, CR gloves were only worn to perform activities outside of the cab/cockpit.

Table 3 ETU exposure estimates and cancer risk for occupational handlers

Crop	Application equipment	Form	PPE [1]	AR [2] (kg a.i./ha)	ATPD [3]	Total ETU ADD [4] (µg/kg bwday)	LADD (µg/kg bwday) [5]	Cancer risk [6]
Short-, Intermediate-term Exposure								
Potatoes, Onion (foliar), Sugar beets	Open Cab Groundboom (farmer)	DF, WG	MLA – Single layer, CR gloves ML – Respirator	1.69	60	0.56	2.34E-02	1E-06
		SN [7]	MLA – Single layer, CR gloves			0.37	1.55E-02	9E-07
	Open Cab Groundboom (custom)	DF, WG	MLA – Single layer, CR gloves, respirator		240	1.63	6.87E-02	4E-06
		SN [7]	MLA – Single layer, CR gloves			1.47	6.19E-02	4E-06
	Closed Cab Groundboom (custom)	DF, WG	MLA – Single layer, CR gloves ML – Respirator			1.47	6.19E-02	4E-06
Potatoes	Aerial (mix/load)	DF, WG	ML – Single layer, CR gloves, respirator	1.69	318	1.79	7.55E-02	5E-06
		SN	ML – Single layer, CR gloves			0.79	3.34E-02	2E-06
	Aerial (application)	DF, WG, SN	A – Single layer, CR gloves [8]			0.03	1.46E-03	9E-08
Apples	Open Cab Airblast	DF, WG	MLA – Single layer, CR gloves ML – Respirator	4.5	7	2.80	0.118	7E-06
		SN	MLA – Single layer, CR gloves			2.74	0.1115	7E-06
Apples	Open Cab Airblast	DF, WG	MLA – Single layer, CR gloves ML – Respirator A – CR hat	4.5	7	0.64	2.71E-02	2E-06
		SN	MLA – Single layer, CR gloves A – CR hat			0.58	2.46E-02	1E-06
Onion (in-furrow)	Open Cab Groundboom	DF, WG	MLA – Single layer, CR gloves ML – Respirator	6.6	12	0.43	1.83E-02	1E-06
	Open Cab Solid Broadcast Spreader	WG	MLA – Single layer, CR gloves ML – Respirator			0.41	1.74E-02	1E-06
Ginseng	Open Cab Groundboom	DF, WG	MLA – Single layer, CR gloves ML – Respirator	3.3	12	0.22	9.14E-03	5E-07
		SN	MLA – Single layer, CR gloves			0.14	6.04E-03	4E-07
Grapes	Airblast	DF, WG	MLA – Single layer, CR gloves	2.25	7	1.71	7.20E-02	4E-06
Cucumbers, Tomatoes,	Open Cab Groundboom	DF, WG	MLA – Single layer, CR gloves	2.44	12	0.71	2.98E-02	2E-06

Crop	Application equipment	Form	PPE [1]	AR [2] (kg a.i./ha)	ATPD [3]	Total ETU ADD [4] (µg/kg bwday)	LADD (µg/kg bwday) [5]	Cancer risk [6]
Pumpkin, Squash, Melons		SN				0.11	4.46E-03	3E-07

ML = mixer/loader; A = applicator; Form = formulation; DF = dry flowable; WG = wettable granule; SN = solution; PPE = personal protective equipment; CR = chemical resistant; AR = application rate; MCZ = mancozeb; ETU = ethylene thiourea; ADD = absorbed daily dose; LADD = lifetime average daily dose.

[1] Single layer = long pants, long-sleeved shirt

[2] Registrant supported application rate.

[3] Based on default assumptions for cancer risk assessments.

[e4] Where ETU ADD µg/kg bw/day = ETU dermal exposure + ETU inhalation exposure + metabolic conversion from MCZ = ((dermal unit exposure × area treated × application rate × tank mix conversion factor (0.1% for mixer/loader and 0.2% for applicator) × 45% dermal absorption)/80 kg bw) + ((inhalation unit exposure × area treated × tank mix conversion factor (0.1% for mixer/loader and 0.2% for applicator) × application rate)/80 kg bw) + (MCZ Exp × metabolic conversion of mancozeb to ETU (7.5%)).

[5] $\text{LADD} = \frac{\text{Absorbed Daily Dose (mg/kg bw/day)} \times \text{Treatment Frequency (30 days per year)} \times \text{Working Duration (40 yrs)}}{\text{365 days/yrs} \times \text{Life Expectancy (78 yrs)}}$

[6] Cancer Risk = LADD (mg/kg bw/day) × q_1^* (0.0601 mg/kg bw/day)$^{-1}$. Cancer risk are considered to acceptable if below 1×10^{-5}.

[7] The registrants did not support a solution formulation for sugar beets.

[8] For closed cab/cockpit scenarios, CR gloves were only worn to perform activities outside of the cab/cockpit.

Table 4 Mancozeb non-cancer dermal exposure estimates and MOEs for postapplication workers

Crops	Rate [1] (kg a.i./ha)	Applications [2]		Activity [9]	TC [3] (cm^2/hr)	Peak DFR [4] (µg/cm^2)	Dermal exposure [5] (µg/kg bw/day)	MOE [6] (day 0)	REI [7] (days)	DFR [4] (µg/cm^2) (REI)	MOE (REI) [6]
		Number	Interval								
Potatoes	1.69	8	5	Hand set/Hand line irrigation related activities involving foliar contact	1750	6.96	12.17	1200	0.5	NA	NA
Apples	4.5	4	7	Hand thinning fruit	3000	27.44	82.83	180	7	16.22	310
				Hand harvesting	1400		38.42	390	0.5	NA	NA
Onions (foliar)	1.69	6	7	Hand weeding	4400	6.96	30.60	490	0.5	NA	NA
Sugar beets	1.69	5	7	Hand harvesting	1100	6.96	7.65	2000	0.5	NA	NA
Ginseng [8]	3.3	6	14	Hand set/Hand line irrigation related activities involving foliar contact	1750	13.58	23.77	630	0.5	NA	NA
Cantaloupe, Cucumbers (field), Melons, Pumpkin, Squash	2.44	3	7	Hand set/Hand line irrigation related activities involving foliar contact	1750	10.04	17.57	850	0.5	NA	NA

Crops	Rate [1] (kg a.i./ha)	Applications [2]		Activity [9]	TC [3] (cm^2/hr)	Peak DFR [4] (µg/cm^2)	Dermal exposure [5] (µg/kg bw/day)	MOE [6] (day 0)	REI [7] (days)	DFR [4] (µg/cm^2) (REI)	MOE (REI) [6]
		Number	Interval								
Tomatoes	2.44	2	7	Hand set/Hand line irrigation related activities involving foliar contact	1750	10.04	17.57	850	0.5	NA	NA
Grapes	2.25	1	NA	Girdling, turning	19 300	4.77	91.99	160	21	1.63	480
				Tying/training, hand harvest, leaf pulling by hand	8500		40.51	370	0.5	NA	NA

TC = transfer coefficient; DFR = dislodgeable foliar residue; MOE = margin of exposure; REI = restricted-entry interval; NA = not applicable

[1] Registrant supported application rate.

[2] Registrant supported number of applications and application intervals.

[3] Transfer coefficients are based on PMRA defaults (PMRA# 2115788).

[4] Based on the DFR data from the studies (PMRA# 1746114; PMRA# 1746112; PMRA# 1752407─1752419) adjusted for differences in application rate. For apples, the residues were also adjusted for differences in the number of applications.

[5] Dermal exposure = DFR × TC × 8 hr × DA/80 kg. Where DA = dermal absorption of 1% for mancozeb.

[f6]Dermal MOE on day 0 on the day of application or the REI day. If there are multiple applications, the dermal MOE is presented for the day of the last application or the REI day to account for any possible accumulation of residues. Calculated using the dermal short-, intermediate-term NOAEL of 15 mg/kg bw/day with at target MOE of 300. Shaded cells indicate MOEs that do not meet the target MOE.

[7] Refers to the day following application that residues are less than the target DFR and calculated MOEs approach the target.

[8] Surrogate TCs based on sweet potato and strawberry for harvesting.

[9] The activities with higher TCs were used to be protective of activities with lower TCs when applicable. When the activities with higher TCs showed unacceptable risk at the peak DFR, activities with lower TCs are shown until risk is acceptable at the peak DFR.

Table 5 ETU non-cancer dermal exposure estimates and MOEs for postapplication workers

Crops	Rate[1] (kg a.i./ha)	Applications[2]		Activity[9]	TC[3] (cm^2/hr)	Peak DFR[4] (µg/cm^2)	Dermal Exposure[5] (µg/kg bw/day)	MOE[6] (day 0)	REI[7] (days)	DFR[4] (µg/cm^2) (REI)	MOE (REI) [6]
		Number	Interval								
Potatoes	1.69	8	5	Hand set/Hand line irrigation related activities involving foliar contact	1750	0.036	3.73	1300	0.5	NA	NA
Apples	4.5	4	7	Hand thinning fruit	3000	0.088	18.08	270	35	0.03	840
				Hand harvesting	1400		8.44	590	14	0.06	970
				Pruning, scouting, training	580		3.49	1400	0.5	NA	NA
Onions (foliar)	1.69	6	7	Hand weeding	4400	0.036	9.37	530	1	0.012	1400

Crops	Rate[1] (kg a.i./ha)	Applications[2]		Activity[9]	TC[3] (cm^2/hr)	Peak DFR[4] (µg/cm^2)	Dermal Exposure[5] (µg/kg bw/day)	MOE[6] (day 0)	REI[7] (days)	DFR[4] (µg/cm^2) (REI)	MOE (REI)[6]
		Number	Interval								
				Hand set/Hand line irrigation related activities involving foliar contact	1750		3.73	1300	0.5	NA	NA
Sugar beets	1.69	5	7	Hand harvesting	1100	0.036	2.35	2100	0.5	NA	NA
Ginseng[8]	3.3	6	14	Hand set/Hand line irrigation related activities involving foliar contact	1750	0.07	7.28	690	1	0.024	1900
				Hand harvesting	1100		4.58	1100	0.5	NA	NA
Cantaloupe, Cucumbers (field), Melons, Pumpkin, Squash	2.44	3	7	Hand set/Hand line irrigation related activities involving foliar contact	1750	0.052	5.39	930	0.5	NA	NA
Tomatoes	2.44	2	7	Hand set/Hand line irrigation related activities involving foliar contact	1750	0.052	5.39	930	0.5	NA	NA
Grapes	2.25	1	NA	Girdling, turning	19 300	0.089	83.81	60	21	0.003	1000
				Tying/training, hand harvest, leaf pulling by hand	8500		36.91	140	7	0.005	1200
				Hand set/Hand line irrigation related activities involving foliar contact	1750		7.60	660	1	0.019	2400
				Bird control, propping, pruning, scouting, trellis repair, weeding, transplanting	640		2.78	1800	0.5	NA	NA

ETU = ethylene thiourea; TC = transfer coefficient; DFR = dislodgeable foliar residue; MOE = margin of exposure; REI = restricted-entry interval; NA = not applicable

[1] Registrant supported application rate.

[2] Registrant supported number of applications and application intervals.

[3] Transfer coefficients are based on PRMA defaults (PMRA# 2115788).

[4] Based on the DFR data from the studies (PMRA# 1746114; PMRA# 1746112; PMRA# 1752407─1752419) adjusted for differences in application rate. For apples, the residues were also adjusted for differences in the number of applications. For grapes day 14 ETU residue = 0.007 µg/cm^2 (Tying/training, hand harvest, leaf pulling by hand MOE = 990); day 35 ETU residue = 0.006 µg/cm^2 (Girdling, turning MOE = 730).

[5] ETU Dermal exposure =ETU DFR × TC × 8 hr × DA/80 kg. ETU exposure from metabolic conversion of mancozeb, calculated by multiplying mancozeb exposure on day 0 or the REI day by 7.5%.

Total ETU exposure = ETU dermal exposure + metabolic conversion from mancozeb. Where DA = dermal absorption of 45% for ETU.
[6] Dermal MOE on day 0 on the day of application or REI day. If there are multiple applications, the dermal MOE is presented for the day of the last application or the REI day to account for any possible accumulation of residues. Calculated using the dermal short-, intermediate-term NOAEL of 5 mg/kg bw/day with at target MOE of 1000. Shaded cells indicate MOEs that do not meet the target MOE.
[7] Refers to the day following application that residues are less than the target DFR and calculated MOEs approach the target.
[8] Surrogate TCs based on sweet potato and strawberry for harvesting
[9] The activities with higher TCs were used to be protective of activities with lower TCs when applicable. When the activities with higher TCs showed unacceptable risk at the peak DFR, activities with lower TCs are shown until risk is acceptable at the peak DFR.

Table 6 ETU dermal exposure estimates and cancer risk for postapplication workers

Crops	Rate[1] (kg a.i./ha)	Applications[2]		Activity[9]	TC[3] (cm^2/hr)	Peak DFR[4] (µg/cm^2)	Total LADD[5] (µg/kg bw/day)	Cancer risk[6] (day 0)	REI[7] (days)	DFR[4] (µg/cm^2) (REI)	Cancer risk[6] (REI)
		Number	Interval								
Potatoes	1.69	8	5	Hand set/Hand line irrigation related activities involving foliar contact	1750	0.036	0.157	1E-05	0.5	NA	NA
Apples	4.5	4	7	Hand thinning fruit	3000	0.088	0.762	5E-05	35	0.03	2E-05
				Hand harvesting	1400		0.356	2E-05	14	0.06	1E-05
				Pruning, scouting, training	580		0.147	9E-06	0.5	NA	NA
Onions (foliar)	1.69	6	7	Hand weeding	4400	0.036	0.395	2E-05	1	0.012	9E-06
				Hand set/Hand line irrigation related activities involving foliar contact	1750		0.157	1E-05	0.5	NA	NA
Sugar beets	1.69	5	7	Hand harvesting	1100	0.036	0.099	6E-06	0.5	NA	NA
Ginseng[8]	3.3	6	14	Hand set/Hand line irrigation related activities involving foliar contact	1750	0.070	0.307	2E-05	1	0.024	7E-06
				Hand harvesting	1100		0.193	1E-05	0.5	NA	NA
Cantaloupe, Cucumbers (field), Melons, Pumpkin, Squash	2.44	3	7	Hand set/Hand line irrigation related activities involving foliar contact	1750	0.052	0.227	1E-05	0.5	NA	NA
Tomatoes	2.44	2	7	Hand set/Hand line irrigation related activities involving foliar contact	1750	0.052	0.227	1E-05	0.5	NA	NA
Grapes	2.25	1	NA	Girdling, turning	19 300	0.089	3.53	2E-04	21	0.003	1E-05

Crops	Rate[1] (kg a.i./ha)	Applications[2]		Activity[9]	TC[3] (cm^2/hr)	Peak DFR[4] (µg/cm^2)	Total LADD[5] (µg/kg bw/day)	Cancer risk[6] (day 0)	REI[7] (days)	DFR[4] (µg/cm^2) (REI)	Cancer risk[6] (REI)
		Number	Interval								
				Tying/training, hand harvest, leaf pulling by hand	8500		1.56	9E-05	7	0.005	1E-05
				Hand set/Hand line irrigation related activities involving foliar contact	1750		0.320	2E-05	1	0.019	5E-06
				Bird control, propping, pruning, scouting, trellis repair, weeding	640		0.117	7E-06	0.5	NA	NA

ETU = ethylene thiourea; TC = transfer coefficient; DFR = dislodgeable foliar residue; LADD = lifetime average daily dose; REI = restricted-entry interval; NA = not applicable

[1] Registrant supported application rate.

[2] Registrant supported number of applications and application intervals.

[3] Transfer coefficients are based on PRMA defaults (PMRA# 2115788).

[4] Based on the DFR data from the studies (PMRA# 1746114; PMRA# 1746112; PMRA# 1752407─1752419) adjusted for differences in application rate. For apples, the residues were also adjusted for differences in the number of applications.

[5] Lifetime Average Daily Dose (LADD), calculated using the following formula: $\frac{\text{Absorbed Daily Dose (mg/kg bw/day)} \times \text{Treatment Frequency (30 days per year)} \times \text{Working Duration (40 yrs)}}{365 \text{ days/yrs} \times \text{Life Expectancy (78 yrs)}}$

Total LADD = ETU LADD + metabolic conversion from mancozeb LADD

Metabolic conversion from mancozeb LADD = Mancozeb LADD * 7.5%

[f6]Cancer risk on day 0 on the day of application or the REI day. If there are multiple applications, the cancer risk is presented for the day of the last application or the REI day to account for any possible accumulation of residues. Calculated using the following formula: LADD (mg/kg bw/day) × q_1^* $(0.0601 \text{ mg/kg bw/day})^{-1}$. Shaded cells indicate cancer risk above 1×10^{-5}. For grapes, day 14 ETU residue = 0.007 µg/cm^2 (Tying/training, hand harvest, leaf pulling by hand Cancer risk = 2E-05); day 35 ETU residue = 0.006 µg/cm^2 (Girdling, turning Cancer risk = 1E-05). For apples, the cancer risk is 1.5E-05 for hand thinning fruit on day 35 based on the study.

[7] Refers to the day following application that residues are less than the target DFR and calculated cancer risk is 1×10^{-5} or less.

[8] Surrogate TCs based on sweet potato and strawberry for harvesting

[9] The activities with higher TCs were used to be protective of activities with lower TCs when applicable. When the activities with higher TCs showed unacceptable risk at the peak DFR, activities with lower TCs are shown until risk is acceptable at the peak DFR.

Table 7 Mancozeb non-cancer inhalation exposure assessment and MOEs for bystanders

Population	Air concentration (µg/m^3)[1]	Inhalation rate (m^3/hr)	Exposure time (hrs/day)	Inhalation exposure (µg/kg bw/day)[2]	MOE[3]
Adult	4.76	0.64	2.3	0.088	60 000
Youth		0.63	1.9	0.100	53 000
Children (1<2 yrs)		0.33	2.3	0.328	16 000

MOE = margin of exposure
[1] Maximum air concentrations based on PMRA# 2044210.
[2] Where inhalation exposure = air concentration inhalation rate × exposure time/body weight. Body weight (80 kg for an adult, 57 kg for youth, 11 kg for a toddler).
[3] Based on short-, intermediate-term NOAEL of 5.27 mg/kg bw/day with a target MOE of 300.

Table 8 ETU non-cancer inhalation exposure assessment and MOEs for bystanders

Population	Air concentration (µg/m^3)[1]	Inhalation rate (m^3/hr)	Exposure time (hrs/day)	Inhalation exposure (µg/kg bw/day)[2]	MOE[3]
Adult	4.76	0.64	2.3	0.0066	760 000
Youth		0.63	1.9	0.0075	670 000
Children (1<2 yrs)		0.33	2.3	0.025	200 000

MOE = margin of exposure
[1] Maximum concentrations based on PMRA# 2044210.
[2] Where inhalation exposure = 7.5% × MCZ inhalation exposure from Table 7.
[3] Based on short-, intermediate-term NOAEL of 5 mg/kg bw/day with a target MOE of 1000.

Table 9 ETU inhalation exposure assessment and cancer risk for bystanders

Population	MCZ exposure[1] (µg/kg bw/day)	ETU exposure[2] (µg/kg bw/day)	Exposure days/year	LADD[3] (µg/kg bw/day)	Total LADD (µg/kg bw/day)	Cancer Risk[4]
Adult	0.088	0.0066	10	1.45E-04	2.02E-04	1E-08
Youth	0.100	0.0075		1.32E-05		
Children (1<2 yrs)	0.328	0.0246		4.33E-05		

ETU = ethylene thiourea; MCZ = mancozeb; LADD = Lifetime average daily dose
[1] Based on mancozeb inhalation exposure calculated in Table 7.
[2] ETU Exposure calculated based on the metabolic conversion of mancozeb = MCZ exposure × 7.5%.
[3] LADD = ETU exposure × exposure frequency (10 days) × exposure duration (5 years for youth and children and 63 years for adults)/(365 days/year × Life expectancy (78 yrs))
[4] Cancer risk = LADD × q_1^* (0.0601 (mg/kg bw/day)$^{-1}$)

Table 10 MCZ non-cancer aggregate exposure assessment for bystanders

Population	MCZ Bystander enhalation exposure[1] (mg/kg bw/day)	MCZ chronic dietary exposure[2] (mg/kg bw/day)	Inhalation MOE[3]	Dietary MOE[4]	Aggregate MOE[5]
Adult	8.76E-05	0.000012	60 000	1 250 000	57 000
Youth	1.00E-04	0.000018	53 000	830 000	50 000
Children (1<2 yrs)	3.28E-04	0.000074	16 000	200 000	15 000

MCZ = mancozeb, MOE = margin of exposure
[1] MCZ bystander exposure based on Table 7 converted to mg.
[2] MCZ chronic dietary exposure based on the dietary risk assessment.
[3] Based on short-, intermediate-term NOAEL of 5.27 mg/kg bw/day with a target MOE of 300.
[4] Based on short-, intermediate-term NOAEL of 15 mg/kg bw/day with a target MOE of 300.
[5] Aggregate MOE = 1/ ((1/inhalation MOE) + (1/dietary MOE)) with a target MOE of 300.

Table 11 ETU aggregate non-cancer exposure assessment, MOEs, and cancer risk for bystanders

Population	ETU bystander inhalation exposure[1] (mg/kg bw/day)	ETU chronic dietary exposure[2] (mg/kg bw/day)	Aggregate exposure[3] (mg/kg bw/day)	MOE[4]	ETU bystander cancer risk[5]	ETU dietary cancer risk[6]	Aggregate cancer risk[7]
Adult	6.57E-06	0.000015	2.16E-05	9300	1E-08	1E-06	1E-06
Youth	7.50E-06	0.000017	2.45E-05	8200			
Children (1<2 yrs)	2.46E-05	0.000076	1.01E-04	2000			

ETU = ethylene thiourea; MOE = margin of exposure; LADD = lifetime average daily dose
[1] ETU bystander exposure based on Table 8 converted to mg.
[2] ETU chronic dietary exposure based on the dietary risk assessment.
[3] ETU Aggregate exposure = ETU exposure + ETU chronic dietary exposure
[4] Based on short-term NOAEL of 0.2 mg/kg bw/day with a target MOE of 100.
[5] ETU Bystander Cancer Risk based on Table 8.
[6] .ETU Dietary Cancer Risk based on the dietary risk assessment.
[7] Aggregate Cancer risk = Bystander Cancer risk + Dietary cancer risk.

Appendix VIII Fate, toxicity, and risks to the environment

Table 1 Summary of fate and behaviour of mancozeb in the environment

Process	$t_{½}$ or DT_{50}	DT_{90}	Kinetics	Comments	PMRA#
Hydrolysis (25°C)	0.8 days pH 5 0.7 days pH 7 1.4 days pH 9	NR	SFO	Rapidly hydrolyzes in water	USEPA RED 2005 (1807553)
	0.9 days pH 4 1.9 days pH 7 1.9 days pH 9	2.8 days pH 4 6.2 days pH 7 6.3 days pH 9	SFO	Rapidly hydrolyzes in water Non-persistent	2950663
Phototransformation soil	CND			Mancozeb is not shown to photolytically degrade on dry soil, however, rapid decomposition would be expected in moist soil due to hydrolysis.	1215599
Photolysis water	A half-life for phototransformation in water could not be determined because of the spontaneous hydrolysis of mancozeb in water. Photolysis in water is not an important route of transformation.				1215610
Aerobic soil biotransformation 120 days Sandy loam: pH 6.5, 0.71% OC Loamy sand: pH 5.7, 2.17% OC Silt loam: pH 5.8, 0.99% OC	< 1 hour	CND	CND		1729981
Aerobic soil biotransformation 3 months Silt loam	< 2 days	CND	CND	The study results are unreliable in terms of quantitative estimation of a soil half-life due to issues interpreting the data and analytical problems. However, the study results are useful with respect to a worst-case derivation of aerobic soil biotransformation.	1216524
Aerobic soil biotransformation 8 weeks Silt loam: pH 6.8, 1.7% OC	<1 hour	25 hours	NR		EC 2018 (3017377)
Aquatic biotransformation					
Aquatic biotransformation 106 days. Two aerobic water/sediment systems: River system: water pH 8; sediment: sand, 1.06% OC Pond System: water pH 8; sediment: silt, 1.59% OC	0.97 days 1.03 days	25 days 27.3 days	DFOP DFOP		1728579
Aquatic biotransformation					1764935

Process	$t_{½}$ or DT_{50}	DT_{90}	Kinetics	Comments	PMRA#
105 days. Two aerobic water/sediment systems: River system: water pH 6.9; sediment: sand, 1.35% OC Pond System: water pH 6.6; sediment: silt, 5.03% OC	0.21 days 0.40 days	25.3 days 18.8 days	DFOP IORE		
Adsorption	Sand	*K*d = 11.4	K_{oc} = 2279	Slight mobility	1215600
	Sandy Loam	*K*d = 8.8	K_{oc} = 551	Low mobility	
	Silt Loam	*K*d = 5.7	K_{oc} = 283	Moderate mobility	
	Clay loam	*K*d = 8.4	K_{oc} = 562	Low mobility	
Leaching	Radioactivity recovered in the leachate was 19.1, 8.7 and 4.2 % of AR in sandy loam and two silt loam soil, respectively. The majority of the residues remained in the soil – 77.8, 98.9 and 90.2% of AR, respectively. The greatest concentration of ^{14}C residues left in the soils were in the top 1 inch, 56.8, 84.2 and 83% of AR, respectively. No significant ^{14}C volatiles were formed. Radioactivity in leachates and remaining in soil was not characterized.				1132308
Terrestrial Field Dissipation (California)	Mancozeb 31–66 d	NR	SFO		1699407
	ETU 41–89	NR	SFO		
CND = could not determine NR = not reported					

Table 2 Summary of the fate and behaviour of ETU in the environment

Property	Test substance	Value	Transformation products	Comments	PMRA#
Phototransformation on soil	ETU	$t_{1/2}$ = 1.28 d	Not measured		1744702
Phototransformation in air	maneb and zineb	$t_{1/2}$ = 8 and 9 d	Not measured	micro agroecosystem	1750246
		$t_{1/2}$ = <1 h	Not measured	EPI Suite v 3.12	1744702
Phototransformation in water	ETU	$t_{1/2}$ = 2.35 d sensitized (confirmed by EC PMRA# 3017377)	EU and two unknowns at 31, 10 and 36% of AR (in sensitized treatments)	In natural water (non-sterile) phototransformation is rapid	1580898
		$t_{1/2}$ = 76.2 to 358 d in deionized water			
Hydrolysis	ETU	$t_{1/2}$= 96.7 d (pH 7)	Insufficient transformation of ETU to determine	Stable (from dark control of photolysis study)	1580898
		stable (pH 5,7,9)			1744702
Aerobic soil biotransformation	ETU	$t_{1/2}$ = 1.4–3.2 d	EU <1 to 3.4% of applied	Non-persistent	1744702, 1216524
	ETU	$t_{1/2}$ = <2 d	EU 54–94%, 2 unknowns		1216524
	ETU	$t_{1/2}$ = 0.1–3.1 days	Not measured		3017377
	parent EBDCs	ETU $t_{1/2}$ = 0.2–6.6 d	No info		1744708, 1744712, 1744713
Anaerobic soil biotransformation	No information				
Aerobic aquatic biotransformation	nabam	DT_{50} = 21.1 days in water	Major: EBIS, EU	Slightly persistent	1580892
Anaerobic water biotransformation	ETU	DT50 whole system = 15.4 to 30.1 days DT50 water = 9.5 and 30.2 days	Major: EU, EDA and CO_2	Slightly persistent	2950667, 2950666
Adsorption/desorption	ETU	K_F = 0.51 clay loam K_F = 0.67 sandy loam K_F = 0.73 sand K_F = 1.14 silt loam $K_{oc\text{-}ads}$ = 35–141 (all soils)	EU 0–14% of applied	High to very high mobility	1580895
	ETU	K_{oc} = 54, 165, 276, 464, 783, 855	Not measured	Low to Very high mobility	1744702
	ETU	K_F = 0.027 to 0.067, Kfoc = 3.4 – 4.6	Not measured	Very high mobility	3017377

Property	Test substance	Value	Transformation products	Comments	PMRA#
Leaching	ETU residues	22–91% of AR in leachate	Not measured	Highly mobile	1580902
Volatilization	maneb and zineb	$t_{1/2}$ = < 2 h to 9 d	Not measured	Not persistent in air	1750246, EPISuite v 3.12
Field dissipation	metiram, New York	Apparent DT_{50} = 21 d	Not measured	Slightly to moderately persistent	1589667
	mancozeb, California	Apparent DT_{50} = 41, 93 d	Not measured		1699407
	EBDC, European review	DT_{50} <7 days	Not measured	Non persistent	1744708, 1744712, 1744713
Field leaching	metiram, New York	ND >15.2 cm soil depth	Not measured	Leaching does not appear to be a concern.	1589667
	mancozeb, California	ND >15.2 cm soil depth	Not measured		1699407
	ETU	ND > 12.7 cm	Not reported		3017377

Table 3 Effects on terrestrial organisms

Organism	Exposure	Test substance	Endpoint value[1]	PMRA#
Invertebrates				
Earthworm (*Eisenia foetida*)	Acute	Dithane M-45 84.6% mancozeb	14-d LC_{50} > 299.1 mg a.i./kg soil NOEC = 299.1 mg a.i./kg soil	1132316; EC 2018 (3017379)
	Acute	Penncozeb 80 WP (mancozeb 80.3%)	**14-d LC_{50} > 1000 mg a.i./kg soil**	EC 2018 (3017381)
	Acute	Fortuna 800 WP (794.4 g mancozeb/kg)	14-d LC_{50} > 794.4 mg a.i./kg soil	EC 2018 (3017383)
	Chronic	81.7% mancozeb	Mortality and biomass: 28-d NOEC ≥ 161 mg a.i./kg soil Reproduction (number of offspring): 56-d NOEC = 20 mg a.i./kg soil	1699413; EC 2018 (3017379)
	Chronic	Dithane M-45 (mancozeb 82.6%)	Mortality and biomass: 28-d NOEC ≥ 316 mg a.i./kg soil Reproduction (number of offspring): 56-d NOEC = 56.2 mg a.i./kg soil EC_{10} = 59.4 mg a.i./kg soil LOEC = 100 mg a.s./kg soil	EC 2018 (3017382)
Springtail (*Folsamia candida*)	Chronic	Dithane M-45 (84.6% a.i.)	Mortality: 28-d LC_{50} = 21.6 mg a.i./kg soil 28-d NOEC = 17.8 mg a.i./kg soil Reproduction (number of	EC 2018 (3017379)

Organism	Exposure	Test substance	Endpoint value[1]	PMRA#
			juveniles): 28-d LC_{50} = 20.1 mg a.i./kg soil **28-d NOEC = 10 mg a.i./kg soil**	
		Mancozeb technical (89.8% a.i.)	Mortality: 28-d LC_{50} = 0.397 mg a.i./kg soil 28-d NOEC = 0.14 mg a.i./kg soil Reproduction (number of juveniles): 28-d LC_{50} = 0.083 mg a.i./kg soil 28-d NOEC = 0.014 mg a.i./kg soil	EC 2018 (3017379)
		Mancozeb 75 WG (86% a.i.)	Mortality: 28-d LC_{50} = 40.7 mg a.i./kg soil 28-d NOEC = 30.9 mg a.i./kg soil LC_{10} = 15.8 mg a.i./kg soil LOEC = 55.6 mg a.i./kg soil Reproduction (number of juveniles): 28-d LC_{50} = 43.6 mg a.i./kg soil 28-d NOEC = 30.9 mg a.i./kg soil EC_{10} = 28.6 mg a.i./kg soil LOEC = 55.6 mg a.i./kg soil	EC 2018 (3017381)
Bee (*Apis mellifera*)	Acute contact adult	Technical (% a.i. not reported)	LD_{50} > 179 µg a.i./bee	USEPA RED 2005 (1807553)
	Acute contact adult	Fortuna 800 WP (794.4 g mancozeb/kg	48-h LD_{50} > 100 µg product/bee	EC 2018 (3017383)
	Acute contact adult	Mannex II (purity not reported)	48-h LD_{50} > 400 µg /bee **Note:** It is unclear whether the reported endpoints is based on active or product.	EC 2018 (3017381)
	Acute oral adult		48-h LD_{50} > 208.89 µg/bee **Note:** It is unclear whether the reported endpoints is based on active or product.	
	Acute contact adult	Dithane M-45 (86% a.i.)	8 – d LD_{50} > 344 µg a.i./hl	EC 2018 (3017381); Study authors: Loveaux, J., Missonnier, J; & Mesquida, J. 1980
	Acute oral adult		72-h LD_{50} > 7280 µg a.i./bee	
	Acute contact adult	Mancozeb technical (86.2% a.i.)	**72-h LD_{50} = 161.7 µg a.i./bee**	EC 2018 (3017379); Study author: Amutha, S., 1999
	Acute oral adult		**72-h LD_{50} = 68.9 µg a.i./bee**	
	Acute contact adult	69% mancozeb 8.26%	72-h LD_{50} > 200 µg formulation/bee	1699414

Organism	Exposure	Test substance	Endpoint value[1]	PMRA#
		zoxamide		
	Acute oral adult	69% mancozeb 8.26% zoxamide	72-h LD_{50} > 153 µg formulation/bee	
	Acute oral adult	Manzate Prostick (75% a.i.)	48-h LD_{50} > 133.3 µg a.i./bee	2950668
	Chronic oral adult	Mancozeb technical (89.8% a.i.)	10-d LD_{50} > 51.4 µg a.i./bee 10-d NOED ≥ 51.4 µg a.i./bee	EC 2018 (3017379); Study author: Galvez 2015
	Chronic oral adult	Mancozeb 80% WP	10-d LD_{50} > 125.4 µg a.i./bee **10-d NOED = 68.9 µg a.i./bee**	EC 2018 (3017379); Study author: Kleebaum, K., 2014a
	Chronic oral larval	Mancozeb 80% WP	22-d LD_{50} = 21.0 µg a.i./larvae **22-d NOED = 12.5 µg a.i./larvae**	EC 2018 (3017379); Study author: Kleebaum, K., 2014b
	Honey bee field trial	Mancozeb 80% WP 33 day study Two treatments: 0.266 and 0.455 g/ 500 g sugar solution	Honeybee brood feeding study conducted under field conditions. No adverse effects on survival, behaviour and development of honeybees were observed at feeding rates equivalent to 1.6 and 2.4 kg a.i./ha; the European Commission (2018) does not report how these rates were obtained from the treatment doses used in the study and the PMRA is unaware of pollen/nectar residue data the could be used as bridging data to estimate equivalent field rates.	EC 2018 (3017379); Study author: Hecht-Rost, S. 2015
Bumblebee *(Bombus terrestris)*	Acute contact	Mancozeb 80% WP	96-h LD_{50} > 2000 µg a.i./bee	EC 2018 (3017379); Study author: Amsel, K. 2014
	Acute oral		96-h LD_{50} = 1351 µg a.i./bee	
Solitary bee (*Osmia bicornis*)	Acute contact	Mancozeb 80% WP	96-h LD_{50} > 800 µg a.i./bee	EC 2018 (3017379); Study author: Shnurr, A. 2015

Organism		Exposure	Test substance	Endpoint value[1]	PMRA#
Beneficial arthropods	Parasitoid wasp *Aphidius rhopalosiphi*	Tier 1 study	Manex II (Mancozeb 35.1%)	Limit test: 913 g a.i./ha. 0% effect on mortality 36.3% effect on reproduction	EC 2018 (3017381)
		Tier 1 study	Sancozeb 800 WP (84.8%)	Tested at 350 and 3500 g a.i./ha At 3500 g a.i./ha, 0% effect on mortality and 36.3% effect on reproduction.	EC 2018 (3017381)
		Tier 1 study	Agria mancozeb 80 WP (83.5%)	48-h LR_{50} > 8350 g a.i./ha 14 ER_{50} < 3340 g a.i./ha 14-d NOEC < 3340 g a.i./ha	EC 2018 (3017383)
		Extended lab study	Penncozeb 75 DG (Mancozeb: 76.5 %)	48-h LR_{50} > 1530 g a.i./ha 50% effects on reproduction at 1530 g a.i./ha	EC 2018 (3017381)
	Predatory mite *Typhlodromus pyri*	Tier 1 study	Dithane M-45 (80.5%)	7-d LR_{50} = 26.67 g a.i./ha 14-d ER_{50} > 9.2 g a.i./ha 14-d NOEC = 9.2 g a.i./ha (based on eggs produced per female)	EC 2018 (3017382)
		Tier 1 study	Agria mancozeb 80 WP (83.5%)	7-d LR_{50} = 162 g a.i./ha 14-d ER_{50} < 1.71 g a.i./ha 14-d NOEC < 1.71 g a.i./ha (based on eggs produced per female)	EC 2018 (3017383)
		Extended lab study	Dithane M-45 (81.8% a.i.)	**7-d LR_{50} = 107 g a.i./ha** 14-d NOEC < 20.45 g a.i./ha (based on eggs produced per female)	1699434; EC 2018 (3017382)
		Extended lab study	Penncozeb 75 DG 76.5% a.i.) Granular product	7-d LR_{50} ~ 1530 g a.i./ha (>56% mortality at 1530 g a.i./ha) Reproduction (cumulative no of offspring per female): 14-d NOER = 76.5 g a.i./ha	EC 2018 (3017381)
		Field trial	technical	Three separate outdoor experiments were conducted in apple orchards in summer; sites were chosen based on adequate populations of *T. pyri* (25 per 100 leaves (and phytophagous mites present on leaves. The experimental design was a randomised complete block consisting of 12 treatments with four replicates. Mancozeb was applied at a rate of 3600 g a.i./ha five times at intervals at approximately 7-day intervals for the first two experiments and at 14-day intervals in the third. Leaves were samples prior to spraying and after applications. *T. pyri* and eggs were counted. The study summary provides limited details on method and results and it is unclear whether other pesticides were included in the experiments. The study	EC 2018 (3017379); Study author: Cross J.V. and A.M. Berrie, 1994

Organism		Exposure	Test substance	Endpoint value[1]	PMRA#
				summmary states that "further investigation on long term effect of mancozeb in the field are desirable". Another study cited as Walker et al. 1988, found mancozeb to be disruptive to integrated mite management on apples in New Zealand.	
	Cydnodromus californicus (adult)	Extended lab study	Dithane M-45 (80%)	Limit test: 1600 g a.i./ha. 0% effect on mortality	EC 2018 (3017382)
	Pirate bug *Orius laevigatus* (second instar nymph)	Extended lab study	Dithane M-45 (80.5%)	9-d LR_{50} > 3200 g a.i./ha 14-d ER_{50} > 3200 g a.i./ha	EC 2018 (3017382)
	Spider *Pardosa sp*	Extended lab study	Dithane M-45 (Mancozeb: 80.5 %)	14-d LR_{50} > 1600 g a.i./ha 14-d ER_{50} > 1600 g a.i./ha	EC 2018 (3017382)
	Seven spotted ladybird *Coccinella septempunctata* (larvae)	Extended lab study	Penncozeb 80 (Mancozeb: 83.8%)	Two test concentrations: 1676 and 2514 g a.i./ha 21-d LR_{50} > 2514 g a.i./ha NOEC ≥ 2514 g a.i./ha	EC 2018 (3017381)
	Ground beetle *Poecilus cupreus* (adult)	Tier 1	Manex II (Mancozeb: 35.1%)	Limit test: 842 g a.i./ha 0% effect on mortality and 8.6% effect on feeding capacity	EC 2018 (3017381)
		Tier 1	Penncozeb 80 WP (Mancozeb 80%)	Limit test: 1600 g a.i./ha LR_{50} > 1600 g a.i./ha ER_{50} > 1600 g a.i./ha	EC 2018 (3017381)
	Green lacewing *Chrysoperla carnea* (larvae)	Tier 1	Manex II (Mancozeb: 35.1%)	Limit test: 842 g a.i./ha 0% effect on mortality and 12.2% effect on reproduction	EC 2018 (3017381)
	Polyphagous wasp *Trichogramma cacoeciae* (adult)	Extended laboratory study - aged residues	Dithane Ultra WG (Mancozeb: 75.3%)	Parasitic capacity: > 50% decreased 0, 7, 14, 21 and 28 day aged residues Parasitic capacity >50% effects after 15 to 28 days aged residues Parasitic capacity <50% effects after 35 days aged residues ER_{50} = <1355 g a.i./ha	EC 2018 (3017382)
	Predatory mite *Hypoaspis (Geolaelaps) aculeifer*	Contact (soil)	Mancozeb (86% a.i.)	Adult mortality: 14-d LC_{50} > 1000 mg a.i./kg soil 14-d NOEC = 132 mg a.i./kg soil Reproduction (number of juveniles): 14-d LC_{50} = 155.6 mg a.i./kg soil 14-d NOEC = 58.5 mg a.i./kg soil 14-d EC_{10} = 72.3 mg a.i./kg soil 14-d LOEC = 87.8mg a.i./kg soil	EC 2018 (3017379); Study author: Scheffczyk, A. 2014
		Contact (soil)	Mancozeb technical (89.8% a.i.)	Adult mortality: 14-d LC_{50} > 372 mg a.i./kg soil 14-d NOEC = 35.6 mg a.i./kg soil	EC 2018 (3017379); Study

Organism		Exposure	Test substance	Endpoint value[1]	PMRA#
				Reproduction (number of juveniles): 14-d LC_{50} = 231 mg a.i./kg soil 14-d NOEC = 115 mg a.i./kg soil 14-d EC_{10} = 26.5 mg a.i./kg soil 14-d LOEC = 207 mg a.i./kg soil	author: Definod, C. 2015b
		Contact (soil)	Mancozeb 80 WP (80.3%)	Adult mortality: 14-d LC_{50} = 382 mg a.i./kg soil 14-d NOEC = 152 mg a.i./kg soil Reproduction (number of juveniles): 14-d NOEC = 152 mg a.i./kg soil 14-d EC_{10} = 89.5 mg a.i./kg soil 14-d LOEC = 273 mg a.i./kg soil	EC 2018 (3017381)
		Contact (soil)	Dithane M-45 (82.3% a.i.)	LR_{50} and ER_{50} > 4.3 mg a.i./kg soil (equivalent to 3200 g a.i./ha) **Note:** Exposure duration was only 1.5 hours; mortality and reproduction was assessed at 21 days	EC 2018 (3017382)
Birds					
Mallard duck (*Anas Platyrhynchos*)		Acute	Dithane M-45 (86% a.i.)	10-d LD_{50} > 1376 mg a.i./kg/day	1699431; EC 2018 (3017379)
			Mancozeb technical (86.2% a.i.)	Limit test 14-d LD_{50} > 1724 mg a.i./kg /day)	EC 2018 (3017379)
Japanese quail *(Coturnix japonica)*			Dithane M-45 (86% a.i.)	10-d LD_{50} > 2752 mg a.i./kg/day	1699431; EC 2018 (3017379)
			Mancozeb technical (86.2% a.i.)	Limit test 14-d LD_{50} > 1724 mg a.i./kg /day)	EC 2018 (3017379)
			Fortuna 800 WP (794.4 g mancozeb/kg)	Limit test: 2000 mg Fortuna 800 WP/kg 14-d LD_{50} > 1589 mg a.i./kg /day)	EC 2018 (3017382)
English sparrow (*Passer domesticus*)			Not reported	**10-d LD_{50} = 1500 mg a.i./kg**	USEPA RED 2005 (1807553)
Bobwhite quail (*Colinus virginianus*)		Reproduction	86.2–88.5% mancozeb	NOEL = 25.5 mg a.i./kg bw/day	1788050; EC 2018 (3017379)
			81.9% mancozeb	**NOEL = 13.2 mg a.i./kg bw/day**	1788051
Mallard duck		Reproduction	80.1% mancozeb	NOEL = 18.1mg a.i./kg bw/day	1788049; EC 2018 (3017379)
Mammals					
Rat		Acute oral	95% mancozeb	**LD_{50} > 5000 mg/kg bw**	1570258

Organism	Exposure	Test substance	Endpoint value[1]	PMRA#
Rat - CD(BR)	2 generation reproduction	88.4 mancozeb (Penncozeb)	NOEL: Repro >110 **offspring: 2.5** parental: 15 (mg a.i./kg bw/day)	1624102
	2 generation reproduction	84 % mancozeb	NOEL: Parental: 7.0/7.5 Repro: 69/79 Offspring: 69/79 (mg a.i./kg bw/day)	1173163
Vascular Plants				
Crop species	Seedling emergence	60% mancozeb 9% dimethomorph Tier I study : (155/0.20 kg a.i./ha).	Most sensitive monocot: Onion – 12% plant dw inhibition Most sensitive dicot: Soybean + tomato – 4% plant dw inhibition	USEPA RED 2005 (1807553)
	Vegetative vigour		Most sensitive monocot: Corn + onion – 2% plant dw inhibition Most sensitive dicot: Cucumber – 10% plant dw inhibition	
	Seedling emergence Monocots: Corn, oat, onion, ryegrass Dicots: cucumber, lettuce, oilseed rape, radish, soybean, tomato	Dithane M-45 (81% a.i.) Tier 1 study: 17.4 lbs a.i./acre (19.5 kg a.i./ha). Applied pre-emergent.	No adverse effects were reported for any species based on the parameters tested: emergence, survival, phytotoxicity, shoot height and dry weight. NOER: 19.5 kg a.i./ha **EC_{25}: >19.5 kg a.i./ha**	2363967
	Vegetative vigour Monocots: Corn, oat, onion, ryegrass Dicots: cucumber, lettuce, oilseed rape, radish, soybean, tomato	Tier 1 study: 17.4 lbs a.i./acre (19.5 kg a.i./ha). Applied post-emergent at 1 or 2 leaf stage (depending on species).		2363969
	Seedling emergence Monocots: Corn, wheat, onion,	Mancozeb ProStick (75.2% a.i.), applied pre-emer	No adverse effects were reported for any species based on the parameters tested: emergence, survival, phytotoxicity, shoot height and dry weight.	2950689

Organism	Exposure	Test substance	Endpoint value[1]	PMRA#
	ryegrass Dicots: sugar beets, oilseed rape, cabbage, soybean, sunflower, tomato	Tier 1 study: 12 lbs a.i./acre (13.5 kg a.i./ha). Applied pre-emergent.	NOER: 13.5 kg a.i./ha EC_{25}: >13.5 kg a.i./ha	
	Vegetative vigour Monocots: oat, onion Dicots: oilseed rape, soybean, tomato, carrot	Tridex 75 DG (76.7% a.i.) Tier 1 study: 1.408 kg a.i./ha). Applied post-emergent at 2 to 4 leaf stage	No adverse effects: survival, phytotoxicity, shoot height, fresh and dry weight. Some phytotoxic effects were observed albeit infrequently and some occurences were found in the control replicates (for example, stunting, chlorosis). NOER: 1.408 kg a.i./ha EC_{50}: >1.408 kg a.i./ha	EC 2018 (3017379); Study author: Cross, N. 2010.
Weed species	Various species	Dithane M-45 (80% a.i.) Tier 1 study: 4.0 kg a.i./ha Pre and post emergent	Findings reported: Dithane® M-45 did not show any activity against any of the weed species tested at 4.0 kg a.i./ha. NOER ≥ 4.0 kg a.i./ha EC_{25} > 4.0 kg a.i./ha	EC 2018 (3017379); Study author: Musco, V. 1994.

1 - Endpoints values shown in bold were used in the risk assessment

Table 4 Effects on aquatic organisms

Organism	Study type	Species	Test material	Endpoint	Value (nominal / mean measured)	Comments	Reference
Freshwater Organisms							
Invertebrates	Acute	*Daphnia magna*	80.0% mancozeb	48-h EC_{50}	580 µg a.i./L (nominal)	The study results are not considered appropriate for risk assessment.[1]	USEPA RED 2005 (1807553)
			Mancozeb technical 90%	48-h EC_{50}	**73 µg a.i./L** (measured)	Static test conditions. Immobility. Verification of the test concentrations at 0 and 48 hours showed the test material to be unstable in water. As a result of the instability observed, the European Commission (2018) reports that the analysis of immobility was carried out using **actual concentration** instead of nominal concentrations **at 48 hours.** European Commission (2018) reports the same endpoint as the study authors (48-hour EC_{50} = 73 µg a.i./L) but also states that this endpoint is based on **mean measured** concentrations. The reviewer notes that this endpoint is considerably lower than other *Daphnia magna* acute toxicity endpoints.	EC 2018 (3017379)

Organism	Study type	Species	Test material	Endpoint	Value (nominal / mean measured)	Comments	Reference
			Dithane M-45 (81.3% mancozeb)	48-h EC_{50} NOEC	3800 µg a.i./L 470 µg a.i./L (mean measured)	Flow-through conditions. Mean measured concentrations ranged from 90 to 116% of the nominal concentrations.	EC 2018 (3017379)
			Penncozeb 80 WP (82% mancozeb)	48-h EC_{50}	390 µg a.i./L (nominal)	Static test conditions. The results are inconsistent with some studies conducted under static conditions that show significant loss of mancozeb over the course of the exposure period. Concentrations were maintained within 20% of nominal after 48 hours. For this reason the nominal based endpoint is considered acceptable.	EC 2018 (3017380)
			Penncozeb technical (purity not reported)	48-h EC_{50}	660 µg a.i./L (nominal)	Static test conditions. No information on the percentage of mancozeb in the formulation used is provided in the study report. It is therefore not possible to conclude an endpoint in terms of active substance from this study. In addition, no measurements of the test substance concentration in test vessels are reported in the study. The study results are not considered appropriate for risk assessment.[1]	EC 2018 (3017380)
			Sancozeb 800WP (80% mancozeb)	48-h EC_{50}	900 µg a.i./L (nominal)	Static test conditions. The study results are not considered appropriate for risk assessment.[1]	EC 2018 (3017380)
			Mancozeb 80 WDP (80% mancozeb)	24-h EC_{50}	11.2 µg a.i./L (nominal)	Static test conditions. Only 24 hours instead of standard 48 hours. The study results are not considered appropriate for risk assessment.[1]	EC 2018 (3017380)
			Formulated product (37%)	48-h EC_{50} NOEC	8500 µg g a.i./L (nominal)	Static test conditions. The study results are not considered appropriate for risk assessment.[1]	1788052
			66.6% mancozeb 4.09% benalaxyl	48-h EC_{50} NOEC	1800 µg total product/L 980 µg total product/L (mean measured)	See note[2]	1788053
			69 % mancozeb 8.26% zoxamide	48-h EC_{50} NOEC	3300 µg total product/L 820 µg total product/L (mean measured)	See note[2]	1699415

Organism	Study type	Species	Test material	Endpoint	Value (nominal / mean measured)	Comments	Reference
			Dithane M-45 (82.4% mancozeb)	48-h EC_{50} NOEC	1040 µg a.i/L 460 µg a.i/L (nominal)	Static test conditions. The study results are not considered appropriate for risk assessment.[1]	1132317
			Mancozeb 80 WP (83.2% mancozeb)	48-h EC_{50}	350 µg a.i/L (nominal)	Static test conditions. The study results are not considered appropriate for risk assessment.[1]	EC 2018 (3017383)
			Fortuna 800 WP (794.4 g mancozeb/kg)	48-h EC_{50}	1096 µg a.i/L (nominal)	Static test conditions. The results are inconsistent with some studies conducted under static conditions that show significant loss of mancozeb over the course of the exposure period. Concentrations were maintained within 20% of nominal at test initiation and after 48 hours. For this reason the nominal based endpoint is considered acceptable.	EC 2018 (3017383)
	Acute	Freshwater snail *Lymnea stagnalis*	Penncozeb 80 WP (80% mancozeb)	48-h EC_{50}	>45 359 µg a.i./L (mean measured)	Static test conditions. The study was performed as a limit test. A geomean of the mean initial and the lowest 48-h measured values is reported.	EC 2018 (3017379)
	Acute	*Gammarus* sp.	Penncozeb 80 WP (80% mancozeb)	48-h EC_{50}	3000 µg a.i./L (initial measured)	Static test conditions. The study results are not considered appropriate for risk assessment.[1]	EC 2018 (3017379)
	Acute	*Asellus sp.*	Penncozeb 80 WP (80% mancozeb)	48-h EC_{50}	4400 µg a.i./L (initial measured)		EC 2018 (3017379)
	Chronic	*Daphnia magna*	Dithane M-45 (82.4% mancozeb)	21-d LC_{50} (survival) **NOEC** EC_{10} (reproductive effects)	>53 ug a.i./L **7.3 µg a.i/L** 10.9 µg a.i/L (mean measured)	Flow through conditions. NOEC based on mean young/adult reproduction day. The study is considered acceptable.	1169756; EC 2018 (3017379)
			Sancozeb 800 WP (80.5% mancozeb)	21-d LC_{50} (survival) NOEC (reproductive effects)	100 ug a.i./L 29 µg a.i/L (nominal)	Static renewal conditions. The study results are not considered appropriate for risk assessment.[1]	EC 2018 (3017380)

Organism	Study type	Species	Test material	Endpoint	Value (nominal / mean measured)	Comments	Reference
			Dithane DG (77.1% mancozeb)	28-d LC_{50} (survival) NOEC (reproductive effects)	24 µg a.i/L 18 µg a.i/L (mean measured)	Flow-through test conditions. NOEC based on mean young/adult reproduction day. The study is considered acceptable.	1699416
		Chironomus riparius	Mancozeb 80 WP (80.5% mancozeb)	28-d EC_{50} NOEC (emergence) NOEC (developmental rate)	≥ 7160 µg a.i/L 430 µg a.i/L 1090 µg a.i/L (initial measured)	Static water/sediment test system. Spiked water; there was no renewal of the test medium during the test. The results show that test substance concentrations were not maintained under the conditions of the test. The study results are not considered appropriate for risk assessment.[1]	EC 2018 (3017379)
		Oligochaete *Lumbriculus variegatus*	Mancozeb 80 WP (80.5% mancozeb)	Reproduction (number of worms): 28-d EC_{50} NOEC Developmental rate (dry biomass of worms): 28-d EC_{50} NOEC	547 µg a.i/L 150 µg a.i/L 298 µg a.i/L 31 µg a.i/L (initial measured)		EC 2018 (3017379)
Fish	Acute	Rainbow trout (*Oncorhynchus mykiss*)	>90% mancozeb	96-h LC_{50} NOEC 96-h LC_{50} NOEC	210 µg a.i/L 180 µg a.i/L (nominal) 74 µg a.i/L 41 µg a.i/L (mean measured)	Static renewal every 24 hours. It is not clear whether concentration measurements were made in fresh water media samples or used samples (after each 24-hour period of renewal). Based on these uncertainties, the LC_{50} reported (mean measured) potentially represents an overestimate of toxicity. The study results are not considered in the risk assessment.	1699424; 1726834; EC 2018 (3017379)

Organism	Study type	Species	Test material	Endpoint	Value (nominal / mean measured)	Comments	Reference
			85% mancozeb	96-h LC_{50} NOEC	88 µg a.i/L 49 µg a.i/L (mean measured)	Static renewal every 24 hours. The EC (2018) states that raw analytical results were not presented in the study report and only an abbreviated summary table of geomeaned concentrations values was provided. The geomeaned concentration values in the table indicate that mancozeb was unstable. The geomeaned values were measured in fresh media and prior to each 24-hour renewal. However, the summary does not contain information on when measurements of test substance were taken, nor of what measurements were included in the calculations of mean measured concentrations. Based on the above uncertainties in reporting, the study results will not be considered for the PMRA's risk assessment.	EC 2018 (3017379)
			Mancozeb 80% WPD (80% mancozeb)	96-h LC_{50} NOEC	88 µg a.i/L 32 µg a.i/L (nominal)	The study results are not considered appropriate for risk assessment.[1]	EC 2018 (3017380)
			Dithane M-45	96-h LC_{50} NOEC	1000 µg a.i/L 270 µg a.i/L (mean measured)	Flow through conditions. EC (2018) states that the study reports that measurements made in all concentrations at days 0 and 4 were within ±20% of the nominal. The 96-hour endpoint is considered acceptable for the acute risk assessment.	EC 2018 (3017379)
			86% mancozeb	48-h LC_{50}	1860 µg a.i/L (nominal)	Static test conditions. The study results are not considered appropriate for risk assessment.[1]	1699421
			Dithane Flowable F45 (37%)	96-h LC_{50}	410 µg a.i./L (nominal)	Static test conditions. The study results are not considered appropriate for risk assessment.[1]	1788055

Organism	Study type	Species	Test material	Endpoint	Value (nominal / mean measured)	Comments	Reference
			81.3% mancozeb	96-h LC_{50} NOEC 96-h LC_{50} NOEC	990 µg a.i./L 250 µg a.i./L (nominal) 910 µg a.i./L 270 µg a.i./L (mean measured)	The USEPA classifies the study as supplemental (study is scientifically sound, but does not satisfy guideline); no explanation is provided. Flow through conditions. The measured concentrations rangedfrom 86.6–113% of nominal concentrations on Day 0 and 87.0–124% on Day 4. The 96-hour endpoint based on mean measured concentration is considered acceptable for the acute risk assessment.	1788057
			Penncozeb 80 WP (82% mancozeb)	96-h LC_{50}	150 µg a.i./L	Flow-through conditions. Measurements of test substance were made at 0, 24, and 96 h throughout the study. Measurements of test concentration were in the range of 48–136.5% of the nominal test concentrations. The LC_{50} is reported as based on "actual concentration"; it is not clear if this is defined as initial test concentrations measured or mean measured concentration values over the exposure period. Based on this uncertainty, the PMRA will not consider the endpoint for risk assessment. The EC (2018) reports an LC_{50} value of 150 µg a.i./L; this value was estimated from the reported "actual concentration" based LC_{50} value of 180 µg/L using the percentage purity of product (82%).	EC 2018 (3017380)
			80% mancozeb	96-h LC_{50}	640µg a.i./L (not reported)	The USEPA classifies the study as supplemental (study is scientifically sound, but does not satisfy guideline); no explanation is provided. It is unclear whether the endpoint was estimated using nominal or measured test concentrations. Nor is it know whether the study employed a static, static renewal or flow through test design. Due to these uncertainties, the study will not be considered for risk assessment**.**	USEPA RED 2005 (1807553)
					460 µg a.i./L (mean measured)	Static test conditions. The USEPA classifies the study as core (study satisfies guideline).	
			8.9% dimethomorph / 59.7% mancozeb	96-h LC_{50}	550 µg a.i./L (nominal)	See note[2]	

Organism	Study type	Species	Test material	Endpoint	Value (nominal / mean measured)	Comments	Reference
			8.9% dimethomorph / 59.7% mancozeb		680 µg a.i./L (nominal)		
			7.5% dimethomorph / 67.7% mancozeb		390 µg a.i./L (nominal)		
			8.26 zoxamide / 69.0% mancozeb		1900 µg a.i./L (not reported)		
		Bluegill sunfish (*Lepomis macrochirus*)	>90% mancozeb	96-h LC_{50} NOEC	83 µg a.i./L 56 µg a.i./L (mean measured)	Nominal based endpoints are not reported. EC (2018) states that the endpoints were based on mean measured concentrations of test substance measured every 24 hours. However, it is not reported whether measurements were made from samples taken from the freshly prepared media, or the spent media after each 24-h period. The measured values imply that measurements at 24, 48, 72, and 96 h were in fact made in the used media, as they are consistently lower (14–44.5% of the nominal) than the measurements made at 0 h (52–71% of the nominal). Mean measured values excluded the 0 h measurements. Based on these uncertainties, the LC_{50} reported (mean measured) potentially represents a potential overestimate of toxicity, and will not be considered for the risk assessment.	EC 2018 (3017379)
			Dithane M45 (81.3% mancozeb)	96-h LC_{50} NOEC 96-h LC_{50} NOEC	>4000 µg a.i./L 500 µg a.i./L (nominal) >3600 µg a.i./L 440 µg a.i./L (mean measured)	Flow through conditions. Recoveries (all test levels) were 86.5–104% of nominal concentrations at time 0 and 89.4–110% at 96 hours. Mortality was 45% at the highest test concentration (3600 µg a.i./L mean measured). The 96-h endpoint based on mean measured concentration is considered acceptable for the acute risk assessment.	1699425; EC 2018 (3017379)
			80% mancozeb	96-h LC_{50}	3850 µg a.i./L (nominal)	Static test conditions. The study results are not considered appropriate for risk assessment.[1]	USEPA RED 2005 (1807553)

Organism	Study type	Species	Test material	Endpoint	Value (nominal / mean measured)	Comments	Reference
					1350 µg a.i./L (not reported)	Static test conditions. The study results are not considered appropriate for risk assessment.[1]	
					1540 µg a.i./L (not reported)	Static test conditions. The study results are not considered appropriate for risk assessment.[1]	
					2040 µg a.i./L (mean measured)	Static test conditions. The USEPA classifies the study as supplemental (study is scientifically sound, but does not satisfy guideline); no explanation is provided. As other acceptable endpoints are available, the study endpoint was not be considered in the risk assessment.	
		Mirror carp *Cyprinus carpio*	Mancozeb WPD (80% mancozeb)	96-h LC_{50} NOEC	5780 µg a.i./L 4000 µg a.i./L (measured)	Semi-static design. Due to the lack of test substance measurements after 24 h and the fact that it is not clear whether measurements were made in fresh or spent media, the endpoint was not considered in the risk assessment.	EC 2018 (3017380)
			Penncozeb 80 WP (82% mancozeb)	96-h LC_{50} NOEC	1840 µg a.i./L 1340 µg a.i./L (mean measured)	Flow-through conditions.	EC 2018 (3017380)
		Zebrafish (*Brachydanio rerio*)	Sancozeb 800 WP (80% mancozeb)	96-h LC_{50} NOEC	4600 µg a.i./L 3000 µg a.i./L (nominal)	The study results are not considered appropriate for risk assessment.[1]	EC 2018 (3017380)
		Zebrafish (*Danio rerio*)	Fortuna 800 WP (794.4 g mancozeb/kg, 79.4%)	96-h LC_{50} NOEC	2620 µg a.i./L 993 µg a.i./L (nominal)	Semi-static conditions with media renewals at daily intervals. It is not possible to know if the concentrations of the test substance were maintained above 80% of the nominal as it has not been reported whether samples taken for analysis were from the spent media or the fresh media. The study results are not considered appropriate for risk assessment.[1]	EC 2018 (3017383)

Organism	Study type	Species	Test material	Endpoint	Value (nominal / mean measured)	Comments	Reference
	Chronic	Fathead minnow (*Pimephales promelas*)	79.3% mancozeb (radiolabelled)	28 day early life stage NOEC LOEC NOEC LOEC	Survival (28 days post hatch): 2.19 µg a.i/L 4.56 µg a.i/L (CS_2 mean measured) 4.65 µg a.i/L 9.57 µg a.i/L (LSC mean measured)	Flow-through conditions.	1171150; EC 2018 (3017379)
			Dithane M-45 (82.4% mancozeb)	33-day early life stage NOEC LOEC	Survival: 5.2 µg a.i/L 10 µg a.i/L (mean measured)	Flow-through conditions. The NOEC value is considered accceptable for risk assessment.	EC 2018 (3017379)

Organism	Study type	Species	Test material	Endpoint	Value (nominal / mean measured)	Comments	Reference
			84.8% mancozeb	215-day full life cycle	Parental generation (F0) Survival: NOEC = 5.05 µg a.i/L LOEC > 5.05 µg a.i/L Reproduction: **NOEC = 1.35 µg a.i/L** EC_{10} = 1.27 µg a.i/L LOEC = 2.58 µg a.i/L (based on # eggs/female/day and cumulative # of eggs) F1 generation Survival: NOEC = 2.58 µg a.i/L LOEC > 5.05 µg a.i/L (mean measured)	Flow-through conditions.	2950671; EC 2018 (3017379)
		Rainbow trout (*Oncorhynchus mykiss*)	77.1% mancozeb	21-day LC_{50} NOEC 21-day LC_{50} NOEC	149 µg a.i./L 13 µg a.i./L (nominal) 102 µg a.i./L 8 µg a.i./L (mean measured)	Flow-through conditions.	1699422
		Rainbow trout (*Oncorhynchus mykiss*)	Mancozeb 80 WP (purity not reported; based on other studies purity expected ~80%)	35-day LC_{50} NOEC	Survival and growth: > 67.3 µg a.i./L 67.3 µg a.i./L (initial mean measured)	All results were based on the mean of initial measured concentrations. As the concentrations were below the MQL between substance renewals and at the end of the study, the reported endpoints may represent an under estimation of toxicity. The study results, therefore, are not considered appropriate for risk assessment.	1169755; EC 2018 (3017379)

Organism	Study type	Species	Test material	Endpoint	Value (nominal / mean measured)	Comments	Reference
		Rainbow trout (*Oncorhynchus mykiss*)	Sancozeb 800 WP (80% mancozeb)	14-day LC_{50} NOEC NOEC	Survival: > 660 µg a.i./L 660 µg a.i./L Growth (weight and length): 490 µg a.i./L	Flow-through conditions. No mortality occurred up to the highest test concentration. It is unclear whether the endpoint values reported are based on mean measured or initial measured test concentrations. Due to this uncertainty, the results reported are not considered in the risk assessment.	EC 2018 (3017380)
		Zebrafish *(Danio rerio)*	mancozeb (87.4% purity)	LC_{10}	10.5 µg a.i./L (fry survival at 35d post-fertilisation)	Zebrafish were exposed to a total of 8 pulses of mancozeb (4 pulses for the parent generation and four for the F1 generation) with 7 days between pulses. The study design, therefore, represents a relevant and realistic worst case exposure scenario relative to the available standard chronic fish toxicity studies (based on continuous mancozeb exposure).	EC 2018 (3017379)
Algae	Acute	Green algae *Pseudokirchneriella subcapitata* (formerly known as *Selenastrum capricornutum*)	Dithane M-45 (82.4% mancozeb)	120-h EC_{50} NOEC 120-h EC_{50} EC_{10}	63 µg a.i./L 33 µg a.i./L (nominal) 32 µg a.i/L 9.5 µg a.i/L (mean measured)	Endpoints based on biomass production and growth rate. EC (2018) was provided EC# data from the applicant based on the geometric mean of measured concentrations at 0, 48 and 120 hours: 32.2 and 9.05 for the EC_{50} and EC_{10}, respectively. The geometric mean measured values from the study are appropriate for reporting endpoints.	1169755; EC 2018 (3017379)
			Mancozeb 80 WP (83.2% mancozeb)	72-h EC_{50}	1130 µg a.i./L (nominal)	Endpoints based on biomass production and growth rate. The study results are not considered appropriate for risk assessment.[1]	EC 2018 (3017383)
			Fortuna 800 WP (794.4 g a.s./kg)	72-h EC_{50}	81.7 µg a.i./L (nominal)	Endpoints based on growth rate. The study results are not considered appropriate for risk assessment.[1]	EC 2018 (3017383)
			69.0% mancozeb 8.26% zoxamide	96-h EC_{50} NOEC	31.4 µg a.i/L 234 µg a.i/L 8.43 µg a.i./L (mean measured total product)	See note[2]	1699433

Organism	Study type	Species	Test material	Endpoint	Value (nominal / mean measured)	Comments	Reference
			62.9% mancozeb 3.96% CGA 329351 (unknown active)	72-h EC_{50} NOEC	31.4 µg a.i/L 234 µg a.i/L 8.43 µg a.i./L (mean measured total product)	See note[2]	1171060
			89.14% mancozeb	120-h EC_{50} 48-h EC_{50} NOEC	390 µg a.i/L 430 µg a.i/L 200 µg a.i./L (nominal)	The study results are not considered appropriate for risk assessment.[1]	1169754
			Mancozeb TK (86.1% mancozeb)	72-h EC_{50} 72-h EC_{10} 72-h EC_{50} 72-h EC_{10} NOEC	Growth rate: 50.9 µg a.i/L 16 µg a.i/L Yield: **16 µg a.i/L** 4.27 µg a.i/L growth rate and yield: 2.01 µg a.i/L (mean measured)	The test concentrations were measured at 0, 24, 48 and 72 hours. For the lowest test concentration (10 µg a.i./L nominal), measured recoveries were below the LOQ (Limit of Quantification) and an LOQ/2 value (1.08 µg a.i./L /2 = 0.54 µg a.i./L) was used for the calculation of the geometric mean measured concentration according to specifications of OECD 23. Endpoints based on initial mean measured concentrations (0 h) were also calculated: the 72-h EC50 (yield) was calculated to be 66.6 µg a.i./L and the 72-h EC_{50} (growth rate) was calculated to be 195 µg a.i../L. The geometric mean measured values from the study are appropriate for reporting endpoints.	EC 2018 (3017379)
			67.7% mancozeb 7.5% dimethomorph	72-h EC_{50} NOEC	19 µg total product/L 4.3 µg total product/L	See note[2]	USEPA RED 2005 (1807553)
			60% mancozeb 9% dimethomorph	120-h EC_{50} NOEC	112 µg total product/L 28 µg total product/L		

Organism	Study type	Species	Test material	Endpoint	Value (nominal / mean measured)	Comments	Reference
		freshwater diatom *(Navicula pelliculosa)*	Penncozeb technical (86.3%)	96-h EC_{50} NOEC	**3.0 µg a.i/L** <0.88 µg a.i/L (initial measured)	Additional endpoints reported based on growth rate and yield: 96-h EC_{50} = 44 µg a.i/L; NOEC = 5.1 µg a.i/L (growth rate) 96-h EC_{50} = 11 µg a.i/L; NOEC = 5.1 µg a.i/L (yield) 72-h endpoint values (EC_{50} and NOECs) were all lower than 96-h endpoints indicating recovery. The 96-h EC_{50} represents the lowest algal toxicity endpoint. A higher tier aquatic toxicity study (considered in PRVD2018-17) demonstrates that phytoplankton and periphyton community response is measured at much higher concentrations. A formal review of this study was not conducted.	2950673
			60% mancozeb 9% dimethomorph	120-h EC_{50} NOEC	13.71 µg total product/L 2.88 µg total product/L	See note[2]	USEPA RED 2005 (1807553)
		freshwater blue-green algae *(Anabaena flos-aquae)*	Penncozeb technical (86.3% mancozeb)	96-h EC_{50} NOEC	17 µg a.i/L 11 µg a.i/L (initial measured)	Additional endpoints reported based on growth rate and yield: 96-h EC_{50} = 70 µg a.i/L; NOEC = 11 µg a.i/L (growth rate) 96-h EC_{50} = 20 µg a.i/L; NOEC = 11 µg a.i/L (area under growth curve) As a more sensitive endpoint is available (96 hour EC50 = 3.0 µg a.i/L for *Navicula pelliculosa*; PMRA# 2950673) and a higher tier aquatic toxicity study which demonstrates that phytoplankton and periphyton community response is measured at much higher concentrations, a formal review of this study was not conducted.	2950674

Organism	Study type	Species	Test material	Endpoint	Value (nominal / mean measured)	Comments	Reference
			Mancozeb 80 WP (80.5% mancozeb)	72-h EC_{50} NOEC 72-h EC_{50} NOEC 72-h EC_{50} NOEC	Growth rate: 267 µg a.i/L 71 µg a.i/L Biomass: 155 µg a.i/L 34 µg a.i/L Yield: 146 µg a.i/L 15 µg a.i/L (initial mean measured)	Measurement of mancozeb concentrations at 0 and 72 hours showed that mancozeb is unstable in this system. Not all initial measured concentrations were within ±20% of the nominal concentrations. Mancozeb were undetectable in all but the highest test concentration after 72 hours. The endpoint values reported are based on initial measured concentration only. The study results are not appropriate for consideration in the risk assessment.	1169755; EC 2018 (3017379)
			60% mancozeb 9% dimethomorph	120-h EC_{50} NOEC	130 µg total product/L 28 µg total product/L	See note[2]	USEPA RED 2005 (1807553)
		Scenedesmus subspicatus	Penncozeb 80 WP (838 g/kg mancozeb)	72-h EC_{50}	990 µg a.i/L (growth rate) (initial measured concentration)	The study invalid based on a number of study discrepancies, abnormalities and inconsistencies. The study is unacceptable for use in the risk assessment.	EC 2018 (3017380)
Vascular Plants	Acute	Duckweed (*Lemna gibba* G3)	Penncozeb technical (86.3% mancozeb)	7-d EC_{50} NOEC	>175 µg a.i/L 175 µg a.i/L	As no effects were observed and a definitive endpoint is available for *Lemna minor* (7-d EC_{50} = 1042 µg a.i/L based on biomass, PMRA# 1169755), a formal review of the study was not conducted.	2950669
		Duckweed (*Lemna minor*)	Mancozeb 80 WP (80.5% mancozeb)	7-d EC_{50} EC_{10} NOEC	1811 µg a.i/L (# fronds), **1042 µg a.i/L (biomass)** 82.2 µg a.i/L (# fronds), 37.1 µg a.i/L (biomass) 24.6 µg a.i/L (# fronds/biomass) (mean measured)	Semi-static regime, with renewal of the test media on days 3 and 5.	1169755; EC 2018 (3017379)
Amphibians	Acute	*B. Americanus* *R. pipiens*	Dithane DG (76–80% mancozeb)	96-h LC_{50}	1400 µg a.i/L (nominal) **200 µg a.i/L** (nominal)	Hatching success Exposure at Gosner stage 8 – embryo stage	2137153

Organism	Study type	Species	Test material	Endpoint	Value (nominal / mean measured)	Comments	Reference
		R. pipiens	Dithane DG (guarantee: 76–80% mancozeb) and Manzate		> 1000 µg a.i/L (nominal)	Mortality Stage 25 tadpoles	2137165
		R. clamitans	Dithane DG (76–80% mancozeb)	Continuous exposure 96 hour LC_{50} 13-day LC_{50}	2210 µg a.i/L 23 µg a.i/L (nominal)	96 hour LC_{50} based on hatching success; 13-d LC_{50} based on tadpole survival. Exposure began at stage 8 (embryo stage).	2137156
				Discontinuous exposure 96-h LC_{50} 16-day LC_{50} EC_{50} 16-d NOEC	960 µg a.i/L 200 µg a.i/L 40 µg a.i/L 7.8 µg a.i/L (nominal)	96-h LC_{50} based on hatching success; 16-d LC_{50} based on tadpole survival; EC_{50} based on deformities at hatching (day 8); NOEC based on growth inhibition observed at 78 ug a.i./L treatment. Exposure began at stage 8 (embryo stage).	
	Chronic	*B.americanus*		Sex ratio NOEC LOEC	0.8 µg a.i./L 80 µg a.i./L (nominal)	Exposure at stage 8 (embryo) for 96 hours then again at stage 42 (limb emergence) for 48 hours. **Note:** the NOEC may be 8 ug/L; sex ratio was not reported for this treatment level.	2137153
				NOEC LOEC	**8.0 µg a.i./L** 80 µg a.i./L (nominal)	Based on 14% skeletal deformities at stage 20 and 5% deformities (abnormal eye) at 80 ug a.i./L. Exposure at stage 8 (embryo) for 96 hours then again at stage 42 (limb emergence) for 48 hours. The most sensitive NOEC endpoint is 8.0 ug a.i./L for *B. americanus* based on skeletal deformities in stage 20 tadpoles following exposure to mancozeb for a short acute duration (96 hours) at the embryonic stage; in the absence of chronic data for amphibians, this endpoint was chosen for the risk assessment in PRVD2018-17.	
		R. pipiens	Manzate 75 DF (guarantee: 75 % mancozeb)	49 day LOEC	16 µg a.i./L (nominal)	The exposure period followed tadpoles from 4-days post hatch to 49 days thereafter. However, an NOEC was not determined in the study; the LOEC was 16 µg a.i./L based on survival and growth rate.	2137159

Organism	Study type	Species	Test material	Endpoint	Value (nominal / mean measured)	Comments	Reference
Freshwater Aquatic community	Aquatic mesocosm	Rotifer *Brachionus leydigi*	Penncozeb 80 WP/L (81.7% mancozeb)	EC_{20} EC_{50}	**4.5 µg a.i./L** 7.5 µg a.i./L (nominal)	Outdoor mesocosm study. Mancozeb was applied as a direct overspray to water once a week over an eight week period at nominal concentrations of 0 (controls), 1.25, 4.0, 12.5, 40, 125, 400 and 1250 µg Penncozeb 80 WP/L. The EC_{20} and EC_{50} values are based on the most sensitive organism, the rotifer *Brachionus leydigi.* *Brachionus leydigi* showed total recovery within three weeks after the last test application due to their short generation period even in the mesocosm pond of the highest test concentration where the population was constantly suppressed during the treatment period. The EC_{20} for *Brachionus leydigi* was considered in the initial risk assessment as representative of the aquatic community level endpoint.	1788072
Marine and estuarine Organisms							
Invertebrates	Acute	Mysid shrimp (*Mysidopsis bahia*)	82.4% mancozeb	96-h EC_{50}	10.5 µg a.i/L (mean measured) 21.9 µg a.i/L (nominal)	Acute 96-h toxicity test conducted under flow-through test conditions.	1788059
			Formulated product (37%)	96-h EC_{50} NOEC 96-h EC_{50} NOEC	**9.5 µg a.i/L** 1.9 µg a.i/L (mean measured) 21.9 µg a.i/L 3.7 µg a.i/L (nominal)	Acute 96-h toxicity test conducted under flow-through test conditions.	1788061

Organism	Study type	Species	Test material	Endpoint	Value (nominal / mean measured)	Comments	Reference
	Chronic		Dithane M-45 (78.8% mancozeb)	28-d NOEC 28-d LOEC 28-d NOEC 28-d LOEC 11-d NOEC 11-d LOEC 11-d NOEC 11-d LOEC	F0 generation: Survival: 1.64 µg a.i/L 3.25 µg a.i/L Length: 3.25 µg a.i/L >3.25 µg a.i/L F1 generation: **Survival: 1.64 µg a.i/L** 3.25 µg a.i/L Length: 3.25 µg a.i/L >3.25 µg a.i/L (mean measured)	Flow-through conditions. Because not all measured concentrations were within ±20% of the day-0 measured concentrations, all biological response results were based upon the arithmetic mean measured concentrations of mancozeb during the 28 days of exposure. The test acceptability criteria for this study were met.	EC 2018 (3017379)
		Eastern oysters (*Crassostrea virginica*)	Formulated product (37%)	96-h EC_{50}	1530 µg a.i/L (mean measured) 1850 µg a.i/L (nominal)	Flow-through test conditions. Shell deposition study.	1788062
			Dithane M-45 (82.4% mancozeb)	96-h EC_{50}	1600 µg a.i/L (mean measured) 2100 µg a.i/L (nominal)	Flow-through test conditions. Shell deposition study.	1788063
Fish	Acute	Sheepshead minnow (*Cyprinodon variegatus*)	Formulated product (% a.i. not reported)	96-h EC_{50} NOEC 96-h EC_{50} NOEC	**1100 µg a.i/L** 560 µg a.i/L (mean measured) 5660 µg a.i/L 1700 µg a.i/L (nominal)	Flow-through test conditions.	1788064
			82.4% mancozeb	96-h EC_{50} NOEC 96-h EC_{50} NOEC	1700 µg a.i/L 820 µg a.i/L (mean measured) 2300 µg a.i/L 1700 µg a.i/L (nominal)	Flow-through test conditions.	1788065
			Formulated product (% a.i. not reported)	96-h EC_{50}	4200 µg a.i/L (nominal)	The USEPA categorized these studies as supplemental based on the rationale that actual concentrations were not measured in two of the	1788071

Organism	Study type	Species	Test material	Endpoint	Value (nominal / mean measured)	Comments	Reference
			82.4% mancozeb	96-h EC_{50}	4200 µg a.i/L (nominal)	lowest treatment vessels in which a precipitate was formed.	1788070
	Chronic	Sheepshead minnow (*Cyprinodon variegatus*)	Dithane M-45 (Mancozeb 78.8%)	39 days (29 days post hatch)	Hatchability, fry survival and growth: **NOEC = 19.5 µg a.i/L** LOEC > 19.5 µg a.i/L (mean measured)	Flow-through conditions. As no apparent dose response was observed, the NOEC is 19.5 µg a.i/L (the highest test concentration).	EC 2018 (3017379)
Algae	Acute	*Skeletonema costatum*	Penncozeb technical (86.3% a.i.)	96-h EC_{50} NOEC	Growth rate: 27 µg a.i/L 11 µg a.i/L Yield: 19 µg a.i/L 11 µg a.i/L Area under growth curve: **16 µg a.i/L** 11 µg a.i/L (initial measured)	As a higher tier aquatic toxicity study demonstrates that phytoplankton and periphyton community response is measured at much higher concentrations, a formal review of this study was not conducted.	2950675
			Formulated product (60% mancozeb, 9% dimethomorph)	120-h EC_{50} NOEC	139 µg total product/L 104 µg total product/L	See note[2]	USEPA RED 2005 (1807553)

NA – not applicable

1 - Given that some studies demonstrate that mancozeb is unstable under testing conditions, results based on nominal test concentrations may represent a considerable underestimate of toxicity.

2 - Formulated product contains another active; study results are not suitable for risk assessment.

Table 5 Summary of effects of ETU on terrestrial organisms.

Study Type/Species	Endpoint	Reference
Invertebrates:	**No data, not required**	
Birds - Acute Oral		
Bobwhite Quail	LD_{50} >2250 mg a.i./kg bw - practically non-toxic	2950680
Zebra Finch	LD_{50} = 2000 mg a.i./kg bw - slightly toxic	2950681
Birds – Reproduction		
Mallard Duck	NOEC = 13.6 mg a.i./kg bw/d	2950688
Bobwhite Quail	NOEC = 8.9 mg a.i./kg bw/d	2950687
Small Mammals		
Acute Toxicity		
Oral mouse/pregnant mouse	LD50 = 2400–4000 mg a.i./kg bw Low Toxicity	As reported in PRVD

Study Type/Species	Endpoint	Reference
Oral Rat/Pregnant rat	LD50 = 545–1832 mg a.i./kg bw (600 mg/kg bw for pregnant rats) Moderately Toxic	2018-17
Oral Hamster and Pregnant hamster	LD50>2400 mg a.i./kg bw Low Toxicity	
Inhalation Rat	LC50 >10.4 mg/L	
Subchronic Toxicity		
90-d Mouse dietary	NOAEL =1.7 mg a.i./kg/bw/d	As reported in PRVD 2018-17
90-d Rat dietary	NOAEL =1.7 mg a.i./kg bw/d	
120-d rat dietary	NOAEL =2.5 mg a.i./kg bw/d	
Chronic Toxicity		
1-yr dog	NOAEL =0.18 mg a.i./kg bw/d	As reported in PRVD 2018-17
Reproductive and Developmental Toxicity		
2 generation rat repro	Parental 2.5 ppm; offspring 25 ppm; Repro >125 ppm NOAELs on a mg a.i./kg bw basis could not be determined because of stability problems of test material, unknown feed consumption and missing pups	As reported in PRVD 2018-17
Developmental rat	NOAEL = Maternal 40 mg/kg bw/d; developmental 5 mg a.i./kg bw/d	
Developmental rat	NOAEL = Maternal: 35 mg/kg bw/d; developmental 15 mg a.i./kg bw/d	
Developmental Rat, mice, hamsters and guinea pigs	NOAEL =5 mg a.i./kg bw/d rats No apparent effects in hamsters or guinea pigs	
Vascular Plants	**No data, not required.**	

Table 6. Summary of effects of ETU on aquatic organisms

Data type	Species	Endpoint (% a.i.)	Value	Reference
Invertebrates (Acute)	*Daphnia magna*	EC_{50} (99.6%)	26.9 mg a.i./L	1744702
Invertebrates (Chronic)	*Daphnia magna*	NOEC	2.0 mg a/i/L	1744708
Fish (Acute)	Rainbow trout (*Oncorhynchus mykiss)*	LC_{50} (99.6%)	>502 mg a.i./L	1744702
	Bluegill sunfish (*Lepomis macrochirus)*	LC_{50} (100%)	>990 mg a.i./L	1619167
Fish (Chronic)	No study available			
Amphibians (acute)	No study available			
Amphibians (chronic)	*X. laevis*	NOEC (survival)	28-d and 90 day = 10 mg a.i./L	1744709
		NOEC (thyroid changes)	90-d 1.0 mg a.i./L	1744712
Freshwater plants and algae	Green Algae	EC_{50} (99.6%)	23.0 mg a.i./L	1744702

Data type	Species	Endpoint (% a.i.)	Value	Reference
(Acute)	(*P. subcapitata*)	NOEC (99.6%)	12.5 mg a.i./L	
	Duckweed	EC_{50} (100%)	>960mg a.i./L	1619169
	(*L. gibba*)	NOEC (100%)	960 mg a.i./L	
Freshwater plants and algae (Chronic)	No study available			
Estuarine/marine invertebrates (Acute)	Eastern oyster (*Crassostrea virginica*)	LC_{50} (100%)	>110 mg a.i./L	1619166
		NOEC (100%) shell growth	42 mg a.i./L	
	Mysid	LC_{50} (100%)	9.2 mg a.i./L	1619165
	(*Americamysis bahia*)	NOEC (100%) mortality	6.4 mg a.i./L	
Estuarine/marine invertebrates (Chronic)	No study available			
Estuarine/Marine fish (Acute)	sheepshead minnow (*Cyprinodon variegatus*)	LC_{50} (100%)	>900 mg a.i./L	1619168
		NOEC (100%)	900 mg a.i./L	
Estuarine/Marine fish (Chronic)	No study available			
Estuarine/Marine Diatom	No study available			

Table 7 Acute contact risk to bees based on screening level exposure estimates for foliar application of mancozeb

Application rate (EEC)	Koch and Weiber (adjustment factor)	Exposure Estimate for Bees[1]	Toxicity endpoint	RQ[2]	LOC exceeded
kg a.i./ha	**µg a.i./bee per kg a.i./ha**	**µg a.i./bee/day**	**µg a.i./bee/day**		
4.5	2.4	10.8	LD_{50}: 161.7	0.07	No
2.44	2.4	5.86	LD_{50}: 161.7	0.04	No

1 - Exposure estimate for bees= application rate (kg a.i./ha) × adjustment factor
2 - Exposure estimate for bees/toxicity endpoint
Note: LOC for bees is set at 0.4.

Table 8 Acute and chronic dietary risk to bees based on screening level exposure estimates for foliar application of mancozeb

Application rate kg a.i./ha	Adjustment factor µg a.i./bee per kg a.i./ha	Exposure Estimate for Bees[1] µg a.i./bee/day	Toxicity endpoint µg a.i./bee/day	RQ[2]	LOC exceeded
Adults (Acute)					
4.5	28.6	128.8	LD_{50}: 68.9	1.9	Yes
2.44	28.6	69.8	LD_{50}: 68.9	1.01	Yes
Adults (Chronic)					
4.5	28.6	128.8	NOEL: 68.9	1.9	Yes
2.44	28.6	69.8	NOEL: 68.9	1.01	Yes
Brood (Chronic)					
4.5	12.15	54.7	NOED: 12.5	4.4	Yes
2.44	12.15	29.7	NOED: 12.5	2.4	Yes

NA – Not available
1 - Exposure estimate for bees= application rate (kg a.i./ha) × adjustment factor (28.6 µg a.i./bee per kg a.i./ha for adults and 12.15 µg a.i./bee per kg a.i./ha for larvae)
2 - Exposure estimate for bees/toxicity endpoint
Note: LOC for bees is set at 0.4 for acute endpoints and 1.0 for chronic endpoints.

Table 9 Risk assessment for predatory arthropods (based on the most sensitive LR_{50} for the predatory mite *T. pyri,* 107 g a.i./ha).

Crop Application rate (g a.i./ha)	Application method	On field			Off-field		
		EEC[1] (g a.i./ha)	RQ	LOC exceeded	EEC[2] (g a.i./ha)	RQ [3]	LOC exceeded
Apples (4500 g a.i./ha × 3 app. at 7 days)	Airblast	7323	68	Yes	677	6.3	Yes
Apples (single application – 4500 g a.i./ha)	Airblast	3600	34	Yes	333	3.1	Yes
Potato (1690 g a.i./ha × 8 app. at 5 days)	Field sprayer	3802	36	Yes	29	0.3	No
	Aerial				109	1.0	No
Cucumber (2440 g a.i./ha × 3 at 7 days)	Field sprayer	3636	34	Yes	27	0.3	No No
Potato (1690 g a.i./ha)	Field sprayer	1352	13	Yes	10	0.1	No
	Aerial				39	0.4	No

1 - In-field EEC = cumulative rate × crop interception factor (80%);
2 - Off-field EEC = cumulative rate × drift factor (6% for field sprayer application, 74% for early season airblast application and 23% for aerial application) × vegetation distribution factor – 10%. The vegetation distribution factor is applied since drift is overestimated to the lower or interior portions of a three-dimensional habitat structure. Most of the drift would be intercepted by the top or side portions of the habitat.
3 – Exceedance of LOC (RQ > 1) highlighted

Table 10 Screening level risk assessment for mancozeb for birds and mammals

	Toxicity (mg a.i./kg bw/d)	Feeding Guild (food item)	EDE (mg a.i./kg bw)	RQ[1]
Small Bird (0.02 kg)				
Acute	150	Insectivore	635	4.2
Reproduction	13.2	Insectivore	635	48
Medium Sized Bird (0.1 kg)				
Acute	150	Insectivore	495	3.3
Reproduction	13.2	Insectivore	495	38
Large Sized Bird (1 kg)				
Acute	150	Herbivore (short grass)	376	2.5
Reproduction	13.2	Herbivore (short grass)	376	28
Small Mammal (0.015 kg)				
Acute	500.00	Insectivore	365	0.7
Reproduction	2.50	Insectivore	365	146
Medium Sized Mammal (0.035 kg)				
Acute	500.00	Herbivore (short grass)	831	1.7
Reproduction	2.50	Herbivore (short grass)	831	332
Large Sized Mammal (1 kg)				
Acute	500.00	Herbivore (short grass)	444	0.9
Reproduction	2.50	Herbivore (short grass)	444	178

1 – Exceedance of LOC (RQ > 1) highlighted.

Table 11 Avian risk assessment using maximum and mean mancozeb residue values based on the cumulative proposed application rate for apples (4500 g a.i./ha × 4 at 7-day intervals, airblast application; 9153 g a.i./ha).

			Maximum nomogram residues				Mean nomogram residues			
			On-field		Off Field		On-field		Off field	
	Toxicity (mg a.i./kg bw/d)	Food guild (food item)	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]
Small Bird (0.02 kg)										
Acute	150	Insectivore	635	4.2	470	3.1	438	2.9	324	2.2
	150	Granivore (grain and seeds)	115	0.8	85	0.6	55	0.4	41	0.3
	150	Frugivore (fruit)	231	1.5	171	1.1	110	0.7	81	0.5
Reproduction	13.20	Insectivore	635	48	470	36	438	33	324	25
	13.20	Granivore (grain and seeds)	115	8.7	85	6.5	55	4.2	41	3.1
	13.20	Frugivore (fruit)	231	17.5	171	13	110	8.3	81	6.2
Medium Sized Bird (0.1 kg)										
Acute	150	Insectivore	495	3.3	366	2.4	342	2.3	253	1.7
	150	Granivore (grain and seeds)	90	0.6	67	0.4	43	0.3	32	0.2
	150	Frugivore (fruit)	180	1.2	133	0.9	86	0.6	64	0.4
Reproduction	13.20	Insectivore	495	38	366	28	342	26	253	19
	13.20	Granivore (grain and seeds)	90	6.8	67	5.0	43	3.3	32	2.4
	13.20	Frugivore (fruit)	180	14	133	10	86	6.5	64	4.8
Large Sized Bird (1 kg)										
Acute	150	Insectivore	145	1.0	107	0.7	100	0.7	74	0.5
	150	Granivore (grain and seeds)	26	0.2	19	0.1	13	<0.1	9.3	<0.1
	150	Frugivore (fruit)	52	0.4	39	0.3	25	0.2	19	0.1
	150	Herbivore (short grass)	375	2.5	278	1.9	133	0.9	99	0.7
	150	Herbivore (long grass)	229	1.5	170	1.1	75	0.5	55	0.4
	150	Herbivore	347	2.3	257	1.7	115	0.8	85	0.6

			Maximum nomogram residues				Mean nomogram residues			
			On-field		Off Field		On-field		Off field	
	Toxicity (mg a.i./kg bw/d)	Food guild (food item)	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]
		(broadleaf plants)								
Reproduction	13.20	Insectivore	145	11	107	8.1	100	7.6	74	5.6
	13.20	Granivore (grain and seeds)	26	2.0	19	1.5	13	0.9	9.3	0.7
	13.20	Frugivore (fruit)	52	4.0	39	2.9	25	1.9	19	1.4
	13.20	Herbivore (short grass)	375	29	277	21	133	10	99	7.5
	13.20	Herbivore (long grass)	229	17	170	13	75	5.7	55	4.2
	13.20	Herbivore (broadleaf plants)	347	26	257	20	115	8.7	85	6.4

1 – Exceedance of LOC (RQ > 1) highlighted.

Table 12 Avian risk assessment using maximum and mean mancozeb residue values based on the proposed cumulative application rate for cucumber (2440 g a.i./ha × 3 at 7-day intervals, ground application; 4546 g a.i./ha)

			Maximum nomogram residues				Mean nomogram residues			
			On-field		Off Field		On-field		Off Field	
	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]
Small Bird (0.02 kg)										
Acute	150	Insectivore	326	2.2	20	0.1	225	1.5	14	<0.1
	150	Granivore (grain and seeds)	57	0.4	3.4	<0.1	27	0.2	1.6	<0.1
	150	Frugivore (fruit)	115	0.8	6.9	<0.1	55	0.4	3.3	<0.1
Reproduction	13.20	Insectivore	326	25	20	1.5	225	17	14	1.0
	13.20	Granivore (grain and seeds)	57	4.3	3.4	0.3	27	2.1	1.6	0.1
	13.20	Frugivore (fruit)	115	8.7	6.9	0.5	55	4.1	3.3	0.3
Medium Sized Bird (0.1 kg)										

			Maximum nomogram residues				Mean nomogram residues			
			On-field		Off Field		On-field		Off Field	
	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]
Acute	150	Insectivore	255	1.7	15	0.1	176	1.2	11	<0.1
	150	Granivore (grain and seeds)	45	0.3	2.7	<0.1	21	0.1	1.3	<0.1
	150	Frugivore (fruit)	89	0.6	5.4	<0.1	43	0.3	2.6	<0.1
Reproduction	13.20	Insectivore	255	19	15	1.2	176	13	11	0.8
	13.20	Granivore (grain and seeds)	45	3.4	2.7	0.2	21	1.6	1.3	0.1
	13.20	Frugivore (fruit)	89	6.8	5.4	0.4	43	3.2	2.6	0.2
Large Sized Bird (1 kg)										
Acute	150	Insectivore	74	0.5	4.5	<0.1	51	0.3	3.1	<0.1
	150	Granivore (grain and seeds)	13	0.1	0.8	<0.1	6.2	<0.1	0.4	<0.1
	150	Frugivore (fruit)	26	0.2	1.6	<0.1	12	<0.1	0.8	<0.1
	150	Herbivore (short grass)	187	1.2	11	0.1	66	0.4	4.0	<0.1
	150	Herbivore (long grass)	114	0.8	6.8	<0.1	37	0.3	2.2	<0.1
	150	Herbivore (broadleaf plants)	173	1.2	10	0.1	57	0.4	3.4	<0.1
Reproduction	13.20	Insectivore	74	5.6	4.5	0.3	51	3.9	3.1	0.2
	13.20	Granivore (grain and seeds)	13	<1.0	0.8	0.1	6.2	0.5	0.4	<0.1
	13.20	Frugivore (fruit)	26	2.0	1.6	0.1	12	0.9	0.8	<0.1
	13.20	Herbivore (short grass)	187	14	11	0.8	66	5.0	4.0	0.3
	13.20	Herbivore (long grass)	114	8.6	6.8	0.5	37	2.8	2.2	0.2
	13.20	Herbivore (broadleaf plants)	173	13	10	0.8	57	4.3	3.4	0.3

1 – Exceedance of LOC (RQ > 1) highlighted.

Table 13 Avian risk assessment using maximum and mean mancozeb residue values based on the proposed single application rate for potato (1690 g a.i./ha)

			Maximum nomogram residues				Mean nomogram residues			
			On-field		Off Field		On-field		Off Field	
	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]
Small bird (0.02 kg)										
Acute	150	Insectivore	138	0.9	32	0.2	95	0.6	22	0.2
	150	Granivore (grain and seeds)	21	0.1	4.9	0.0	10	<0.1	2.3	<0.1
	150	Frugivore (fruit)	43	0.3	10	0.1	20	0.1	4.7	<0.1
Reproduction	13.2	Insectivore	138	10	32	2.4	95	7.2	22	1.7
	13.2	Granivore (grain and seeds)	21	1.6	4.9	0.4	10	0.8	2.3	0.2
	13.2	Frugivore (fruit)	43	3.2	10	0.7	20	1.5	4.7	0.4
Medium Sized Bird (0.1 kg)										
Acute	150	Insectivore	107	0.7	25	0.2	74	0.5	17	0.1
	150	Granivore (grain and seeds)	17	0.1	3.8	0.0	7.9	<.1	1.8	<0.1
	150	Frugivore (fruit)	33	0.2	7.6	0.1	16	0.1	3.6	<0.1
Reproduction	13.2	Insectivore	107	8.1	25	1.9	74	5.6	17	1.3
	13.2	Granivore (grain and seeds)	17	1.3	3.8	0.3	7.9	0.6	1.8	0.1
	13.2	Frugivore (fruit)	33	2.5	7.6	0.6	16	1.2	3.6	0.3
Large Sized Bird (1 kg)										
Acute	150	Insectivore	31	0.2	7.2	<0.1	22	0.1	5.0	<0.1
	150	Granivore (grain and seeds)	4.9	<0.1	1.1	<0.1	2.3	<0.1	0.5	<0.1
	150	Frugivore (fruit)	9.7	0.1	2.2	<0.1	4.6	<0.1	1.1	<0.1
	150	Herbivore (short grass)	69	0.5	16	0.1	25	0.16	5.7	<0.1
	150	Herbivore (long grass)	42	0.3	9.7	0.1	14	<0.1	3.2	<0.1
	150	Herbivore (broadleaf plants)	64	0.4	15	0.1	21	0.1	4.9	<0.1

			Maximum nomogram residues				Mean nomogram residues			
			On-field		Off Field		On-field		Off Field	
	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]
Reproduction	13.2	Insectivore	31	2.4	7.2	0.5	22	1.6	5.0	0.4
	13.2	Granivore (grain and seeds)	4.9	0.4	1.1	0.1	2.3	0.2	0.5	<0.1
	13.2	Frugivore (fruit)	9.7	0.7	2.2	0.2	4.6	0.4	1.1	<0.1
	13.2	Herbivore (short grass)	69	5.3	16	1.2	25	1.9	5.7	0.4
	13.2	Herbivore (long grass)	42	3.2	9.7	0.7	14	1.1	3.2	0.2
	13.2	Herbivore (broadleaf plants)	64	4.9	15	1.1	21	1.6	4.9	0.4

1 – Exceedance of LOC (RQ > 1) highlighted.

Table 14 Mammalian risk assessment using maximum and mean mancozeb residue values based on the proposed cumulative application rate for apples (4500 g a.i./ha × 4 at 7-day intervals, airblast application; 9153 g a.i./ha)

			Maximum nomogram residues				Mean nomogram residues			
			On-field		Off Field		On-field		Off Field	
	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]
Small Mammal (0.015 kg)										
Acute	500	Insectivore	365	0.7	270	0.5	252	0.5	186	0.4
	500	Granivore (grain and seeds)	66	0.1	49	0.1	32	0.1	23	<0.1
	500	Frugivore (fruit)	133	0.3	98	0.2	63	0.1	47	0.1
Reproduction	2.50–110	Insectivore	365	3.3–146	270	2.5–108	252	2.3–101	187	1.7–75
	2.50–110	Granivore (grain and seeds)	66	0.6 – 27	49	0.4 – 20	32	0.3 – 13	23	0.2 – 9.4
	2.50–110	Frugivore (fruit)	133	1.2–53	98	0.9 – 39	63	0.6–25	47	0.4–19
Medium Sized Mammal (0.035 kg)										
Acute	500	Insectivore	320	0.6	237	0.5	221	0.4	163	0.3

			Maximum nomogram residues				Mean nomogram residues			
			On-field		Off Field		On-field		Off Field	
	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]
	500	Granivore (grain and seeds)	58	0.1	43	0.1	28	0.1	21	<0.1
	500	Frugivore (fruit)	116	0.2	86	0.2	55	0.1	41	0.1
	500	Herbivore (short grass)	831	1.7	615	1.2	295	0.6	218	0.4
	500	Herbivore (long grass)	507	1.0	376	0.8	166	0.3	123	0.2
	500	Herbivore (forage crops)	769	1.5	569	1.1	254	0.5	188	0.4
Reproduction	2.50–110	Insectivore	320	2.9–128	237	2.2–95	221	2.0–88	163	1.5–65
	2.50–110	Granivore (grain and seeds)	58	0.5 – 23	43	0.4 – 17	28	0.3 – 11	21	0.2 – 8.2
	2.50–110	Frugivore (fruit)	116	1.1 – 47	86	0.8 – 34	55	0.5 – 22	41	0.4 – 16
	2.50–110	Herbivore (short grass)	831	7.5 – 333	615	5.6 – 246	295	2.7 – 118	218	2.0 – 87
	2.50–110	Herbivore (long grass)	507	4.6–203	376	3.4–150	166	1.5–66	123	1.1–49
	2.50–110	Herbivore (broadleaf plants)	769	7.0–308	569	5.2–228	254	2.3–102	188	1.7–75
Large Sized Mammal (1 kg)										
Acute	500	Insectivore	171	0.3	127	0.3	118	0.2	87	0.2
	500	Granivore (grain and seeds)	31	0.1	23	0.0	15	0.0	11	0.0
	500	Frugivore (fruit)	62	0.1	46	0.1	30	0.1	22	0.0
	500	Herbivore (short grass)	444	0.9	329	0.7	158	0.3	117	0.2
	500	Herbivore (long grass)	271	0.5	201	0.4	89	0.2	66	0.1
	500	Herbivore (broadleaf plants)	411	0.8	304	0.6	136	0.3	101	0.2
Reproduction	2.50–110	Insectivore	171	1.6–68	127	1.2–51	118	1.1–47	87	0.8–35
	2.50–110	Granivore (grain	31	0.3–12	23	0.2–9.2	15	0.1–5.9	11	0.1–4.4

			Maximum nomogram residues				Mean nomogram residues			
			On-field		Off Field		On-field		Off Field	
	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]
		and seeds)								
	2.50–110	Frugivore (fruit)	62	0.6–25	46	0.4–18	30	0.3–12	22	0.2–8.8
	2.50–110	Herbivore (short grass)	444	4.0–178	329	2.9 – 132	158	1.4–63	117	1.1–47
	2.50–110	Herbivore (long grass)	271	2.5–109	201	1.8 – 80	89	0.8–35	66	0. –26
	2.50–110	Herbivore (broadleaf plants)	411	3.7–164	304	2.7–122	136	1.2–54	101	0.9–40

1 – Exceedance of LOC (RQ > 1) highlighted.

Table 15 Mammalian risk assessment using maximum and mean mancozeb residue values based on the proposed cumulative application rate for cucumber (2440 g a.i./ha × 3 at 7-day intervals ground application; 4546 g a.i./ha)

			Maximum nomogram residues				Mean nomogram residues			
			On-field		Off Field		On-field		Off Field	
	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]
Small Mammal (0.015 kg)										
Acute	500	Insectivore	187	0.4	11	<0.1	130	0.3	7.8	<0.1
	500	Granivore (grain and seeds)	33	<0.1	2.0	<0.1	16	<0.1	0.9	<0.1
	500	Frugivore (fruit)	66	0.1	4.0	<0.1	31	<0.1	1.9	<0.1
Reproduction	2.50–110	Insectivore	187	1.7–75	11	0.1–4.5	130	1.2–52	7.8	<0.1–3.1
	2.50–110	Granivore (grain and seeds)	33	0.3–13	2.0	<0.1–0.8	16	0.1–6.3	0.9	<0.1–0.4
	2.50–110	Frugivore (fruit)	66	0.6–26	4.0	<0.1–1.6	31	0.3–13	1.9	<0.1–0.8

			Maximum nomogram residues				Mean nomogram residues			
			On-field		Off Field		On-field		Off Field	
	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]
Medium Sized Mammal (0.035 kg)										
Acute	500	Insectivore	165	0.3	9.9	<0.1	114	0.2	6.8	<0.1
	500	Granivore (grain and seeds)	29	<0.1	1.7	<0.1	14	<0.1	0.8	<0.1
	500	Frugivore (fruit)	58	0.1	3.5	<0.1	28	<0.1	1.7	<0.1
	500	Herbivore (short grass)	413	0.8	25	<0.1	147	0.3	8.8	<0.1
	500	Herbivore (long grass)	252	0.5	15	<0.1	82	0.2	4.9	<0.1
	500	Herbivore (forage crops)	382	0.8	23	<0.1	126	0.3	7.6	<0.1
Reproduction	2.50–110	Insectivore	165	1.5–66	9.9	<0.1 – 4.0	114	1.0–46	6.8	<0.1–2.7
	2.50–110	Granivore (grain and seeds)	29	0.3–125	1.7	<0.1–0.7	14	0.1–5.5	0.8	<0.1–0.3
	2.50–110	Frugivore (fruit)	58	0.5–23	3.5	<0.1–1.4	28	0.3–11	1.7	<0.1–0.7
	2.50–110	Herbivore (short grass)	413	3.8–165	25	0.2–9.9	147	1.3–59	8.8	<0.1–3.5
	2.50–110	Herbivore (long grass)	252	2.3–101	15	0.1–6.0	82	0.7–33	4.9	<0.1–2.0
	2.50–110	Herbivore (broadleaf plants)	382	3.5–153	23	0.2–9.2	126	1.1–50	7.6	<0.1–3.0
Large Sized Mammal (1 kg)										
Acute	500	Insectivore	88	0.2	5.3	<0.1	61	0.1	3.6	<0.1
	500	Granivore (grain and seeds)	15	<0.1	0.9	<0.1	7.4	<0.1	0.4	<0.1
	500	Frugivore (fruit)	31	<0.1	1.9	<0.1	15	<0.1	0.9	<0.1
	500	Herbivore (short grass)	221	0.4	13	<0.1	78	0.2	4.7	<0.1
	500	Herbivore (long grass)	135	0.3	8.1	<0.1	44	<0.1	2.6	<0.1
	500	Herbivore (broadleaf plants)	204	0.4	12	<0.1	67	0.1	4.1	<0.1
Reproduction	2.50–110	Insectivore	88	0.8–35	5.3	<0.1–2.1	61	0.6–24	3.6	<0.1 –1.5
	2.50–110	Granivore (grain and seeds)	15	0.1–6.2	0.9	<0.1–0.4	7.4	<0.1–2.9	0.4	<0.1–0.2
	2.50–110	Frugivore (fruit)	31	0.3 –	1.9	<0.1–	15	0.1–5.9	0.9	<0.1–0.4

			Maximum nomogram residues				Mean nomogram residues			
			On-field		Off Field		On-field		Off Field	
	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]
				12		0.7				
	2.50–110	Herbivore (short grass)	221	2.0 – 88	13	0.1–5.3	78	0.7–31	4.7	<0.1–1.9
	2.50–110	Herbivore (long grass)	135	1.2 – 54	8.1	<0.1–3.2	44	0.4–18	2.6	<0.1–1.1
	2.50–110	Herbivore (broadleaf plants)	204	1.9–82	12	0.1–4.9	67	0.6–27	4.1	<0.1–1.6

1 – Exceedance of LOC (RQ > 1) highlighted.

Table 16 Mammalian risk assessment using maximum and mean mancozeb residue values based on the proposed single application rate for potato (1690 g a.i./ha, aerial application)

			Maximum nomogram residues				Mean nomogram residues			
			On-field		Off Field		On-field		Off Field	
	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]
Small Mammal (0.015 kg)										
Acute	500	Insectivore	79	0.2	18	<0.1	55	<0.1	12.56	<0.1
	500	Granivore (grain and seeds)	12	<0.1	2.8	<0.1	5.8	<0.1	1.34	<0.1
	500	Frugivore (fruit)	25	<0.1	5.6	<0.1	12	<0.1	2.69	<0.1
Reproduction	2.50–110	Insectivore	79	0.7–32	18	0.2–7.3	55	0.5–22	13	0.1–5.0
	2.50–110	Granivore (grain and seeds)	12	0.1–4.9	2.8	<0.1–1.1	5.8	<0.1–2.3	1.3	<0.1–0.5
	2.50–110	Frugivore (fruit)	25	0.2–9.8	5.6	<0.1–2.3	12	0.1–4.7	2.7	<0.1–1.1
Medium Sized Mammal (0.035 kg)										
Acute	500	Insectivore	69	0.1	16	<0.1	48	<0.1	11	<0.1
	500	Granivore (grain and seeds)	11	<0.1	2.5	<0.1	5.1	<0.1	1.2	<0.1
	500	Frugivore (fruit)	21	<0.1	4.9	<0.1	10	<0.1	2.4	<0.1
	500	Herbivore (short grass)	153	0.3	35	<0.1	55	0.1	13	<0.1

			Maximum nomogram residues				Mean nomogram residues			
			On-field		Off Field		On-field		Off Field	
	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]
	500	Herbivore (long grass)	94	0.2	22	<0.1	31	<0.1	7.0	<0.1
	500	Herbivore (forage crops)	142	0.3	33	<0.1	47	<0.1	11	<0.1
Reproduction	2.50–110	Insectivore	69	0.6–280	16	0.1–6.4	48	0.4–19	11	0.1–4.4
	2.50–110	Granivore (grain and seeds)	11	<0.1–4.3	2.5	<0.1–<1.0	5.1	<0.1–2.0	1.2	<0.1–0.5
	2.50–110	Frugivore (fruit)	21	0.2–8.6	4.9	<0.1–2.0	10	<0.1–4.1	2.4	<0.1–0.9
	2.50–110	Herbivore (short grass)	153	1.4–61	35	<0.1–14	55	0.5–22	13	<0.1–5.0
	2.50–110	Herbivore (long grass)	94	0.9–37	22	<0.1–8.6	31	0.3–12	7.0	<0.1–2.8
	2.50–110	Herbivore (broadleaf plants)	142	1.3–57	33	<0.1–13	47	0.4–19	11	<0.1–4.3
Large Sized Mammal (1 kg)										
Acute	500	Insectivore	37	<0.1	8.5	<0.1	26	<0.1	59	<0.1
	500	Granivore (grain and seeds)	5.7	<0.1	1.3	<0.1	2.7	<0.1	0.6	<0.1
	500	Frugivore (fruit)	11	<0.1	2.6	<0.1	5.5	<0.1	1.3	<0.1
	500	Herbivore (short grass)	82	0.2	19	<0.1	29	<0.1	6.7	<0.1
	500	Herbivore (long grass)	50	0.1	12	<0.1	16	<0.1	3.8	<0.1
	500	Herbivore (broadleaf plants)	76	0.2	17	<0.1	25	<0.1	5.8	<0.1
Reproduction	2.50–110	Insectivore	37	<0.1–15	8.5	0.01–3.4	26	0.05–10	5.9	0.01–2.4
	2.50–110	Granivore (grain and seeds)	5.7	<0.1–2.3	1.3	<0.1–0.5	2.7	<0.1–1.1	0.6	<0.1–0.3
	2.50–110	Frugivore (fruit)	11	0.1–4.6	2.6	<0.1–1.1	5.5	<0.1–2.0	1.3	<0.1–0.5
	2.50–110	Herbivore (short grass)	82	0.7–33	19	0.2–7.5	29	0.3–13	6.7	<0.1–2.7
	2.50–110	Herbivore (long grass)	50	0.5–20	12	0.1–4.6	16	0.1–6.5	3.8	<0.1–1.5
	2.50–110	Herbivore (broadleaf plants)	76	0.7–30	17	0.2–7.0	25	0.2–10	5.8	<0.1–2.3

1 – Exceedance of LOC (RQ > 1) highlighted.

Table 17 Summary of risk of mancozeb to aquatic organisms: screening level

Organism	Exposure	Species	Endpoint value (µg a.i./L)	Endpoint for RA[1] (µg a.i./L)	EEC[2] (µg a.i./L)	RQ	LOC Exceeded
Freshwater species							
Invertebrate	Acute	*Daphnia magna*	48-h LC_{50} = 73	31.5	570	118	Yes
	Chronic	*Daphnia magna*	21-d NOEC = 7.3	7.3	570	78	Yes
Rainbow trout	Acute	*Oncorynchus mykiss*	96-h LC_{50} = 460	46	570	12	Yes
Fathead minnow	Chronic	*Pimephales promelas*	215-d full life cycle NOEC = 1.35	1.35	570	422	Yes
Amphibians	Acute	*Rana pipiens*	96-h LC_{50} = 200	20	3020	151	Yes
	Chronic	*Bufo americanus*	NOEC = 8.0	8.0	3020	378	Yes
Freshwater diatom	Acute	*Navicula pelliculosa*	96-h EC_{50} = 3.0	1.5	570	380	Yes
Freshwater aquatic community	Chronic	rotifer *Brachionus leydigi*	EC_{20} = 4.5	4.5	570	127	Yes
Vascular plant	Acute	Pondweed *Lemna minor*	7-d EC_{50} = 1042	521	570	1.1	Yes
Estuarine and marine species							
Invertebrate	Acute	Mysid shrimp *(Mysidopsis bahia)*	96-h EC_{50} = 9.5	4.25	570	124	Yes
Fish	Acute	Sheepshead minnow *(Cypronodon variegates)*	96-h LC_{50} = 1100	550	570	1.0	Yes
Marine diatom	Acute	*Skeletonema costatum*	96-h EC_{50} = 16	8	570	71	Yes

1 - Endpoints used in the acute exposure risk assessment (RA) are derived by dividing the EC_{50} or LC_{50} from the appropriate laboratory study by a factor of two (2) for aquatic invertebrates and plants, and by a factor of ten (10) for fish and amphibians.
2 - EEC based on a 15-cm water body depth for amphibians and a 80-cm water depth for all other aquatic organisms for the highest cumulative application rate for apples (4500 g a.i./ha × 4 applications at 7-day intervals).

Table 18 Spray drift risk assessment for non-target aquatic organisms

Organism	Exposure	Species	Endpoint reported (µg a.i./L)	Endpoint for RA[1] (µg a.i./L)	Use pattern / method of application	Cummulative application rate (g a.i./ha)[2]	EEC Exposure from drift (µg a.i./L)	RQ	LOC exceeded
Freshwater Invertebrate	Acute	*Daphnia magna*	48-h LC_{50} = 73	31.5	apples (airblast):	3360	420	13	Yes
					potato (aerial)	403	50	1.6	Yes
					cucumber and melon (field sprayer)	147	18	0.6	No
					Potato (single application – field sprayer)	101	13	0.4	No
	Chronic	*Daphnia magna*	21-d NOEC = 7.3	7.3	apples (airblast):	3360	420	58	Yes
					potato (aerial)	403	50	6.8	Yes
					cucumber and melon (field sprayer)	147	18	2.5	Yes
					Potato (single application – field sprayer)	101	13	1.8	Yes
Freshwater fish	Acute	*Onkorynchus mykiss*	96–h LC_{50} = 460	46	apples (airblast):	3360	420	9.1	Yes
					potato (aerial)	403	50	1.1	Yes
					cucumber and melon (field sprayer)	147	18	0.4	No
					Potato (single application – field sprayer)	101	13	0.3	No
	Chronic (pulsed dose)	*Danio rerio*	LC_{10} = 10.5 (fry survival at 35d post-fertilisation)	10.5	apples (airblast):	3360	420	40	Yes
					potato (aerial)	403	50	4.8	Yes
					cucumber and melon (field sprayer)	147	18	1.7	Yes
					Potato (single application – field sprayer)	101	13	1.2	Yes

Organism	Exposure	Species	Endpoint reported (µg a.i./L)	Endpoint for RA[1] (µg a.i./L)	Use pattern / method of application	Cummulative application rate (g a.i./ha)[2]	EEC Exposure from drift (µg a.i./L)	RQ	LOC exceeded
Amphibian	Acute	*Rana pipiens*	96–h LC_{50} = 200	20	apples (airblast):	3360	2240	112	Yes
					potato (aerial)	403	269	14	Yes
					cucumber and melon (field sprayer)	147	98	4.9	Yes
					Potato (single application – field sprayer)	101	68	3.4	Yes
	Chronic	*Bufo americanus*	NOEC = 8.0	8.0	apples (airblast):	3360	2240	280	Yes
					potato (aerial)	403	269	34	Yes
					cucumber and melon (field sprayer)	147	98	12	Yes
					Potato (single application – field sprayer)	101	13	1.6	Yes
Freshwater aquatic community	Chronic	rotifier *Brachionus leydigi*	EC_{20} = 4.5	4.5	apples (airblast):	3360	420	93	Yes
					potato (aerial)	403	50	11	Yes
					cucumber and melon (field sprayer)	147	18	4.0	Yes
					Potato (single application – field sprayer)	101	13	2.9	Yes
Marine Invertebrate	Acute	Mysid shrimp *(Mysidopsis bahia)*	96-h EC_{50} = 9.5	4.25	apples (airblast):	3360	420	99	Yes
					potato (aerial)	403	50	12	Yes
					cucumber and melon (field sprayer)	147	18	4.2	Yes
					Potato (single application – field sprayer)	101	13	3.1	Yes
Marine fish	Acute	Sheepshead	96-h LC_{50} =	550	apples (airblast):	3360	420	0.8	No

Organism	Exposure	Species	Endpoint reported (µg a.i./L)	Endpoint for RA[1] (µg a.i./L)	Use pattern / method of application	Cummulative application rate (g a.i./ha)[2]	EEC Exposure from drift (µg a.i./L)	RQ	LOC exceeded
		minnow *(Cypronodon variegates)*	1100		potato (aerial)	403	50	0.1	No
					cucumber and melon (field sprayer)	147	18	<0.1	No
					Potato (single application – field sprayer)	101	13	<0.1	No
Marine diatom	Acute	*Skeletonema costatum*	96-h EC_{50} = 16	8.0	apples (airblast):	3360	420	53	Yes
					potato (aerial)	403	50	6.3	Yes
					cucumber and melon (field sprayer)	147	18	2.3	Yes
					Potato (single application – field sprayer)	101	13	1.6	Yes

1 - Endpoints used in the acute exposure risk assessment (RA) are derived by dividing the EC_{50}, LC_{50} from the appropriate laboratory study by a factor of two (2) for aquatic invertebrates and plants, and by a factor of ten (10) for fish and amphibians.
2 - Cumulative application rates were estimated based on the percentages for off-site drift to non-target aquatic habitats for each of the application methods and by adjusting the sum of the applications for dissipation between applications using the longest whole system DT_{50} value of 1.03 days from the aerobic aquatic biotransformation studies.

Table 19 Mammalian risk assessment using maximum and mean nomogram residues for ETU, assuming a foliar half-life of 11.7 days and a mancozeb to ETU conversion rate of 6.8% from dislodgeable foliar studies – airblast applications to apples

	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	Maximum nomogram residues				Mean nomogram residues			
			On-field		Off Field		On-field		Off Field	
			EDE (mg a.i./kg bw)	RQ	EDE (mg a.i./kg bw)	RQ	EDE (mg a.i./kg bw)	RQ	EDE (mg a.i./kg bw)	RQ[1]
Small Mammal (0.015 kg)										
Acute	54.5	Insectivore	34.17	0.63	25.29	0.46	23.59	0.43	17.46	0.32
	54.5	Granivore (grain and seeds)	5.29	0.10	3.91	0.07	2.52	0.05	1.87	0.03
	54.5	Frugivore (fruit)	10.58	0.19	7.83	0.14	5.04	0.09	3.73	0.07
Reproduction	5	Insectivore	34.17	6.83	25.29	5.06	23.59	4.72	17.46	3.49
	5	Granivore (grain and seeds)	5.29	1.06	3.91	0.78	2.52	0.50	1.87	0.37
	5	Frugivore (fruit)	10.58	2.12	7.83	1.57	5.04	1.01	3.73	0.75
Medium Sized Mammal (0.035 kg)										
Acute	54.5	Insectivore	29.95	0.55	22.17	0.41	20.68	0.38	15.31	0.28
	54.5	Granivore (grain and seeds)	4.64	0.09	3.43	0.06	2.21	0.04	1.64	0.03
	54.5	Frugivore (fruit)	9.27	0.17	6.86	0.13	4.42	0.08	3.27	0.06
	54.5	Herbivore (short grass)	66.27	1.22	49.04	0.90	23.54	0.43	17.42	0.32
	54.5	Herbivore (long grass)	40.46	0.74	29.94	0.55	13.21	0.24	9.78	0.18
	54.5	Herbivore (forage crops)	61.32	1.13	45.37	0.83	20.27	0.37	15.00	0.28
Reproduction	5	Insectivore	29.95	5.99	22.17	4.43	20.68	4.14	15.31	3.06
	5	Granivore (grain and seeds)	4.64	0.93	3.43	0.69	2.21	0.44	1.64	0.33
	5	Frugivore (fruit)	9.27	1.85	6.86	1.37	4.42	0.88	3.27	0.65
	5	Herbivore (short grass)	66.27	13.25	49.04	9.81	23.54	4.71	17.42	3.48
	5	Herbivore (long grass)	40.46	8.09	29.94	5.99	13.21	2.64	9.78	1.96
	5	Herbivore (broadleaf plants)	61.32	12.26	45.37	9.07	20.27	4.05	15.00	3.00
Large Sized Mammal (1 kg)										
Acute	54.5	Insectivore	16.01	0.29	11.84	0.22	11.05	0.20	8.18	0.15
	54.5	Granivore (grain and seeds)	2.48	0.05	1.83	0.03	1.18	0.02	0.87	0.02
	54.5	Frugivore (fruit)	4.95	0.09	3.67	0.07	2.36	0.04	1.75	0.03
	54.5	Herbivore (short grass)	35.41	0.65	26.20	0.48	12.58	0.23	9.31	0.17
	54.5	Herbivore (long grass)	21.62	0.40	16.00	0.29	7.06	0.13	5.22	0.10
	54.5	Herbivore (broadleaf plants)	32.76	0.60	24.25	0.44	10.83	0.20	8.01	0.15
Reproduction	5	Insectivore	16.01	3.20	11.84	2.37	11.05	2.21	8.18	1.64
	5	Granivore (grain	2.48	0.50	1.83	0.37	1.18	0.24	0.87	0.17

	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	Maximum nomogram residues				Mean nomogram residues			
			On-field		Off Field		On-field		Off Field	
			EDE (mg a.i./kg bw)	RQ	EDE (mg a.i./kg bw)	RQ	EDE (mg a.i./kg bw)	RQ	EDE (mg a.i./kg bw)	RQ[1]
		and seeds)								
	5	Frugivore (fruit)	4.95	0.99	3.67	0.73	2.36	0.47	1.75	0.35
	5	Herbivore (short grass)	35.41	7.08	26.20	5.24	12.58	2.52	9.31	1.86
	5	Herbivore (long grass)	21.62	4.32	16.00	3.20	7.06	1.41	5.22	1.04
	5	Herbivore (broadleaf plants)	32.76	6.55	24.25	4.85	10.83	2.17	8.01	1.60

1 – Exceedance of LOC (RQ > 1) highlighted.

Table 20 Bird risk assessment using maximum and mean nomogram residues for ETU, assuming a foliar half-life of 11.7 days and a mancozeb to ETU conversion rate of 6.8% from dislodgeable foliar studies – airblast applications to apples

	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	Maximum nomogram residues				Mean nomogram residues			
			On-field		Off Field		On-field		Off Field	
			EDE (mg a.i./kg bw)	RQ	EDE (mg a.i./kg bw)	RQ	EDE (mg a.i./kg bw)	RQ	EDE (mg a.i./kg bw)	RQ[1]
Small Bird (0.015 kg)										
Acute	200	Insectivore	59.41	0.3	43.96	0.2	41.02	0.21	30.36	0.15
	200	Granivore (grain and seeds)	9.19	0.0	6.80	0.0	4.39	0.02	3.24	0.02
	200	Frugivore (fruit)	18.39	0.1	13.61	0.1	8.77	0.04	6.49	0.03
Reproduction	8.9	Insectivore	59.41	6.7	43.96	4.9	41.02	4.61	30.36	3.41
	8.9	Granivore (grain and seeds)	9.19	1.0	6.80	0.8	4.39	0.49	3.24	0.36
	8.9	Frugivore (fruit)	18.39	2.1	13.61	1.5	8.77	0.99	6.49	0.73
Medium Sized Bird (0.035 kg)										
Acute	200	Insectivore	46.36	0.2	34.31	0.2	32.01	0.16	23.69	0.12
	200	Granivore (grain and seeds)	7.18	0.0	5.31	0.0	3.42	0.02	2.53	0.01
	200	Frugivore (fruit)	14.35	0.1	10.62	0.1	6.84	0.03	5.06	0.03
Reproduction	8.9	Insectivore	46.36	5.2	34.31	3.9	32.01	3.60	23.69	2.66
	8.9	Granivore (grain and seeds)	7.18	0.8	5.31	0.6	3.42	0.38	2.53	0.28
	8.9	Frugivore (fruit)	14.35	1.6	10.62	1.2	6.84	0.77	5.06	0.57
Large Sized Bird (1 kg)										
Acute	200	Insectivore	13.54	0.1	10.02	0.1	9.35	0.05	6.92	0.03
	200	Granivore (grain and seeds)	2.09	0.0	1.55	0.0	1.00	0.00	0.74	0.00
	200	Frugivore (fruit)	4.19	0.0	3.10	0.0	2.00	0.01	1.48	0.01
	200	Herbivore (short grass)	29.95	0.1	22.16	0.1	10.64	0.05	7.87	0.04

	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	Maximum nomogram residues				Mean nomogram residues			
			On-field		Off Field		On-field		Off Field	
			EDE (mg a.i./kg bw)	RQ	EDE (mg a.i./kg bw)	RQ	EDE (mg a.i./kg bw)	RQ	EDE (mg a.i./kg bw)	RQ[1]
	200	Herbivore (long grass)	18.29	0.1	13.53	0.1	5.97	0.03	4.42	0.02
	200	Herbivore (broadleaf plants)	27.71	0.1	20.50	0.1	9.16	0.05	6.78	0.03
Reproduction	8.90	Insectivore	13.54	1.5	10.02	1.1	9.35	1.05	6.92	0.78
	8.90	Granivore (grain and seeds)	2.09	0.2	1.55	0.2	1.00	0.11	0.74	0.08
	8.90	Frugivore (fruit)	4.19	0.5	3.10	0.3	2.00	0.22	1.48	0.17
	8.90	Herbivore (short grass)	29.95	3.4	22.16	2.5	10.64	1.20	7.87	0.88
	8.90	Herbivore (long grass)	18.29	2.1	13.53	1.5	5.97	0.67	4.42	0.50
	8.90	Herbivore (broadleaf plants)	27.71	3.1	20.50	2.3	9.16	1.03	6.78	0.76

1 – Exceedance of LOC (RQ > 1) highlighted.

Table 21 Screening level risk of ETU to aquatic organisms

Organism	Exposure	Endpoint for risk assessment (mg a.i./L)	Air blast to apples EEC (mg a.i./L)	Airblast RQ	Ground boom to ginseng EEC (mg a.i./L)	Ground boom RQ[1]
Freshwater species						
Daphnia magna	Acute	13.5	2.25	0.17	2.48	0.18
	Chronic	2.0	2.25	1.13	2.48	1.24
Amphibian	Acute (fish surrogate)	50.2	12.0	0.24	13.2	0.26
	Chronic (endocrine)	10	12.0	1.20	13.2	1.32
Rainbow trout	Acute	50.2	2.25	0.05	2.48	0.05
	Chronic	No data	2.25	-	2.48	-
Bluegill sunfish	Acute	99.0	2.25	0.03	2.48	0.03
	Chronic	No data	2.25	-	2.48	-
Freshwater algae	Acute	11.5	2.25	0.19	2.48	0.22
Vascular plant	Acute	480	2.25	0.005	2.48	0.005
Marine species						
Mollusk	Acute	4.6	2.25	0.49	2.48	0.54
	Chronic	No data	2.25	-	2.48	-

Organism	Exposure	Endpoint for risk assessment (mg a.i./L)	Air blast to apples EEC (mg a.i./L)	Airblast RQ	Ground boom to ginseng EEC (mg a.i./L)	Ground boom RQ[1]
Crustacean	Acute	55	2.25	0.04	2.48	0.05
	Chronic	No data	2.25	-	2.48	-
Sheepshead Minnow	Acute	90	2.25	0.03	2.48	0.03
Marine algae	Acute	No Data	2.25	-	2.48	-

1 – Exceedance of LOC (RQ > 1) highlighted.

Appendix IX Water modelling and monitoring for use in the drinking water risk assessment

Mancozeb is not persistent in natural environments due to rapid hydrolysis. The decomposition process is complex and results in a mixture of variable low molecular weight polymeric chains (in other words, polymer fragments), monomeric species, transient species and EBDC ligands associated with other metal ions that might be present in the environment. Major transformation products produced from mancozeb include ethylenebis-isothiocyanate sulfide (EBIS), M11, ETU and EU.

ETU is a common transformation product of the EBDC fungicides mancozeb, maneb, metiram, zineb and nabam. ETU is formed, as part of the EBDCs complex, in soil pore water/water bodies from hydrolytic transformation of parent EBDCs following application to soils and/or after reaching water bodies by drift, and/or run-off and in soil pore water. Aging of the complex results in enrichment with the transformation product ethylenethiourea (ETU), and ETU transformation products. ETU may be produced continuously at low concentrations from the slow transformation of the soil/sediment associated bound species via hydrolysis. ETU is very soluble in water and does not bind strongly to soils. It is very mobile in soil and has the potential to leach and reach groundwater.

EBIS and M11 are transient and are not expected to pose a chronic exposure concern in water. EU is produced through transformation of ETU. Because EU is formed from ETU, environmental levels are not expected to exceed those of ETU. The 2018 European Commission review (PMRA# 3017377–3017383) determined the toxicity reference values for EU were 30–40 times less than those of ETU, indicating that toxicity of EU is much less than ETU.

As a result, the residue of concern for drinking water was determined to be ETU alone.

Drinking water modelling was conducted with regional scenarios and region-specific weather data for a variety of crops. This resulted in an acute drinking water EEC of 16 µg/L and a chronic drinking water EEC of 2.9 µg/L (as reported in PRVD 2018-17).

Refinement of the chronic drinking water EEC was required. Relatively robust water monitoring data for ETU was available from a two year targeted retrospective monitoring study, initiated in 2001. The study was conducted by the EBDC/ETU Task Force and submitted to the PMRA (PMRA# 1766450). Potential drinking water sourced from surface water was monitored for a period of two years from watersheds in Maine, New York, Michigan, Minnesota and Washington. The sample sites ranged from very small watersheds and reservoirs in Maine to large watersheds draining into the Great Lakes in New York and Michigan. A total of 231 sites were sampled multiple times, resulting in a total of 3,971 samples. Concentrations of ETU in surface water were used in the chronic drinking water assessment because it would be expected that surface water concentrations would be higher than in groundwater.

The data does not allow for the calculation of chronic EEC values as sampling was infrequent. The use of a peak value from the monitoring data set provides a very conservative estimate of chronic drinking water concentrations for the drinking water health risk assessment. The peak value from the monitoring study data (0.57µg/L, New York State) was proposed as a conservative chronic drinking water EEC from monitoring in PRVD2018-17.

The study authors reported a value of 0.21µg/L as a proposed upper bound value from the drinking water monitoring survey. The USEPA used this value in their chronic dietary risk assessment.

Based on a reconsideration of the analysis of this study, the value proposed by the study authors as the upper bound value for drinking water (0.21µg/L) is suitable for use as a conservative estimate of the potential chronic concentration of ETU residues in drinking water from the use of EBDC pesticides. This value has been used in the chronic drinking water assessment in this re-evaluation decision.

Appendix X Label amendments for products containing mancozeb

Information on approved labels of currently registered products should not be removed unless it contradicts the label statements provided below.

1.0 Label amendments for technical class products (Reg. Nos. 19788, 20734, 25166):

On the principal panel, replace “Guarantee” with “Active Ingredient”.

The following statements are to be added to the “Environmental Hazards/Precautions” section:

- TOXIC to aquatic organisms.
- DO NOT discharge effluent containing this product into sewer systems, lakes, streams, ponds, estuaries, oceans or other waters.

The following statements are required under the “Disposal” Section:

- Canadian manufacturers should dispose of unwanted active ingredients and containers in accordance with municipal or provincial regulations. For additional details and clean up of spills, contact the manufacturer or the provincial regulatory agency.

2.0 Label amendments required for all commerial class products

2.1 Directions for use:

- Use instructions for crops which are no longer supported (seed treatment for barley, corn, flax, oat, and wheat (including potato seed pieces), greenhouse uses, pears, carrots, celery, lettuce, watermelon, lentils, wheat, alfalfa grown for seed, ornamentals, and forestry uses) must be removed from the label.
- Tank mix partners must be clearly indicated, by product name, on mancozeb product labels. Specific directions regarding use of the tank mix, or a reference to the tank mix partner label, must be included. A general reference that "this product can be tank mixed with other products" is not acceptable. Therefore, remove any vague or non-specific claims that the product can be tank mixed with another pesticide.
- Remove any vague reference to “apply as needed”, or “apply as required”. Directions for Use should reflect the use-specific re-application interval.

The maximum application rates, maximum number of applications, and application timing on the label must be updated to match the information specified in Table 1, for each crop currently registered on the label and granted continuing registration. Use information must be removed from the labels for uses that are cancelled: seed treatment (including potato seed piece treatment), greenhouse uses, pears, carrots, celery, lettuce, watermelon, lentils, wheat, alfalfa grown for seed, ornamentals, and forestry uses, and application by handheld equipment.

Table 1 Supported use pattern with acceptable risks based on occupational exposure

Site/Crop	Formulation	Maximum Rate (kg a.i./ha)	Number of Applications per Year	Interval Between Applications
Potatoes	DF, WG, SN	1.69	8	5
Apples	DF, WG, SN	4.5	4	7
Onions (foliar)	DF, WG, SN	1.69	6	7
Onion (in-furrow)	DF, WG	6.6	1	NA
Sugar beets	DF, WG	1.69	5	7
Ginseng	DF, WG, SN	3.3	6	14
Cucumbers	DF, WG, SN	2.44	3	7
Tomatoes	DF, WG, SN	2.44	2	7
Grapes	DF, WG	2.25	1	NA
Pumpkin (foliar)	DF, WG, SN	2.44	3	7
Squash (foliar)	DF, WG, SN	2.44	3	7
Melons including cantaloupe, excluding watermelon	DF, WG, SN	2.44	3	7

DF = dry flowable, WG = wettable granule, SN = solution; NA = not applicable

Statements must be amended (or added) to include the following directions to the appropriate labels in order to mitigate the risk of exposure to mancozeb:

"The total seasonal application of mancozeb and metiram combined cannot exceed the maximum number of applications on potatoes of either chemical per year with no more than 3 applications being metiram."

"When applied as a tank-mix combination, read and observe all label directions, including rates, personal protective equipment, restrictions and precautions for each product used in the tank-mix. Always use in accordance with the most restrictive label restrictions and precautions."

"DO NOT apply using handheld equipment."

"DO NOT apply in greenhouses."

For all wettable granular or dry flowable formulations, add the following statement:

"DO NOT apply by hand."

For all products that are in water soluble packaging add the following label statements:

"Water-Soluble Packages (WSPs) are designed to dissolve in water. Agitation may be used, if necessary, to help dissolve the WSP. Failure to follow handling and mixing instructions can increase your exposure to the pesticide products in WSPs.

Handling instructions
Follow these steps when handling pesticide products in WSPs.

1. Mix in spray tank only.

2. Handle WSP(s) in a manner that protects package from breakage and/or unintended release of contents. If package is broken, put on a minimum of coveralls, chemical-resistant gloves, chemical-resistant footwear, and a NIOSH-approved N95 (minimum) filtering facepiece respirator (dust mask) that is properly fit tested and then continue with mixing instructions.
3. Keep the WSP(s) in outer packaging until just before use.
4. Keep the WSP dry prior to adding to the spray tank.
5. Handle with dry gloves and according to the label instructions for PPE.
6. Keep WSP intact. Do not cut or puncture WSP.
7. Reseal the WSP outer packaging to protect any unused WSP(s).

Mixing instructions
Follow the steps below when mixing this product, including if tank mixed with other pesticide products. If being tank mixed, the mixing directions 1 through 9 below take precedence over the mixing directions of the other tank mix products. All other directions for use of all tank mixed products should be followed provided they do not conflict. Do not tank mix this product with products that prohibit tank mixing or have conflicting mixing directions.

1. If a basket or strainer is present in the tank hatch, remove prior to adding the WSP to the tank.
2. Fill tank with water to approximately one-third to one-half of the desired final volume of spray.
3. Stop adding water and stop any agitation.
4. Place intact/unopened WSP(s) into the tank.
5. Do not spray water from a hose or fill pipe to break or dissolve the WSP(s).
6. Start mechanical and recirculation agitation from the bottom of tank without using any overhead recirculation, if possible. If overhead recirculation cannot be turned off, close the hatch before starting agitation.
7. Dissolving the WSP(s) may take up to 5 minutes or longer, depending on water temperature, water hardness and intensity of agitation.
8. Stop agitation before tank lid is opened.
9. Open the lid to the tank, exercising caution to avoid contact with dusts or spray mix, to verify that the WSPs have fully dissolved and the contents have been thoroughly mixed into the solution.
10. Do not add other allowed products or complete filling the tank until the bags have fully dissolved and pesticide is thoroughly mixed.
11. Once the WSP have fully dissolved and any other products have been added to the tank, resume filling the tank with water to the desired level, close the tank lid, and resume agitation.
12. Use the spray solution when mixing is complete.
13. Maintain agitation of the diluted pesticide mix during transport and application.
14. It is unlawful to use any registered pesticide, including WSPs, in a manner inconsistent with its label."

For all products registered for aerial application, the following use directions must be added:

> **Aerial application:** DO NOT apply during periods of dead calm. Avoid application of this product when winds are gusty. DO NOT apply when wind speed is greater than 16 km/h at flying height at the site of application. DO NOT apply with spray droplets smaller than the American Society of Agricultural Engineers (ASAE S572.1) medium classification. Reduce drift caused by turbulent wingtip vortices. Nozzle distribution along the spray boom length MUST NOT exceed 65% of the wing- or rotorspan.
>
> Apply only by fixed-wing or rotary aircraft equipment which has been functionally and operationally calibrated for the atmospheric conditions of the area and the application rates and conditions of this label.
>
> Label rates, conditions and precautions are product specific. Read and understand the entire label before opening this product. Apply only at the rate recommended for aerial application on this label. Where no rate for aerial application appears for the specific use/crop, this product cannot be applied by any type of aerial equipment for that use/crop.
>
> Ensure uniform application. To avoid streaked, uneven or overlapped application, use appropriate marking devices.

Required for all products:

Field sprayer application: DO NOT apply during periods of dead calm. Avoid application of this product when winds are gusty. DO NOT apply with spray droplets smaller than the American Society of Agricultural Engineers (ASAE S572.1) medium classification. Boom height must be 60 cm or less above the crop or ground.

Airblast application: DO NOT apply during periods of dead calm. Avoid application of this product when winds are gusty. DO NOT direct spray above plants to be treated. Turn off outward pointing nozzles at row ends and outer rows. DO NOT apply when wind speed is greater than 16

Buffer zones: Spot treatments using hand-held equipment do not require a spray buffer zone. Use of low-clearance hooded or shielded sprayers that prevent spray contact with crop, fruit or foliage, and soil drench or soil incorporation do not require a spray buffer zone.

The spray buffer zones specified in the table below are required between the point of direct application and the closest downwind edge of sensitive freshwater habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs and wetlands) and estuarine/marine habitats.

Ground buffer zones for all products:

The buffer zones presented in this table are for mancozeb. As buffer zones are active specific, for co-formulated products (in other words, Reg. No. 26842, 28893, and 33565), care must be taken to ensure the correct buffer zones remain on the label. If the currently labelled buffer zones for Reg. No. 26842, 28893, and 33565 are larger than in this table, the buffer zones should remain on the label. For all other products, the buffer zones below apply.

Method of application	Crop		Spray Buffer Zones (metres) Required for the Protection of:			
			Freshwater Habitat of Depths:		Estuarine/Marine Habitat of Depths:	
			Less than 1 m	Greater than 1 m	Less than 1 m	Greater than 1 m
Field sprayer	Onions (foliar), potatoes, sugarbeets		5	1	2	1
	Field tomato, cantaloupe, cucumbers, melons, pumpkins, squash		5	1	3	1
	Ginseng		10	2	4	2
	Onions (in-furrow)		15	1	5	3
Airblast	Apples	Early growth stage	45	25	35	25
		Late growth stage	35	20	25	20
	Grapes	Early growth stage	40	20	30	20
		Late growth stage	30	10	20	10

Aerial buffer zones

The buffer zones presented in this table are for mancozeb. As buffer zones are active specific, for co-formulated products (in other words, Reg. No. 26842, 28893, and 33565), care must be taken to ensure the correct buffer zones remain on the label. If the currently labelled aerial buffer zones for Reg. No. 26842, 28893, and 33565 are larger than in this table, the buffer zones should remain on the label. For all other products, the aerial buffer zones below apply.

Mancozeb Aerial Buffer Zones for Potatoes only

PCP#	Crop		Spray Buffer Zones (metres) Required for the Protection of:			
			Freshwater Habitat of Depths:		Estuarine/Marine Habitat of Depths:	
			Less than 1 m	Greater than 1 m	Less than 1 m	Greater than 1 m
20552	Potatoes	Fixed-wing	250	20	75	20
		Rotary-wing	150	15	50	15
20553, 26842, 28893, 29221, 30241, 33565	Potatoes	Fixed-wing	275	15	50	15
		Rotary-wing	150	10	35	10
21057, 28127, 33292	Potatoes	Fixed-wing	275	15	45	15
		Rotary-wing	150	10	35	10
25397	Potatoes	Fixed-wing	250	15	50	15

PCP#	Crop		Spray Buffer Zones (metres) Required for the Protection of:			
			Freshwater Habitat of Depths:		Estuarine/Marine Habitat of Depths:	
			Less than 1 m	Greater than 1 m	Less than 1 m	Greater than 1 m
		Rotary-wing	125	10	35	10
31181	Potatoes	Fixed-wing	225	20	80	20
		Rotary-wing	150	15	50	15
33299	Potatoes	Fixed-wing	300	15	70	20
		Rotary-wing	175	15	50	15

For tank mixes, consult the labels of the tank-mix partners and observe the largest (most restrictive) spray buffer zone of the products involved in the tank mixture and apply using the coarsest spray (ASAE) category indicated on the labels for those tank mix partners.

The spray buffer zones for this product can be modified based on weather conditions and spray equipment configuration by accessing the Spray Buffer Zone Calculator on the Pest Management Regulatory Agency web site.

Add to GENERAL DIRECTIONS FOR USE after the MIXING INSTRUCTIONS:

- As this pesticide is not registered for the control of pests in aquatic systems, DO NOT use to control aquatic pests.
- DO NOT contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes.
- To protect pollinators, follow the instructions regarding bees in the Environmental Precautions section.

For labels that currently have an early re-entry statement. The statement must be updated to the following [PPE in the label statement must match the PPE required for mixing and loading]:

- "DO NOT enter or allow worker entry into treated areas during the restricted-entry interval (REI) on the label. Employers should make every effort to schedule pesticide applications and worker tasks in order to avoid early entry of workers into treated areas. Under exceptional circumstances, certified pesticide applicators may enter treated areas for short-term tasks not involving hand labour if at least 4 hours have passed since application and a long-sleeved shirt, long pants, chemical-resistant footwear, socks, goggles, 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 is worn. Time spent in the treated area cannot exceed 1 hour in a 24 hour period or until restricted-entry interval is over."

2.2 Use precautions:

There may be potential for exposure to bystanders from drift following pesticide application to agricultural areas. In the interest of promoting best management practices and to minimize human exposure from spray drift or from spray residues resulting from drift, the following label statement is required:

"Apply only when the potential for drift beyond the area to be treated is minimal. Take into consideration wind speed, wind direction, temperature inversions, application equipment, and sprayer settings."

The technical registrants no longer support uses on outdoor ornamentals, therefore these uses were not assessed for re-evaluation. To ensure that mancozeb will not be used in residential areas for the apple use, the following statement should appear on all mancozeb labels:

"This product is not to be used in or around homes or other residential areas such as parks, school grounds and/or playing fields. Residential areas are defined as any use site where the general public, including children, could be exposed during or after application. It is not for use by homeowners."

2.3 Engineering controls and personal protective equipment:

Statements must be amended (or added) to include the following directions to the appropriate labels in order to mitigate the risk of exposure to mancozeb:

For all products add the following label statements:

"Wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes during mixing, loading, application, clean-up and repair. Gloves are not required during application within a closed cab or cockpit."

"In addition, wear chemical-resistant headgear during open cab airblast application. Chemical-resistant headgear includes Sou'Wester hat, chemical-resistant rain hat or large brimmed waterproof hat and hood with sufficient neck protection. Gloves and chemical-resistant hat are not required during application within a closed cab."

For all dry flowable and wettable granule formulations, except those in water soluble packaging, add the following statements:

"A respirator with a NIOSH-approved organic-vapour-removing cartridge with a prefilter approved for pesticides, or a NIOSH-approved canister approved for pesticides is required when mixing/loading."

"During open-cab groundboom application, applicators must wear either a respirator with a NIOSH approved organic-vapour-removing cartridge with a prefilter approved for pesticides OR a NIOSH approved canister approved for pesticides OR use a closed-cab tractor that provides both a physical barrier and respiratory protection (such as dust/mist filtering and/or vapour/gas purification system) when handling more than [350 kg a.i.to be reported as a product equivalent

value] per person per day. The closed cab must have a chemical-resistant barrier that totally surrounds the occupant and prevents contact with pesticides outside the cab. These restrictions are in place to minimize exposure to individual applicators. Application may need to be performed over multiple days or using multiple applicators." As indicated by the square brackets above, the active ingredient amount in this statement (in other words, 350 kg a.i.) is to be converted into the corresponding amount of product by the registrant.

2.4 Restricted-entry interval:

The following table must be added to all labels under PRECAUTIONS. Remove any crops from the table that are not registered on that specific product label. Some of the activities in the REI table are not routinely conducted on every farm for every crop. The REIs specified for an activity must be followed only if that activity is being performed.

Table 2 Required restricted-entry intervals

Crop	Postapplication Activity	REI and/or PHI (days)
Potatoes	Harvesting	3
	All other activities	0.5
Apples	Harvesting	77
	Hand thinning of fruit	35
	All other activities	0.5
Onions (foliar)	Harvesting	14
	Hand weeding	1
	All other activities	0.5
Onions (in-furrow)	Harvesting	100
	All other activities	0.5
Sugar beets	Harvesting	21
	All other activities	0.5
Ginseng	Harvesting	30
	Hand set/Hand line irrigation related activities involving foliar contact	1
	All other activities	0.5
Cucumbers	Harvesting	14
	All other activities	0.5
Tomatoes	Harvesting	30
	All other activities	0.5
Grapes	Harvesting	66
	Girdling, Turning	21
	Leaf pulling by hand, tying, training	7
	Hand set/Hand line irrigation related activities involving foliar contact	1
	All other activities	0.5
Pumpkin, Squash, Melons including Cantaloupe, excluding watermelon	Harvesting	14
	All other activities	0.5

REI = restricted-entry interval; PHI = preharvest interval

2.5 Environmental precautions

The following statements are to be added:

- TOXIC to aquatic organisms. Observe buffer zones specified under DIRECTIONS FOR USE.
- TOXIC to small wild mammals.
- TOXIC to birds
- May be toxic to bees. Minimize spray drift to reduce harmful effects on bees in habitats close to the application site. Avoid application during the crop blooming period. If applications must be made during the crop blooming period, restrict applications to the evening when most bees are not foraging. Avoid applications when bees are foraging in the treatment area in ground cover containing blooming weeds. To further minimize exposure to pollinators, refer to the complete guidance "Protecting Pollinators during Pesticide Spraying – Best Management Practices" on the Health Canada website (www.canada.ca/pollinators).
- Toxic to certain beneficial arthropods (which may include predatory and parasitic insects, spiders, and mites). Minimize spray drift to reduce harmful effects on beneficial arthropods in habitats next to the application site such as hedgerows and woodland.
- To reduce runoff from treated areas into aquatic habitats avoid application to areas with a moderate to steep slope, compacted soil, or clay.
- Avoid application when heavy rain is forecast.
- Contamination of aquatic areas as a result of runoff may be reduced by including a vegetative strip between the treated area and the edge of the water body.
- This product demonstrates the properties and characteristics associated with chemicals detected in groundwater. The use of this product in areas where soils are permeable, particularly where the water table is shallow, may result in ground water contamination.

Non-risk label amendments

On the principal panel, replace "Guarantee" with "Active Ingredient".

Update the "Resistance Management Recommendations" section according to Regulatory Directive DIR2013-04, *Pesticide Resistance Management Labelling Based on Target Site/Mode of Action.*

On the front panel and in the resistance management section, update "GROUP M FUNGICIDE" to "GROUP M3 FUNGICIDE".

Under the DIRECTIONS FOR USE section, just before the use direction tables, insert the following statement: "When applied as directed, (product name) will control the listed diseases, unless otherwise indicated as suppression.".

Replace all Minor Use Liability Statements with the following:

The DIRECTIONS FOR USE for the uses described in this section of the label were developed by persons other than [registrant name] under the User Requested Minor Use Label Expansion program. For these uses, [Registrant name] has not fully assessed performance (efficacy) and/or crop tolerance (phytotoxicity) under all environmental conditions or for all crop varieties when used in accordance with the label. The user should test the product on a small area first, under local conditions and using standard practices, to confirm the product is suitable for widespread application.

For each disease already on the product label, verify that the following Latin pathogen name appears in parenthesis after the common disease name, for each crop in the use directions table:

- Apple – scab (*Venturia inaequalis*), cedar apple rust (*Gymnosporangium juniperi-virginianae)* and quince rust (*Gymnosporangium clavipes*);
- Potato – early blight (*Alternaria solani*) and late blight (*Phytophthora infestans*);
- Ginseng – Alternaria leaf blight (*Alternaria panax*);
- Onions (dry bulb), foliar – Botrytis leaf blight (*Botrytis squamosal*), neck rot (*Botrytis allii*), Downy mildew (*Peronospora destructor*) and purple blotch (*Alternaria porri*);
- Onions (dry bulb), in-furrow – onion smut (*Urocystis cepulac*);
- Sugar beets – Cercospora leaf spot (*Cercospora beticola*);
- Tomatoes, field – anthracnose (*Colletotrichum spp*.), early blight (*Alternaria solani*), gray leaf spot (*Stemphylium solani, S. lycopersici*) and late blight (*Phytophthora infestans*);
- Grapes – downy mildew (*Plasmopara viticola*) and black rot (*Guignardia bidwellii*);
- Cantaloupe, cucumber (field), pumpkin, squash, other melons (except water melon) – anthracnose (*Colletotrichum obiculare*), Alternaria leaf spot (*Alternaria cucumerina*), downy mildew (*Pseudoperonospora cubensis*), gummy stem blight (*Didymella bryoniae*) and scab (*Cladosporium cucumerinum*).

Appendix XI References considered following publication of PRVD2018-17

A. Information considered in the updated toxicological assessment

List of studies/information submitted by registrant

PMRA Document Number	Reference
2039432	2010. Ethylene thiourea (ETU): Developmental Toxicity Study in Rabbits. DACO 4.5.3
2055156	2011. Ethylene thiourea (ETU): Dietary reproduction probe study in Crl:CD(SD) rats. DACO 4.5.1, 4.5.14
2313478	2013. Ethylenethiourea (ETU): An F1 extended one generation reproductive toxicity study in Crl:CD(SD) rats. DACO 4.5.1,4.5.14
2363857	2012. Immunotoxicity study in male Wistar rats. Administration via the diet for 4 weeks. DACO 4.3.8
2047262	2007. A dietary exposure and dose range-finding developmental neurotoxicity study of mancozeb in rats. DACO 4.5.14
2047261	2008. An oral (dietary) developmental neurotoxicity study of mancozeb in rats.DACO 4.5.14
2363852	2012. Mancozeb: assessment of immunotoxic potential using the sheep red blood cell assay after 28-day dietary exposure to male Crl:CD(SD) Rats. DACO: 4.3.8
3016507	2015. A Preliminary Oral (Gavage) Study of Mancozeb in Pregnant Sprague Dawley Rats. DACO 4.5.2
3016508	2015. An Oral (Gavage) Prenatal Developmental Toxicity Study of ETU in Sprague Dawley Rats. DACO 4.5.2
3016509	2015. An Oral (Gavage) Prenatal Developmental Toxicity Study of Mancozeb in Sprague Dawley Rats. DACO 4.5.2
3016506	2015. A 14-Day Oral (Gavage) Tolerability Study of Mancozeb in Nonpregnant Sprague Dawley Rats. DACO 4.5.2

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PMRA Document Number	Reference
2849973	2008. Gavage DNT study of Propylthiouracil (PTU) in Wistar rats. Relationship between transient hypothyroxinemia during development and long-lasting behavioural and functional changes. Marta Axelstad. DACO 4.5.14
2849980	2009. Assessment of developmental effects of hypothyroidism in rats from in utero and lactation exposure to anti-thyroid agents. Makoto Shibutani, Gye-Hyeong. DACO 4.5.2
2849986	2011. Mancozeb Developmental Neurotoxicity study (dose finding) in Wistar rats (HanTac), Axelstad. DACO 4.5.14

2849986	2011. Developmental Neurotoxicity study (main study) in Wistar rats (HanTac), Axelstad. DACO 4.5.14
3131868	EFSA, 2018, Monograph. Volume3-B (Toxicology and metabolism). DACO: 12.5
3131867	Dearfield, 1994. Ethylene thiourea (ETU). A review of the genetic toxicity studies. DACO 4.8
3131869	Elia, 1995. The genetic toxicology of ethylenethiourea. DACO 4.8

B. Information considered in the updated dietary assessment

List of studies/information submitted by registrant

PMRA Document Number	Reference
2363881	1986. Analytical Reports of Dithane and ETU for Winter Squash Residue Samples. DACO 7.4.2.
2363906	1998. Mancozeb: Magnitude of Residue on Ginseng. DACO 7.4.2.
2950649 2969551	2018. Magnitude of the Residue of Mancozeb in Potato Processed Commodities. DACO 7.4.5
2969548	1990. ETU National Food Survey - ETU 89-01 Vol 1 of 8 (Market Basket Survey), Vol 1 of 8. DACO 7.8
2969552	1990. Market Basket (National Food) Survey Fourth Quarter and Interim Final Report ETU 90-09, Vol 5 of 8. DACO 7.8
2969553	1990. Market Basket (National Food) Survey Fourth Quarter and Interim Final Report ETU 90-09, Vol 7 of 8. DACO 7.8
2969554	1990. Market Basket (National Food) Survey Fourth Quarter and Interim Final Report ETU 90-09, Vol 2 of 8. DACO 7.8
2969555	1990. Market Basket (National Food) Survey Fourth Quarter and Interim Final Report ETU 90-09, Vol 4 of 8. DACO 7.8
2969556	1990. Market Basket (National Food) Survey Fourth Quarter and Interim Final Report ETU 90-09, Vol 6 of 8. DACO 7.8
2969557	1990. Market Basket (National Food) Survey Fourth Quarter and Interim Final Report ETU 90-09, Vol 8 of 8. DACO 7.8
2969558	1990. Market Basket (National Food) Survey Fourth Quarter and Interim Final Report ETU 90-90, Vol 3 of 8. DACO 7.8
2969560	2019. Response of the Mancozeb Task Force to the Pest Management Regulatory Agency Consultation on the Proposed Re-evaluation Decision for Mancozeb and its Associated End-Use Products Dietary Evaluation PRVD2018-17. DACO 7.8
2969564	2019. Response of the Mancozeb Task Force to the Pest Management Regulatory Agency Consultation on the Proposed Re-evaluation Decision for Mancozeb and its

PMRA Document Number	Reference
	Associated End-Use Products Overview of Task Force Comments PRVD2018-17. DACO 0.8.24
2969569	2019. Response of the Mancozeb Task Force to the Pest Management Regulatory Agency Consultation on the Proposed Re-evaluation Decision for Mancozeb and its Associated End-Use Products Value of Mancozeb to Canadian Agriculture PRVD2018-17. DACO 10.6
3066998	2019. The EBDC/ETU Task Force Market Basket Survey and Monitory Study Continue to be Valid, Reliable and Appropriate for Dietary Risk Assessment. Project Identification Number TF2019-1. DACO 7.8

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	USEPA, 2003a. Mancozeb, Maneb, and Metiram: Processing and Cooking Factors for Use in Dietary Exposure Assessments to Support Reregistration, dated November 5, 2003.
	USEPA, 2003b. Mancozeb: Anticipated Residues for Dietary Exposure Assessment to Support Reregistration, dated November 5, 2003.
	USEPA, 2013. Mancozeb. Acute, Chronic, and Cancer Dietary Exposure Assessments of Food and Drinking Water to Support the New Use of Mancozeb on Walnuts and the Establishment of a Tolerance on Imported Tangerines for Section 3 Registration.

C. Information considered in the updated occupational and non-occupational assessment

List of studies/information submitted by registrant

PMRA Document Number	Reference
2115788	2008. Data Submitted by the ARTF to Support Revision of Agricultural Transfer Coefficients.
2572744	2009. Agricultural Handler Exposure Scenario Monograph: Open Cab Groundboom Application of Liquid Sprays. DACO 5.4, 5.5
2572745	2012. Agricultural Handler Exposure Scenario Monograph: Closed Cockpit Aerial Application of Liquid Sprays. DACO 5.4, 5.5
2572743	2014. Agricultural Handler Exposure Scenario Monograph: Open Cab Airblast Application of Liquid Sprays. DACO 5.4, 5.5
2172938	2015a. Agricultural Handler Exposure Scenario Monograph: Open Pour Mixing and Loading Dry Flowable Formulations. DACO 5.4, 5.5
1913109	2015b. Agricultural Handler Exposure Scenario Monograph: Open Pour Mixing and Loading of Liquid Formulations. DACO 5.4, 5.5
1746114	1999a. Dissipation of dislodgeable foliar residues of mancozeb applied to apples. DACO 5.9
1746112	1999b. Dissipation of dislodgeable foliar residues of mancozeb applied to grapes. DACO 5.9
1752407-1752419	1992. Mancozeb dislodgeable foliar residue and worker re-entry studies on tomatoes - supplemental report. Supplement to MRID No. 41836902. EPA MRID 42560201. DACO 5.9

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D. Information considered in the updated environmental assessment

List of studies/information submitted by registrant

PMRA Document Number	Reference
2950663	2017. Hydrolysis of [^{14}C]-Mancozeb. DACO 8.2.3.2
2362910	2002. Residual Analysis of Grass Samples and *Poecilus cupreus* treated with Dithane® M-45. DACO 1.5.8.
2959927	2007. Residual Analysis of Grass Samples and *Poecilus cupreus* treated with Dithane® M-45. DACO 1.5.8.
2959928	2006. Mancozeb Residues in Aphids (*Rhopalosiphum padi*) in a Semi-Field Study. DACO 1.5.8.
2959929	2006. Mancozeb Residues on Mealworm (*Tenebrio molitor*) in a Semi-Field Study. DACO 1.5.8.
2959930	2006. Mancozeb Residues on the Cricket (*Acheta domestica*) in a Semi-Field Study. DACO 1.5.8.
2959922	2004. To determine the magnitude of mancozeb residues in grass grown in orchards resulting from a single directed application of DITHANE M45 to fruit trees and vines using commercial spray equipment in the UK and N France. DACO 1.5.8.
2959923	2004. To determine the magnitude of mancozeb residues in grass grown in orchards resulting from a single directed application of DITHANE M45 to fruit trees and vines using commercial spray equipment in Italy and S France. DACO 1.5.8.
2959924	2006. To determine the magnitude of mancozeb residues in grass grown in orchards resulting from a single directed application of DITHANE NEOTEC 75 WG Rainshield to either apple trees using commercial spray equipment, or directly to the orchard floor (UK, 2005). DACO 1.5.8.
2959925	2006. To determine the magnitude of mancozeb residues in grass grown in orchards resulting from a single directed application of DITHANE NEOTEC 75 WG Rainshield to either vines using commercial spray equipment, or directly to the vineyard floor (N France, 2005). DACO 1.5.8.

2959926	2006. To determine the magnitude of mancozeb residues in grass grown in orchards resulting from a single directed application of DITHANE NEOTEC 75 WG Rainshield to either apple trees using commercial spray equipment, or directly to the orchard floor (Italy and Southern France, 2005). DACO 1.5.8.

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PMRA Document Number	Reference
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3017379	European Commission, 2018. Mancozeb Volume 3 – B.9 (AS) – Active Substance: Ecotoxicology Data And Assessment Of Risks For Non-Target Species: Renewal Assessment Report prepared according to the Commission Regulation N° 1107/2009. DACO 12.5.9
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3017381	European Commission, 2018. Mancozeb Volume 3 – B.9 (PPP) – Penncozeb 80WP: Ecotoxicology Data And Assessment Of Risks For Non-Target Species. Renewal Assessment Report prepared according to the Commission Regulation N° 1107/2009. DACO 12.5.9
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3017383	European Commission, 2018. Mancozeb Volume 3 – B.9 (PPP) – Agria Mancozeb 800WP: Ecotoxicology Data And Assessment Of Risks For Non-Target Species. Renewal Assessment Report prepared according to the Commission Regulation N° 1107/2009. DACO 12.5.9
3017377	European Commision, 2018. Mancozeb Volume 3 – CA.B.8 (AS): Environmental Fate and Behaviour. Ecotoxicology Data And Assessment Of Risks For Non-Target Species. Renewal Assessment Report prepared according to the Commission Regulation N° 1107/2009. DACO 12.5.8