Re-evaluation Decision RVD2024-09

# Tebuconazole and Its Associated End-use Products

*Final Decision*

*(publié aussi en français)*

**20 November 2024**

This document is published by the Health Canada Pest Management Regulatory Agency. For further information, please contact:

Publications
Pest Management Regulatory Agency
Health Canada
2 Constellation Drive
8th floor, A.L. 2608 A
Ottawa, Ontario K1A 0K9

Internet: canada.ca/pesticides
pmra.publications-arla@hc-sc.gc.ca

Information Service:
1-800-267-6315
pmra.info-arla@hc-sc.gc.ca

Canada

ISSN: 1925-1017 (print)
1925-1025 (online)

Catalogue number: H113-28/2024-9E (print version)
H113-28/2024-9E-PDF (PDF version)

# Table of Contents

# Re-evaluation decision for tebuconazole 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 meet current health and environmental standards and 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. More details, on the legislative framework, risk assessment and risk management approach, are provided under the Evaluation approach Section of this document.

Tebuconazole is a systemic fungicide registered for foliar uses (including large field crops, asparagus, and turf), seed treatments, and as a heavy-duty wood preservative. The joinery wood use was assessed separately (RVD2017-06, *Re-evaluation Decision for Joinery Use of Tebuconazole*) and is not included in the current re-evaluation decision.

Currently registered products containing tebuconazole can be found in the Pesticide Product Information Database and in Appendix I. The Proposed Re-evaluation Decision PRVD2021-08, *Tebuconazole and Its Associated End-use Products*[1] containing the evaluation of tebuconazole and proposed decision, underwent a 90 day consultation period ending on 21 October 2021. PRVD2021-08 proposed continued registration of tebuconazole and all associated end-use products provided new risk mitigation measures are put in place. The proposed mitigation measures included increased personal protective equipment and engineering controls, restricted-entry intervals for agricultural products, reduction of the total seasonal application rate for turf, precautionary environmental label statements and spray buffer zones.

Health Canada received comments (and information) relating to the health, environmental and value assessments. Commenters are listed in Appendix II. These comments are summarized in Appendix III along with the responses by Health Canada. These comments and new data/information resulted in revisions to the human health and, environmental risk and value assessments (see Science evaluation update), and resulted in changes to the proposed re-evaluation decision described in PRVD2021-08.

A reference list of information used as the basis for the proposed re-evaluation decision is included in PRVD2021-08, and further information used in the re-evaluation decision (RVD2024-09) is listed in Appendix X of this document. Therefore, the complete reference list of all information used in this final re-evaluation decision includes both the information set out in PRVD2021-08 and the information set out in Appendix X herein.

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

This document presents the final decision[2] for the re-evaluation of tebuconazole, including the required amendments (risk mitigation measures) to protect human health and the environment, as well as label amendments required to bring labels to current standards. All products containing tebuconazole that are registered in Canada are subject to this re-evaluation decision. As discussed above, the exception to this decision are products containing tebuconazole registered for joinery wood use.

## Re-evaluation decision for tebuconazole

Health Canada has completed the re-evaluation of tebuconazole. Under the authority of the *Pest Control Products Act*, Health Canada has completed all required evaluations and consultations and has determined that the registration of products containing tebuconazole is required to be amended, in accordance with paragraph 21(2)(a) of the *Pest Control Products Act*. An evaluation of available scientific information respecting the health and environmental risks and value of tebuconazole found that certain uses of tebuconazole products meet current standards for protection of human health and the environment and have acceptable value when used according to the amended conditions of registration which includes new mitigation measures. However, all turf uses of tebuconazole are cancelled as risks due to exposure from drinking water were not shown to be acceptable when used according to the current conditions of registration, or when additional mitigation is considered. Label amendments, as summarized below and listed in Appendix IX, 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/or mitigation measures, as a result of the re-evaluation of tebuconazole, are summarized below. Refer to Appendix IX for details.

### Human health

The following risk-reduction measures are required for continued registration of tebuconazole in Canada:

The following maximum residue limit action is required to address potential dietary food exposure and risks:

- The import maximum residue limit of 5 ppm for grape commodities will be revoked. After revocation, residues of tebuconazole on/in grapes will be regulated under subsection B.15.002(1) of the Food and Drug Regulations, which requires that residues not exceed 0.1 ppm. A proposed maximum residue limit document will be published to inform the public of this decision.

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

The following mitigation measures are required to address potential dietary risks due to exposure from drinking water:

- All turf uses are cancelled. As a result, the registration of Mirage Stressgard (Registration Number 32405) and Dedicate Stress (Registration Number 33236) is cancelled.
- For all other remaining crops, the total seasonal rate is limited to a maximum of 136 g a.i./ha/year, except for those crops where the yearly total rate is currently below 136 g a.i./ha.
- The number of foliar applications per year for asparagus, and short rotation intensive culture (poplar and willow) are reduced to 1 application at 126 g a.i./ha.
- The number of foliar applications per year for soybean are reduced to either 1 application at 136 g a.i./ha or 2 applications at 65 g a.i./ha at a minimum 10-day interval.

For consistency with other labels:

- Rotational plant-back interval of 120 days is required for food and feed crops, unless the current label directions are more restrictive.

To protect workers handling commercial-class products or entering treated sites following application of these products, the following risk reduction measures are required:

- Increased personal protective equipment for mechanically-pressurized handguns and handheld airblast/mistblowers.
- Limit the amount of product handled per day for handheld airblast/mistblowers.
- A restricted-entry intervals of 12 hours for agricultural sites.

To protect workers treating wood and handling treated wood:

- Personal protective equipment as per the "Recommendations for Design and Operation of Wood Preservation Facilities, 2013 Technical Recommendations Document", which is enforced by Environment and Climate Change Canada (ECCC, 2013).

To protect workers treating seed and handling treated seed:

- For corn seed, closed mix/load and transfer systems during commercial treatment.
- For corn seed, respiratory protection for baggers/sewers/stackers and cleaners.
- For wheat, barley, oat, rye, and triticale seed, personal protective equipment for cleaners and when planting commercially treated or imported seed.
- Closed cab tractor for planting treated seed.

**Environment**

To protect the environment, the following risk-reduction measures are required for continued registration of tebuconazole in Canada:

- Precautionary label statements to inform users of the potential toxicity of tebuconazole to non-target terrestrial plants and aquatic organisms.
- Precautionary label statements on all outdoor uses of tebuconazole, except seed treatments, regarding potential for runoff to adjacent aquatic habitats for sites with characteristics that may be conducive to runoff and when heavy rain is forecast.
- Standard label statements to protect the environment from potential discharge or runoff of tebuconazole from wood preservation facilities.
- Spray buffer zones for the protection of non-target terrestrial and aquatic habitats (1–15 metres). See the Spray Buffer Zone Label Statements section for the complete spray buffer zone table and drift mitigation instructions (Appendix IX).

## Implementation of the re-evaluation decision

Regulatory Directive DIR2018-01, *Policy on Cancellations and Amendments Following Re-evaluation and Special Review* provides information and general timelines regarding the implementation of post-market decisions, (for example, up to 24-month timeline for label amendments and up to 36-month phase-out timeline for cancelled registrations), and *Information Note: update on implementation of post-market decisions* provides additional information on phase-out measures for post-market decisions that include cancellations. The post-market decision considers potential health and environmental risks regarding the use of the pest control product, and its value, when establishing the implementation timelines.

The health and environmental considerations for the implementation timeline for this final decision are outlined below.

## Health considerations

Risks to human health from exposure to a pesticide are estimated by comparing potential exposures with the most relevant endpoint from toxicology studies, with standard protection factors incorporated to further protect human health, including the most sensitive population. These factors provide an inherent level of protection from exposures that could result in adverse effects to human health. Furthermore, Health Canada applies additional protection factors if warranted by the hazard profile of the pesticide or by the quality and completeness of the underlying data. When potential risks of concern are identified in the human health exposure scenarios, it does not necessarily mean that exposure will result in adverse effects, but mitigation measures to reduce potential risks would be required.

Potential and relative health risks are considered acceptable during the general 2-year implementation period unless there is evidence from incident reports or other sources of real-world post-market surveillance data suggesting that there are adverse health effects occurring as

a result of the use of the product(s) according to the currently approved label/use conditions. Taking into consideration these factors, the general 2-year implementation timeline for label amendments for tebuconazole is considered appropriate from a human health perspective. Therefore, the required label updates will be implemented within 24 months following the publication of the re-evaluation decision document.

Similarly, Health Canada has determined that the identified health risks from the use of tebuconazole on turf is not expected to be serious or imminent over a three-year phase-out period for cancelled products registered for use on turf.

## Environmental considerations

Registered labels for products containing tebuconazole currently include all the precautionary statements that were determined to be required by the environmental assessment for the re-evaluation. Buffer zones were recalculated based on revisions to the registered use pattern, and, as certain uses/applications rates were reduced or cancelled, the revised spray buffer zones are smaller or within the same range as buffer zones currently on product labels. Therefore, environmental precautionary statements and mitigative measures on product labels will be protective during the general 2-year implementation timeline for label amendments for pest control products containing tebuconazole, and environmental risks are considered to be acceptable.

Similarly, Health Canada has determined that the identified environmental risks from the use of tebuconazole on turf is not expected to be serious or imminent over a three-year phase-out period for cancelled products registered for use on turf.

Taking into consideration these factors, the general 2-year implementation timeline for label amendments for pest control products containing tebuconazole is considered appropriate from a human health and environmental perspective.

## Amendment and cancellation timeframes

Based on the above considerations, the required amendments (mitigation measures and label updates) for pest control products containing tebuconazole must be implemented within 24-months from the date of this decision document. In addition, certain registrations of pest control products containing tebuconazole are cancelled as of the date of this decision document with a 36-month phase-out period.

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

## 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.

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

To comply with this decision, products registered for turf uses are cancelled (as of the date of publication) pursuant to paragraph 21(2)(b) of the *Pest Control Products Act*. Where risks of concern are not considered imminent and serious, existing stocks of the cancelled products are phased out in Canada following a general timeline of three (3) years from the publication date of the decision and following a sequential timeline provided for each level of the supply chain (in other words, at registrant, retail/distribution, and user levels). Health Canada has determined that the identified risks from the use of tebuconazole on turf are not expected to be serious or imminent over the three-year phase-out period.

Therefore, continued possession, handling, storage, and use of existing stock in Canada of these products will be authorized under paragraph 21(5)(a) of the *Pest Control Products Act* during the phase-out period as per the schedule below:

- Authorized for sale (of existing stocks in Canada) by registrant one (1) year from the date of decision, followed by;
- Authorized for sale by retailer/distributor (if applicable) one (1) year from the last date of sale by registrant, followed by;
- Authorized for use one (1) year from the last date of sale by retailer/distributor.

During the phase-out period, importing or manufacturing of products containing tebuconazole for turf use in Canada is prohibited. In addition, registrants are required to continue to comply with sales and incident reporting obligations during the phase-out period.

## Other information

Any person may file a notice of objection[3] regarding this decision on tebuconazole 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 and pest management Section of the Canada.ca website (Public Engagement Portal - Public Engagement Forms - Notice of Objection) or contact PMRA's Pest Management Information Service.

The relevant confidential test data on which the decision is based (as referenced in PRVD2021-08 and in Appendix X of this document) are available for public inspection, upon application, in PMRA's Reading Room. For more information, please contact Health Canada's Pest Management Information Service.

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

# Evaluation approach

## Legislative framework

The Minister of Health's primary objective under the *Pest Control Products Act* (the Act) subsection 4(1) is to prevent unacceptable risks to individuals and the environment from the use of pest control products.

As noted in the preamble of the Act, it is in the national interest that the attainment of the objectives of the federal regulatory system continue to be pursued through a scientifically-based national registration system that addresses risks to human health, the environment and value both before and after registration and applies to the regulation of pest control products throughout Canada; and that pest control products with acceptable risk and value be registered for use only if it is shown that their use would be efficacious and if conditions of registration can be established to prevent unacceptable risks to human health and the environment.

For the purposes of the Act, the health or environmental risks of a pest control product are acceptable if there is reasonable certainty that no harm to human health, future generations or the environment will result from exposure to or use of the product, taking into account its conditions of registration as per subsection 2(2) of the *Pest Control Products Act*.

Risk for the human health and environment, and value are defined under the Act subsection 2(1) as follows:

> **Health risk**, in respect of a pest control product, means the possibility of harm to human health resulting from exposure to or use of the product, taking into account its conditions or proposed conditions of registration.
>
> **Environmental risk**, in respect of a pest control product, means the possibility of harm to the environment, including its biological diversity, resulting from exposure to or use of the product, taking into account its conditions or proposed conditions of registration.
>
> **Value**, in respect of a pest control product, means the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (a) efficacy; (b) effect on host organisms in connection with which it is intended to be used; and (c) health, safety and environmental benefits and social and economic impact.

When evaluating the health and environmental risks of a pesticide and determining whether those risks are acceptable, subsection 19(2) of the *Pest Control Products Act* requires Health Canada to apply a scientifically-based approach. The science-based approach to assessing pesticides considers both the toxicity and the level of exposure of a pesticide in order to fully characterize risk.

## Risk and value assessment framework

Health Canada uses a comprehensive body of modern scientific methods and evidence to determine the nature as well as the magnitude of potential risks posed by pesticides. This approach allows for the protection of human health and the environment through the application of appropriate and effective risk management strategies, consistent with the purpose described in the preambular text set out above.

Health Canada's approach to risk and value assessment is outlined in A Framework for Risk Assessment and Risk Management of Pest Control Products.[4] A high-level overview is provided below.

i) Assessing Potential Health Risks

With respect to the evaluation and management of potential health risks, Health Canada's risk assessments follow a structured, predictable process that is consistent with international approaches and the Health Canada Decision-Making Framework for Identifying, Assessing, and Managing Health Risks.[5]

The evaluation of potential health risks begins with a consideration of the toxicological profile of a pesticide to establish reference doses at which no adverse effect is expected and against which the expected exposure is assessed. This includes, where appropriate, the use of uncertainty (protection) factors to provide additional protection that accounts for the variation in sensitivity among members of human population and the uncertainty in extrapolating animal test data to humans. Under certain conditions, the *Pest Control Products Act* requires the use of another factor to provide additional protection to pregnant women, infants, and children. Other uncertainty factors, such as a database deficiency factor, are considered in specific cases. More details related to the application of the uncertainty factors are provided in SPN2008-01.[6]

Assessments estimate potential health risks to defined populations[7] under specific exposure conditions. They are conducted in the context of the registered conditions of use, such as the use of a pesticide on a particular field crop using specified application rates, methods and equipment. Potential exposure scenarios consider exposures during and after application of the pesticide in occupational or residential settings, food and drinking water exposure, or exposure when interacting with treated pets.

---

4 PMRA Guidance Document, A Framework for Risk Assessment and Risk Management of Pest Control Products

5 Health Canada Decision-Making Framework for Identifying, Assessing, and Managing Health Risks - August 1, 2000

6 Science Policy Note: The Application of Uncertainty Factors and the Pest Control Products Act Factor in the Human Health Risk Assessment of Pesticides

7 Consideration of Sex and Gender in Pesticide Risk Assessment

Also considered are the anticipated durations (short-, intermediate- or long-term) and routes of exposure (oral, inhalation, or skin contact). In addition, an assessment of health risks must consider available information on aggregate exposure and cumulative effects.

ii) Assessing risks to the environment

With respect to the evaluation of environmental risks, Health Canada's environmental risk assessments follow a structured, tiered approach to determine the likelihood that exposure to a pesticide can cause adverse effects on individual organisms, populations, or ecological systems. This involves screening assessments starting with simple methods, conservative exposure scenarios and sensitive toxicity effects metrics, then moving on, where required, to more refined assessments that can include exposure modelling, monitoring data, results from field or mesocosm studies, and probabilistic risk assessment methods.

The environmental assessment considers both the exposure (environmental fate, chemistry, and behaviour, along with the application rates and methods) and hazard (toxic effects on organisms) of a pesticide. The exposure assessment examines the movement of the pesticide in soil, water, sediments and air, as well as the potential for uptake by plants or animals and transfer through the food web. The possibility for the pesticide to move into sensitive environmental compartments such as groundwater or lakes and rivers, as well as the potential for atmospheric transport, is also examined. The hazard assessment examines effects on a large number of internationally recognized indicator species of plants and animals (terrestrial organisms include invertebrates such as bees, beneficial arthropods, and earthworms, birds, mammals, plants; aquatic organisms include invertebrates, amphibians, fish, plants and algae), and includes considering effects on biodiversity and the food chain. Acute and chronic effects endpoints are derived from laboratory and field studies that characterize the toxic response and the dose–effect relationship of the pesticide.

The characterization of environmental risk requires the integration of information on environmental exposure and effects to identify which, if any, organisms or environmental compartments may be at risk, as well as any uncertainties in characterizing the risk.

iii) Value assessment

Value assessments consist of two components: an assessment of the performance of a pest control product and its benefits.

During re-evaluation, value is examined under current conditions and in light of alternative pest control methods (both chemical and nonchemical) that may have been developed since the pesticide was first registered. An assessment of the benefits associated with the pesticide may also be conducted to demonstrate its value in the current context, and to identify potential alternatives.

## Risk management

The outcomes of the assessments of risks to human health and the environment, and the assessment of value, form the basis for identifying risk management strategies. These include appropriate risk mitigation measures and are a key part of decision-making on whether health and environmental risks are acceptable. The development of risk management strategies take place within the context of the pesticide's conditions of registration. Conditions can relate to, among other things, the specific use (for example, application rates, timing, frequency and method of application), personal protective equipment, preharvest intervals, restricted-entry intervals, buffer zones, spray drift and runoff mitigation measures, handling, manufacture, storage or distribution of a pesticide. If feasible conditions of use that have acceptable risk and value cannot be identified, the pesticide use will not be eligible for registration.

The selected risk management strategy is then implemented as part of the re-evaluation decision. The pesticide registration conditions include legally-binding use directions on the label. Any use in contravention of the label or other specified conditions is illegal under the *Pest Control Products Act*. Implementation of post-market decisions follow the framework articulated in the *Policy on Cancellations and Amendments Following Re-evaluation and Special Review*.[8]

Following a decision, continuous oversight activities such as post-market review, monitoring and surveillance, including incident reporting, all play an essential role to help ensure the continued acceptability of risks and value of registered pesticides.

[8] PMRA Regulatory Directive DIR2018-01 *Policy on Cancellations and Amendments Following Re-evaluation and Special Review*

# Science evaluation update

## 1.0 Introduction

Based on the comments and additional information received during consultation, Health Canada revised the human health, environmental health and value assessments.

## 2.0 Revised health risk assessment

### 2.1 Toxicology summary

A detailed review of the toxicology database for tebuconazole was summarized in the proposed re-evaluation decision for tebuconazole and associated end-use products (PRVD2021-08). Comments received during the consultation period for PRVD2021-08 specific to the toxicology assessment pertained to the assessment of the 90-day oral toxicity study in rats, the developmental toxicity studies in mice and rabbits, the two-generation reproductive toxicity study in rats, the one-year studies in dogs, the combined chronic toxicity and carcinogenicity study in rats, the oncogenicity studies in mice, and the acute neurotoxicity study in rats. Additional information including new historical control data and scientific rationales pertaining to the offspring point of departure selected for the rat developmental neurotoxicity study were also provided by the registrant. This point of departure was the basis for establishing the acute dietary reference dose as well as the incidental oral and the dermal and inhalation reference values in PRVD2021-08. No new toxicology studies were submitted during the consultation period.

In response to the comments received, Health Canada re-visited the findings from the 90-day oral toxicity study in rats, the developmental toxicity studies in mice and rabbits, the two-generation reproductive toxicity study in rats, the oncogenicity studies in mice, the acute neurotoxicity study in rats and the developmental neurotoxicity study in rats. Health Canada also conducted an updated search of the published scientific literature for tebuconazole. The scope of the literature review was narrowed to consider only studies that may inform the developmental toxicity or developmental neurotoxicity potential of tebuconazole or identify unique health effects or increased hazard associated with exposure to tebuconazole. Based on the comments received and the additional information retrieved, the toxicology reference values for tebuconazole outlined in PRVD2021-08 were updated. Detailed responses to comments are presented in Appendix III. The updated toxicology assessment and toxicology reference values are also presented in Appendix IV.

## 2.2 Dietary exposure and risk assessment

In the PRVD2021-08, dietary exposure and risks to human health that were estimated using the proposed toxicology reference values (TRVs) were shown to be acceptable with a proposed rate reduction to minimize exposure to tebuconazole from drinking water, in other words, for turf uses, a reduction of the maximum total seasonal rate from 3.10 kg a.i./ha/year to 1.44 kg a.i./ha/year. In addition, for consistency among product labels, a rotational plant back interval of 120 days was proposed for food and feed crops, unless the current label directions were more restrictive.

There were no comments received regarding the dietary food exposure assessment in the PRVD2021-08; however, comments related to the modelling of drinking water estimated environmental concentrations (EECs) were received from the technical registrant, Bayer CropScience Inc. (See Appendix III for the comment and PMRA's response). Due to revisions of the toxicology reference values and refinement of the EECs following the proposed re-evaluation decision (PRVD2021-08), the dietary risk assessment used to support PRVD2021-08 was updated. Additionally, new monitoring data from the United States Department of Agriculture's Pesticide Data Program (USDA PDP), which became available after the 2021 dietary risk assessment was completed, along with updated American percent crop treated (PCT) data, were used to refine the present assessment. This assessment utilized the PMRA's updated weighted percent crop treated (WPCT) calculator. Furthermore, the domestic PCT data for crops not registered in Canada was adjusted from 100% to 0%.

As with the previous dietary risk assessment, revised acute and chronic dietary exposure and risk assessments were conducted using the Dietary Exposure Evaluation Model - Food Commodity Intake Database™ (DEEM-FCID™; Version 4.02 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. When all currently registered uses were included in the revised dietary assessment using the revised and lower toxicology reference values, potential acute and chronic risks were not shown to be acceptable; drinking water and imported grapes were the major contributors to the dietary exposures. To refine the dietary risk assessment, the PMRA requested a list of priority crop uses from the registrants, and cereal crops were identified as the highest priorities. For exposures from food alone, when residues on grape commodities were set at the general maximum residue limit of 0.1 ppm, risks were found to be acceptable (in other words, 60% of the acute reference dose and 6% of the acceptable daily intake). For the exposure from drinking water, risks resulted from turf uses were not shown to be acceptable when used according to the current conditions of registration, or when additional mitigation is considered. Drinking water EECs were refined to lower values using a lower total rate of 136 g a.i./ha per year, which does not produce unacceptable risk to human health. Dietary exposure and risks (from food and drinking water) were found to be acceptable for the most exposed subpopulation (in other words, 94% of the acute reference dose and 22% of the acceptable daily intake for females 13–49). Therefore, for the purposes of risk mitigation, to reduce acute food dietary exposure, the import maximum residue limit of 5 ppm on grape commodities is revoked. After revocation, residues on/in grape commodities will be regulated under subsection B.15.002(1) of the Food and Drug Regulations, which requires that residues not exceed 0.1 ppm.

To reduce exposure from drinking water to an acceptable level, all turf uses are cancelled, and the yearly total rate for the remaining uses is limited to 136 g a.i./ha. Label changes resulting from the dietary assessment are included in Appendix IX of this document.

**Maximum residue limits**

Currently, Canadian maximum residue limits for tebuconazole are established for 97 food commodities, ranging from 0.03 to 10 ppm. PRVD2021-08 proposed that the residue definition for animal commodities be updated to "tebuconazole, including the metabolite hydroxy-tebuconazole and their conjugates (expressed as parent equivalents)", according to current standards. There were no comments received on this proposal during the consultation period; therefore, this revision is final as part of the re-evaluation decision. The present risk assessment of tebuconazole indicated that dietary risks from tebuconazole food exposure are of concern. In the refined dietary risk assessment for the re-evaluation decision, to reduce dietary food exposure to an acceptable level, the import maximum residue limit of 5 ppm for grape commodities will be revoked; as such, residues on grape commodities will be covered by the general maximum residue limit of 0.1 ppm. A proposed maximum residue limit document will be published to inform the public of this decision.

## 2.3 Occupational and non-occupational exposure and risk assessment

In PRVD2021-08, risks were shown to be acceptable for all uses with proposed mitigation measures such as increased personal protective equipment and increased restricted-entry intervals. As a result of the information received during the consultation period, the toxicology reference values were updated resulting in revisions to the occupational and non-occupational (for example, residential) risk assessment of tebuconazole for all uses. Due to this, many of the outcomes of the occupational risk assessment and proposed mitigation in PRVD2021-08 have changed.

As discussed above in Section 2.2, to reduce exposure from drinking water, all turf uses are cancelled; however, all other registered uses are acceptable for continued registration provided that the mitigation measures outlined in Appendix IX are followed.

Health Canada responses to specific comments are presented in Appendix III. Details of the revised occupational and non-occupational risk assessments are presented in Appendix VI.

## 2.4 Aggregate exposure and risk assessment

The aggregate exposure and risk assessment was updated to include those uses and scenarios for which route-specific risks were shown to be acceptable. As all turf uses are cancelled to reduce exposure from drinking water, an aggregate assessment for this scenario was not required. Non-occupational postapplication dermal exposure from the use of tebuconazole as a heavy-duty wood preservative was aggregated with dietary exposure from food and drinking water.

Aggregate risks were shown to be acceptable for tebuconazole used as a heavy-duty wood preservative. Details of the revised aggregate risk assessment is presented in Appendix VII.

### 2.5 Cumulative assessment

The findings related to the cumulative assessment for tebuconazole were previously summarized in PRVD2021-08. No comments specific to the cumulative assessment were received. There were no changes to the cumulative assessment.

### 2.6 Health incident reports

Since the publication of PRVD2021-08 (in other words, from 13 November 2020 to 2 April 2024), 15 human and 5 domestic animal incidents involving tebuconazole were submitted to the PMRA. All incidents involved tebuconazole along with other active ingredients.

Overall, the patterns of exposure (in other words, accidental spray or splash onto the skin and/or eyes during the use of a commercial class product) and the mainly minor adverse effects (in other words, minor skin or eye irritation) following exposure to tebuconazole and other active ingredients, as noted in these incidents, were similar to the previous review of human incidents conducted for PRVD2021-08. Domestic animals were exposed by contact with pesticide residue via drift from an application site, or by accidental ingestion of treated plant material similar to what was noted in PRVD2021-08.

The adverse effect and exposure trends noted in the current review of tebuconazole incidents is similar to that outlined in PRVD2021-08. No additional health concerns were identified following this incident report review. The labels of tebuconazole products contain appropriate precautionary statements to minimize exposure following the use of the products.

## 3.0 Revised environmental risk assessment

No new information was submitted during the consultation period which resulted in a refinement of the environmental risk assessment. The responses to the comments submitted by the registrant are provided in Appendix III. However, the environmental risk assessment and any related mitigation measures were revised based on changes to the use pattern resulting from the human health (drinking water) risk assessment outcomes. The following mitigation measures are required as follows:

- The maximum yearly total application rate has been limited to 136 g a.i./ha/year for all crops.
- Application rates for asparagus, short rotation intensive culture poplar and willow have been reduced to 1 application at 126 g a.i./ha.
- Soybean is reduced to 1 application at 136 g a.i./ha or 2 applications at 65 g a.i./ha (10-day re-treatment interval).
- All turf uses are cancelled [Mirage Stressgard (Registration No. 32405), Dedicate Stressgard (Registration No. 33236)].

### 3.1 Environmental risk characterization

#### 3.1.1 Risks to terrestrial organisms

Risks to beneficial foliar-dwelling arthropods and birds were shown in PRVD2021-08 to be unacceptable only when considering use on turf which was the highest application rate for tebuconazole. As turf uses are cancelled, risks to beneficial arthropods and birds are now acceptable and additional precautionary label statements are not required.

#### 3.1.2 Risks to aquatic organisms and terrestrial plants

The risk assessments for aquatic organisms and terrestrial plants were not revised. However, based on the reduced application rates, buffer zones for aquatic and terrestrial habitats were re-calculated and are lower than proposed in PRVD2021-08. See Appendix IX for the revised buffer zone tables and label statements.

### 3.2 Environmental incident reports

From November 2020 to April 2024, no additional environmental incident reports involving tebuconazole had been submitted to the PMRA.

## 4.0 Value assessment

Comments received in response to PRVD2021-08 did not result in a change to the value assessment for heavy-duty wood preservative uses. Therefore, the value assessment for heavy-duty wood preservative uses are consistent with PRVD2021-08.

However, the value assessment of agricultural uses were revised based on changes to the use pattern resulting from the outcomes of the human health risk assessment. Tebuconazole is used in agriculture as a systemic fungicide registered for seed treatment for control of seed and soil borne diseases of cereal grains and for foliar use on cereals, soybeans, asparagus, short rotation intensive culture poplar and willow, and turf for control of wide range of foliar diseases. Due to its protective, curative, and eradicative properties, tebuconazole is of value to agricultural producers as it will control several fungal diseases of economic importance on crops particularly suppression of mycotoxin (deoxynivalenol) producing Fusarium head blight pathogen in cereals.

From a value perspective, a reduction of the yearly total application rate for all crops for mitigation purposes is expected to have minimal impact on users, since this active ingredient would still be registered for use to manage all listed diseases on different crops, albeit at a lower number of applications. Cancellation of all turf uses will also expected to have minimum impact since alternative fungicides from different mode of action groups are registered for all turf diseases.

During the consultation of PRVD 2021-08, Health Canada received comments relating to the value of tebuconazole. The comments are summarized in Appendix III along with the response by Health Canada.

## 5.0 Conclusion of science evaluation

### Health

It has been determined that the human health risks associated with the use of tebuconazole and associated end-use products are shown to be acceptable with the implementation of additional mitigation measures. Based on the comments provided and additional information retrieved after PRVD2021-08 was published, the toxicology reference values and drinking water EECs for tebuconazole were updated and these changes resulted in revisions to the dietary and occupational/non-occupational risk assessments. To reduce tebuconazole exposures from drinking water to an acceptable level, all turf uses are cancelled, and the yearly total rate for the remaining uses is limited to 136 g a.i./ha. To reduce tebuconazole exposure from food to an acceptable level the import maximum residue limit of 5 ppm for grape commodities is revoked and residues on grapes are set at general maximum residue limit of 0.1 ppm. The revised occupational and non-occupational risk assessments were shown to be acceptable with mitigation measures.

### Environment

It has been determined that the environmental risks associated with the use of tebuconazole and associated end-use products are shown to be acceptable with the implementation of additional mitigation measures. Tebuconazole use pattern has been reduced based on conclusions from the human health risk assessment and turf use has been cancelled. Precautionary label statements to protect beneficial arthropods and birds are not required. Buffer zones and label statements are required to protect aquatic organisms and terrestrial plants.

### Value

It has been determined that tebuconazole and its end-use products have acceptable value. The reduction of the yearly total application rate and the cancellation of turf uses for tebuconazole is expected to have a minimum impact on agricultural users. The value assessment of tebuconazole as a heavy-duty wood preservative is consistent with PRVD2021-08.

# List of abbreviations

| | |
|---|---|
| % | percent |
| ↑ | increased |
| ↓ | decreased |
| µg | microgram |
| a.i. | active ingredient |
| abs | absolute |
| ADI | acceptable daily intake |
| ALP | alkaline phosphatase |
| ALT | alanine aminotransferase |
| AOP | adverse outcome pathway |
| ARfD | acute reference dose |
| ASAE | American Society of Agricultural Engineers |
| AST | aspartate aminotransferase |
| ATPD | area treated per day |
| BMD | benchmark dose |
| BMDL | benchmark dose lower confidence limit |
| bw | body weight |
| bwg | body weight gain |
| CAF | Composite Assessment Factor |
| CFDA | Carboxyfluorescein Diacetate, Acetoxymethyl Ester |
| CNS | central nervous system |
| CRABP | cellular retinoid binding protein |
| CYP | cytochrome-P |
| cm | centimeter |
| $cm^2$ | centimeters squared |
| CR | chemical resistant |
| DA | dermal absorption |
| DEEM | Dietary Exposure Evaluation Model |
| DFR | Dislodgeable Foliar Residue |
| DNT | developmental neurotoxicity |
| DNT IVB | developmental neurotoxicity in vitro battery |
| $DT_{50}$ | dissipation time 50% (time required to observe a 50% decline in concentration) |
| $EC_{50}$ | effective concentration to 50% of the population |
| EEC | estimated environmental concentration |
| ET | exposure time |
| F1 | first generation |
| fc | food consumption |
| g | gram |
| GMRL | general maximum residue limit |
| ha | hectare(s) |
| HH AB/MB | handheld airblast/mistblower |
| HOX | homeobox |
| hr | hour(s) |
| k | kinetic rate constant |
| kg | kilogram |
| L | litre(s) |

| | |
|---|---|
| LOAEL | lowest observed adverse effect level |
| LOEL | lowest observed effect level |
| M/L/A | mixer/loader/applicator |
| max | maximum |
| mg | milligram(s) |
| mmHg | millimeters of mercury |
| MCH | mean corpuscular hemoglobin |
| MCHC | mean corpuscular hemoglobin concentration |
| MOE | margin of exposure |
| MPHG | mechanically pressurized handgun |
| MPHW | manually pressurized handwand |
| MRL | maximum residue limit |
| N/A | not applicable |
| NAFTA | North American Free Trade Agreement |
| N-DEM | n-demethylase |
| NOAEL | no observed adverse effect level |
| NHANES | National Health and Nutrition Examination Survey |
| O-DEM | o-demethylase |
| OECD | Organisation for Economic Co-operation and Development |
| PA | postapplication |
| PCT | percent crop treated |
| PMRA | Pest Management Regulatory Agency |
| PND | postnatal day |
| PPE | personal protective equipment |
| PRVD | Proposed Re-evaluation Decision |
| ppm | parts per million |
| PWC | Pesticide in Water Calculator |
| RA | Retinoic acid |
| REI | restricted-entry interval |
| ROS | reactive oxygen species |
| RVD | Re-evaluation Decision Document |
| SA | surface area |
| SOP | standard operating procedures |
| SRIC | short rotation intensive culture |
| TC | transfer co-efficient |
| TEU | tebuconazole |
| TG | triglyceride |
| TO | treatment operators |
| TRD | technical recommendations document |
| TRV | toxicology reference values |
| TTR | turf transferable residue |
| USDA PDP | United States Department Of Agriculture’s Pesticide Data Program |
| USEPA | United States Environmental Protection Agency |
| WH | wood handlers |
| WoE | weight of evidence |
| WPCT | weighted percent crop treated |
| wt | weight |
| WWEIA | What We Eat In America |

# Appendix I Registered products containing Tebuconazole in Canada[1]

## Table 1 Products containing tebuconazole requiring label amendments

| Registration number | Marketing class | Registrant | Product name | Formulation type | Active ingredient (%, g/L) |
|---|---|---|---|---|---|
| 25763 | Technical Grade Active Ingredient | Bayer CropScience Inc. | Folicur Technical Fungicide | Solid | TEU: 97% |
| 29409 | Technical Grade Active Ingredient | LANXESS Corporation | Preventol A8 Technical Fungicide | Solid | TEU: 95.0% |
| 35258 | Technical Grade Active Ingredient | LANXESS Corporation | Preventol A8 II Technical Fungicide | Solid | TEU: 98% |
| 33447 | Technical Grade Active Ingredient | ADAMA Agricultural Solutions Canada Ltd. | ADAMA Tebuconazole Technical | Solid | TEU: 98.3% |
| 33718 | Technical Grade Active Ingredient | Albaugh LLC | Tebuconazole TG | Solid | TEU: 98% |
| 34371 | Technical Grade Active Ingredient | Albaugh LLC | Tebuconazole Technical | Solid | TEU: 97.9% |
| 33758 | Technical Grade Active Ingredient | Farmer's Business Network Canada, Inc. | FBN Tebuconazole Technical | Solid | TEU: 98.9% |
| 33894 | Technical Grade Active Ingredient | Sharda Cropchem Limited | Tebuconazole Technical Fungicide | Solid | TEU: 98.6% |
| 33994 | Technical Grade Active Ingredient | NewAgco Inc | NewAgco Tebuconazole Technical | Solid | TEU: 97% |
| 34478 | Technical Grade Active Ingredient | Nufarm Agriculture Inc. | Nufarm Tebuconazole Technical | Solid | TEU: 97.5% |
| 34707 | Technical Grade Active Ingredient | Jiangsu Good Harvest-Weien Agrochemical Co., Ltd. | TebuStar Tebuconazole Technical 98% | Solid | TEU: 98.6% |
| 35011 | Manufacturing Concentrate | Bayer CropScience Inc. | Raxil Pro Shield MUP | Suspension | TEU: 3.0 g/L; IMI: 92 g/L; MTA: 6.2 g/L; PRB: 15.3 g/L |
| 35013 | Manufacturing Concentrate | Bayer CropScience Inc. | Raxil Pro MUP | Suspension | TEU: 3.0 g/L; MTA: 6.2 g/L; PRB: 15.4 g/L |

| Registration number | Marketing class | Registrant | Product name | Formulation type | Active ingredient (%, g/L) |
|---|---|---|---|---|---|
| **Plant protection products:** | | | | | |
| 25762 | Commercial | Bayer CropScience Inc. | Raxil 312 FS Seed Treatment Fungicide | Suspension | TEU: 312 g/L |
| 25940 | Commercial | Bayer CropScience Inc. | Folicur 432 F Foliar Fungicide | Suspension | TEU: 432 g/L |
| 26137 | Commercial | Bayer CropScience Inc. | Raxil SP Soluble Pack | Wettable Powder | TEU: 9.55% |
| 26138 | Commercial | Bayer CropScience Inc. | Raxil 250 FL Flowable Fungicide | Suspension | TEU: 6 g/L |
| 27692 | Commercial | Bayer CropScience Inc. | Raxil MD Fungicide | Suspension | TEU: 5.0 g/L; MTA: 6.6 g/L |
| 29819 | Commercial | Bayer CropScience Inc. | Prosaro 421 SC Foliar Fungicide | Suspension | TEU: 210.5 g/L; PRB: 210.5 g/L |
| 29820 | Commercial | Bayer CropScience Inc. | Folicur 250 EW Fungicide | Suspension | TEU: 250 g/L |
| 29821 | Commercial | Bayer CropScience Inc. | Prosaro 250 EC Fungicide | Emulsifiable Concentrate | TEU: 125 g/L; PRB: 125 g/L |
| 30102 | Commercial | Bayer CropScience Inc. | Raxil Pro | Suspension | TEU: 3.0 g/L; MTA: 6.2 g/L; PRB: 15.4 g/L |
| 30491 | Commercial | Bayer CropScience Inc. | Palliser Foliar Fungicide | Suspension | TEU: 432 g/L |
| 32073 | Commercial | Bayer CropScience Inc. | Deflect Fungicide | Suspension | TEU: 5.0 g/L; MTA: 6.6 g/L |
| 32500 | Commercial | Nufarm Agriculture Inc. | Hornet 432 F Foliar Fungicide | Suspension | TEU: 432 g/L |
| 32824 | Commercial | Bayer CropScience Inc. | Prosaro XTR Fungicide | Emulsifiable Concentrate | TEU: 125 g/L; PRB: 125 g/L |
| 33825 | Commercial | Bayer CropScience Inc. | Tilmor 240 EC Fungicide | Emulsifiable Concentrate | TEU: 160 g/L; PRB: 80 g/L |
| 34093 | Commercial | Bayer CropScience Inc. | Prosaro Pro | Suspension | TEU: 100 g/L; FPY: 100 g/L; PRB: 200 g/L |
| 34245 | Commercial | Bayer CropScience Inc. | Raxil Pro Shield | Suspension | TEU: 3.0 g/L; IMI: 92.0 g/L; MTA: 6.2 g/L; PRB: 15.3 g/L |
| 33453 | Commercial | FMC of Canada Limited | F9651-2 Fungicide | Suspension | TEU: 340 g/L; BIX: 160 g/L |
| 33672 | Commercial | ADAMA Agricultural Solutions Canada Ltd. | Custodia | Suspension | TEU: 200 g/L; AZY: 120 g/L |
| 33673 | Commercial | ADAMA Agricultural Solutions Canada Ltd. | Orius 430 SC | Suspension | TEU: 430 g/L |

| Registration number | Marketing class | Registrant | Product name | Formulation type | Active ingredient (%, g/L) |
|---|---|---|---|---|---|
| 34368 | Commercial | ADAMA Agricultural Solutions Canada Ltd. | Soraduo B | Suspension | TEU: 430 g/L |
| 33719 | Commercial | Albaugh LLC | Toledo 250 EW | Emulsifiable Concentrate | TEU: 250 g/L |
| 34339 | Commercial | Albaugh LLC | Toledo 430 SC Foliar Fungicide | Suspension | TEU: 430 g/L |
| 34349 | Commercial | Albaugh LLC | StarPro | Emulsifiable Concentrate | TEU: 125 g/L; PRB: 125 g/L |
| 34372 | Commercial | Albaugh LLC | TebuStar 432 | Suspension | TEU: 432 g/L |
| 35061 | Commercial | Albaugh LLC | Defence 250 | Emulsifiable Concentrate | TEU: 250 g/L |
| 33779 | Commercial | Farmer's Business Network Canada, Inc. | FBN Tebuconazole 250 Fungicide | Suspension | TEU: 250 g/L |
| 34868 | Commercial | Farmer's Business Network Canada, Inc. | FBN ProTEB 250 EC | Emulsifiable Concentrate | TEU: 125 g/L; PRB: 125 g/L |
| 33887 | Commercial | Advantage Crop Protection Inc | Advantage Tebuconazole 250 | Suspension | TEU: 250 g/L |
| 34975 | Commercial | Advantage Crop Protection Inc | Advantage Prothio + Teb 250 EC | Emulsifiable Concentrate | TEU: 125 g/L; PRB: 125 g/L |
| 33901 | Commercial | Sharda Cropchem Limited | Tebbie | Suspension | TEU: 250 g/L |
| 34038 | Commercial | Sharda Cropchem Limited | Sharda Meteb 11ST Fungicide | Suspension | TEU: 5.00 g/L; MTA: 6.60 g/L |
| 34270 | Commercial | Sharda Cropchem Limited | Lixar Pro Fungicide | Suspension | TEU: 3.0 g/L; MTA: 6.2 g/L; PRB: 15.4 g/L |
| 34357 | Commercial | Sharda Cropchem Limited | Shalimar Fungicide | Emulsifiable Concentrate | TEU: 125 g/L; PRB: 125 g/L |
| 33995 | Commercial | NewAgco Inc | Tornado Fungicide | Emulsifiable Concentrate | TEU: 250 g/L |
| 34693 | Commercial | NewAgco Inc | Fusaro Fungicide | Emulsifiable Concentrate | TEU: 125 g/L; PRB: 125 g/L |
| 34128 | Commercial | Maxunitech North America, Inc. | Maxunitech Prothio + Teb EC | Emulsifiable Concentrate | TEU: 125 g/L; PRB: 125 g/L |
| 34639 | Commercial | Nufarm Agriculture Inc. | Stance Fungicide Seed Treatment | Suspension | TEU: 4.6 g/L; DFZ: 36.3 g/L; MTA: 12.6 g/L |
| 34770 | Commercial | Viking Crop Production Partners Inc. | Viking Tebuconazole Fungicide | Emulsifiable Concentrate | TEU: 250 g/L |
| 34794 | Commercial | Viking Crop Production Partners Inc. | Viking Tromso Fungicide | Emulsifiable Concentrate | TEU: 125 g/L; PRB: 125 g/L |

| Registration number | Marketing class | Registrant | Product name | Formulation type | Active ingredient (%, g/L) |
|---|---|---|---|---|---|
| 34928 | Commercial | Corteva Agriscience Canada Company | Straxan Fungicide Seed Treatment | Suspension | TEU: 4.6 g/L; DFZ: 36.3 g/L; MTA: 12.6 g/L |
| 35154 | Commercial | Loveland Products Canada Inc. | Duplex B | Suspension | TEU: 430 g/L |
| 35285 | Commercial | ADAMA Agricultural Solutions Canada Ltd. | Jury B | Suspension | TEU: 430 g/L |
| 35311 | Commercial | Sipcam Agro USA, Inc. | Cortina Pro | Emulsifiable Concentrate | TEU: 125 g/L; PRB: 125 g/L |
| **Heavy-duty wood preservative products:** | | | | | |
| 27132 | Commercial | Arch Wood Protection Canada Corp | Wolman NB | Emulsifiable Concentrate | TEU: 0.37%; CUR: 9.25% |
| 30003 | Commercial | Arch Wood Protection Canada Corp | Wolman AG CN | Solution | TEU: 5%; QAV: 9.68%; PON: 2.43% |
| 30570 | Commercial | Arch Wood Protection Canada Corp | Wolman μNB | Suspension | TEU: 0.37%; CUV: 9.25% |
| 34048 | Commercial | Arch Wood Protection Canada Corp | Wolman MNB | Suspension | TEU: 1.0%; CUV: 25.0% |
| 30379 | Commercial | Timber Specialties Limited | MTZ | Suspension | TEU: 33.95% |
| 31545 | Commercial | Timber Specialties Limited | FIM-3 | Solution | TEU: 2.4%; QAV: 21.7% |
| 32008 | Commercial | Timber Specialties Limited | MP200A-TS | Suspension | TEU: 1.12%; CUV: 28% |
| 33525 | Commercial | Timber Specialties Limited | NW-CA-B | Suspension | TEU: 0.37%; CUR: 9.25% |
| 31160 | Commercial | Viance LLC | Viance CA-B | Emulsifiable Concentrate | TEU: 0.37%; CUR: 9.25% |
| 32361 | Commercial | Viance LLC | Ecolife - CDN | Solution | TEU: 11.43% |

[1]as of 9 October 2024, excluding discontinued products or products with a submission for discontinuation
AZY – Azoxystrobin; BIX – Bixafen; CUR – Copper present as copper monoethanolamine complexes; CUV - Copper present as basic copper carbonate; DFZ – Difenoconazole; FPY – Fluopyram; IMI – Imidacloprid; MTA – Metalaxyl; PON – Propiconazole; PRB – Prothioconazole; QAV - Didecyldimethylammonium present as carbonate and bicarbonate salts; TEU – Tebuconazole; TFY – Trifloxystrobin.

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

| Registration number | Marketing class | Registrant | Product name | Formulation type | Active Ingredient (%, g/L) |
|---|---|---|---|---|---|
| 32405 | Commercial | 2022 Environmental Science CA Inc. | Mirage Stressgard | Suspension | TEU: 240 g/L |
| 33236 | Commercial | 2022 Environmental Science CA Inc. | Dedicate Stressgard | Suspension | TEU: 190 g/L; TFY: 48 g/L |

[1]as of 9 October 2024, excluding discontinued products or products with a submission for discontinuation
TEU – Tebuconazole; TFY – Trifloxystrobin.

# Appendix II List of Commenters to PRVD2021-08

List of commenters' affiliations for comments submitted in response to PRVD2021-08

| Category | Commenter |
|---|---|
| Registrant | Bayer CropScience Inc. |
| General Public | Public |

# Appendix III Comments and responses

Health Canada received 33 written comments during the public consultation for tebuconazole proposed re-evaluation decision. Commenters' affiliations are listed in Appendix II. 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 Comments related to the health risk assessment

In response to the consultation for PRVD2021-08, comments related to the human health assessment were received from Bayer CropScience Inc. and the public.

### 1.1 Comments related to toxicology

#### 1.1.1 Comments related to the assessment of developmental neurotoxicity

**Comment:** The registrant disagreed with the offspring no observed adverse effect level (NOAEL) at the low-dose level of 8.8 mg/kg bw/day established in the rat developmental neurotoxicity (DNT) study. The offspring NOAEL in this study was based on the decrease in offspring pre-weaning body weight and decreased auditory startle response in both sexes on postnatal day (PND) 23, as well as an equivocal decrease in brain weight in males observed at the lowest observed adverse effect level (LOAEL) of 22 mg/kg bw/day. The registrant stated that the effects on offspring body and brain weight noted at the mid-dose level of 22 mg/kg bw/day should not be considered adverse given that the magnitude of change at this dose level was less than the coefficient of variation for concurrent controls. Additionally, the new historical control data not previously submitted to Health Canada showed that offspring body weight and brain weight values were comparable to those from historical controls. The registrant further contended that the differences in auditory startle response should not be considered as compound-related effects based on the inconsistency across gender and age tested.

**Health Canada response:**

The available weight of evidence suggests that tebuconazole may be a developmental neurotoxicant. As outlined in PRVD2021-08, neurobehavioral alterations were reported in a published study that examined the effect of tebuconazole on neurological function in adult rats following perinatal gavage exposure (gestation day 14 to PND 6) (PMRA# 2873583). Additionally, decreased auditory startle response, increased motor activity[9] as well as decreased brain weight and altered brain morphometrics were noted in the available guideline dietary DNT study. The DNT potential of tebuconazole is also supported by its biological activity in several assays from the in vitro DNT test battery (in other words, DNT in vitro battery (IVB)) (PMRA# 3594113, PMRA# 3594116, PMRA# 3594115, PMRA# 3594118). Consisting of 17 complementary assays designed to detect changes in important neurodevelopmental processes, the DNT IVB is based on the assumption that changes in these processes in vitro may result in potential changes in vivo (PMRA# 3599976). Data for the DNT IVB are available through the USEPA's ToxCast pipeline and are also reported in various scientific publications. In a 2022

[9] PRVD2021-08 erroneously reported that motor activity was decreased at PND 22 in high dose animals. Motor activity was in fact increased in these animals.

publication (PMRA# 3594105), it was noted that tebuconazole is cytotoxic to neurons at concentrations that demonstrate little or no bioactivity in other cell types and/or ToxCast assay platforms. Behavioral testing in zebrafish is being explored as an alternative species model for the assessment of DNT. Data from zebrafish behavioral assays are currently available for tebuconazole in the National Toxicology Program (NTP)'s Developmental NeuroToxicity Data Integration and Visualization Enabling Resource (DNT-DIVER). Based on the presented data, tebuconazole was active in several zebrafish behavioral assays. Health Canada recognizes the current limitations of the DNT IVB and of other new approach methodologies, including zebrafish models, to assess the DNT potential of chemicals. However, in the context of the available in vivo data, integration of the available in vitro information supports the overall weight of evidence that tebuconazole has the potential to interfere with normal neurodevelopment.

In the rat dietary DNT study, reductions in pre-weaning offspring body weight were observed at all dose levels when compared to controls. To refine the interpretation and account for data variability, Health Canada conducted benchmark dose (BMD) analysis of the pre-weaning offspring body weight data at PND 5, 8, 12, 14, 18 and 22. Health Canada generally considers reductions of ≥5% in body weight to be of toxicological relevance in establishing a point of departure for hazard assessment; accordingly, Health Canada selected a benchmark response level of 5% for the analysis. Health Canada's refined analysis of the offspring body weight data yielded a $BMDL_5$ (lower BMD confidence limit for a 5% decrease in body weight) of 9.25 mg/kg bw/day based on the body weight effects noted at PND 8.

Health Canada also re-visited its assessment of the auditory startle response and motor activity data from the rat dietary DNT study using statistical modelling. A linear mixed-effects model was used to analyze motor activity and auditory startle response data, considering both equal and unequal variance (when homogeneity tests were not met) across dose groups. In PRVD2021-08, decreases in auditory startle peak response amplitude noted at PND 23 were considered treatment-related and adverse at the mid- and high-dose levels. Based on the revised analysis conducted, statistically significant decreases in auditory startle peak response amplitude were noted in both sexes on PND 23 at the high-dose level only. Health Canada concurs that the magnitude of change observed at the low- and mid-dose levels at PND 23 and PND 63 was slight; and therefore, the effects were not considered biologically significant. In PRVD2021-08, treatment-related effects on motor activity were reported in high-dose males and when both sexes were combined at PND 22. The re-analysis of the motor activity data did not impact the conclusion reported in PRVD2021-08 that the statistically significant increase in motor activity in high-dose animals on PND 22 is considered treatment-related and adverse.

In PRVD2021-08, Health Canada considered there was equivocal evidence of a treatment-related decrease in brain weight in mid-dose males. The historical control data provided by the registrant during the commenting period were not sufficient to revise the conclusions previously established in the proposed re-evaluation decision. In the rat dietary DNT study, at both assessment time points, the mean brain weight values of concurrent control males were above the provided historical control range. While historical control data can provide valuable information to contextualize concurrent controls, it should not be solely relied upon for interpretation of treatment-related effects. Thus, greater weight is typically given to concurrent controls given the technical challenges related to neuropathological assessments. There is currently no consensus in the broader scientific community regarding what magnitude of change constitutes a

toxicologically relevant effect on brain weight. In high-dose males, statistically significant decreases (≥10%) in absolute brain weights were noted at PND 12 and PND 83. At the mid-dose level, non-statistically significant decreases in absolute brain weight were noted at PND 12 (-3.1%) and PND 83 (-4.7%) in males; however, no apparent dose responses were observed. Therefore, Health Canada maintains that the effect of dosing on brain weight is considered equivocal in mid-dose males.

Based on the information provided and the revised statistical modelling conducted, Health Canada concludes that in the dietary DNT study in rats, the NOAEL protective of effects on the developing neurological system is the mid-dose level of 22 mg/kg bw/day and the revised LOAEL for DNT is 65 mg/kg bw/day, the highest dose tested.

In PRVD2021-08, the *Pest Control Products Act* factor (PCPA factor) was reduced to threefold when the offspring NOAEL of 8.8 mg/kg bw/day, the low-dose level from the rat dietary DNT study, was used to establish the point of departure for risk assessment. A threefold PCPA factor was considered appropriate at the time as, although the effects on brain weight and neurobehavioral parameters were noted in the absence of maternal toxicity at the mid-dose level, concern for these findings was tempered by the fact that they were considered either equivocal or of questionable biological concern given that the auditory startle response may not be fully mature early in the post-weaning period. Furthermore, the effect on auditory startle response was only observed in juveniles and not maintained at the later assessment time point (PND 63) at this dose level.

As a result of the revised statistical modelling conducted by Health Canada, the offspring NOAEL for DNT effects in the rat dietary DNT study has been updated to the mid-dose level of 22 mg/kg bw/day. Consequently, effects on neurobehavioral parameters in offspring are now only identified at the high-dose level in the presence of significant maternal toxicity (mortality, and decreases in body weight, body weight gain and food consumption) in the rat dietary DNT study. At the high-dose level, other evidence of DNT included decreased brain weight and altered brain morphometrics. The DNT effects observed in offspring were considered serious in nature; however, the concern was tempered by the presence of maternal toxicity. On the basis of this information, the PCPA factor was reduced to threefold for scenarios in which the point of departure for the DNT endpoints was used as the basis for risk assessment. The effects on offspring pre-weaning body weight noted in the rat dietary DNT study were present in the absence of maternal toxicity; however, this is not considered a serious effect and consequently the PCPA factor was reduced to onefold for scenarios in which this endpoint was used as a point of departure for risk assessment.

The offspring $BMDL_5$ of 9.25 mg/kg bw/day established on the basis of decreased offspring body weight provides a more conservative point of departure for the rat dietary DNT study than the offspring NOAEL (22 mg/kg bw/day) established for the neurobehavioral effects. However, when the application of the PCPA factor is considered, the offspring $BMDL_5$ does not provide a sufficient margin to the serious neurodevelopmental effects noted at the high-dose level in this study. Therefore, Health Canada concluded that the use of the NOAEL established for the offspring neurodevelopmental effects in the rat dietary DNT study was more appropriate for use in risk assessment and protective of the effects on offspring body weight. Therefore, Health Canada has revised the acute reference dose for the general population (excluding females 13–49 years of age), as well as reference values for the short- and intermediate-term non-dietary

incidental oral; the short-, intermediate-, and long-term dermal; and the general population short- and intermediate-term aggregate exposure scenarios based on the offspring NOAEL of 22 mg/kg bw/day for neurodevelopmental effects from the dietary DNT study. The PCPA factor was reduced to threefold as the serious findings noted in this study were observed in the presence of significant maternal toxicity. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were be applied, resulting in a composite assessment factor or target margin of exposure of 300. The resulting acute reference dose for the general population (excluding females 13–49 years of age) is 0.07 mg/kg bw.

### 1.1.2 Comments related to the assessment of the 90-day oral toxicity study in rats, the two-generation reproductive toxicity study in rats, the one-year oral toxicity studies in dogs, the combined chronic toxicity and carcinogenicity study in rats, the oncogenicity studies in mice, and the acute neurotoxicity study in rats.

**Comment:** The registrant submitted executive summaries of updated data evaluation records prepared by the United States Environmental Protection Agency (USEPA) in the context of their registration review of tebuconazole. The USEPA's registration review was published following the completion of the PMRA's human health hazard assessment. These summaries, which included the 90-day oral toxicity study in rats, the two-generation reproductive toxicity study in rats, the one-year studies in dogs, the combined chronic toxicity and carcinogenicity study in rats, the oncogenicity studies in mice, and the acute neurotoxicity study in rats were revised by the USEPA to reflect the updated conclusions following their re-evaluation of these studies.

**Health Canada's response:**

Health Canada re-visited the findings from the 90-day oral toxicity study in rats, the two-generation reproductive toxicity study in rats, the one-year oral toxicity studies in dogs, and the acute neurotoxicity study in rats in the context of the information provided and concluded that the existing NOAELs were appropriate, and that no revisions to Health Canada's assessment of these studies were necessary. Health Canada's conclusions for these studies are included in Appendix IV.

Health Canada also re-examined the findings from the 2-year combined chronic toxicity/ carcinogenicity study in rats. An inadvertent dose calculation error was corrected. Additionally, the NOAEL from this study was re-evaluated and revised to reflect the absence of adverse findings in male rats up to the highest dose level tested. Furthermore, Health Canada re-visited the findings in the oncogenicity studies in mice. In one study, a slight non-statistically significant increase in the incidence of histiocytic sarcomas was noted in the high-dose group. At the high dose level, the incidence of these tumours was only slightly above the provided historical control range and the relationship to treatment for this finding was considered equivocal. Overall, the concern for this finding was low as these tumors are benign, and the increase was not statistically significant when compared to concurrent controls and only slightly above the provided historical control range. Furthermore, the acceptable daily intake provides a margin of >2800 to the NOAEL for this finding. Therefore, Health Canada concluded that no change to the tebuconazole cancer risk assessment was warranted based on the revised assessment. The revised assessment from these studies can be found in Appendix IV.

### 1.1.3 Comments related to the assessment of the developmental toxicity studies in mice and rabbits.

**Comment:** The registrant submitted executive summaries of data evaluation records prepared by the USEPA in the context of the tebuconazole registration review. The executive summaries for the developmental toxicity studies in mice and rabbits were revised by the USEPA to reflect their updated conclusions following the re-evaluation of these studies.

**Health Canada's response:**

Health Canada re-visited the findings from the gavage developmental toxicity studies in rabbits and concluded that no change to the maternal or developmental NOAEL values previously established in these studies, and described in PRVD2021-08, was warranted. The points of departure selected by Health Canada for these studies are in agreement with those established by the USEPA. Health Canada's conclusions for these studies are included in Appendix IV.

The findings from the gavage developmental toxicity studies in mice were also re-examined. In PRVD2021-08, in consideration of available historical control data for the individual incidences of serious craniofacial malformations (exencephaly, open eye, cleft palate, protruding tongue), Health Canada established a developmental NOAEL of 10 mg/kg bw/day for the 1995 developmental toxicity study in mice (PMRA# 1038120–1038123). The incidences of serious malformations noted in this study were reconsidered in light of published scientific literature suggesting that disruption of the retinoic acid (RA) signalling pathway is responsible for the craniofacial and central nervous system (CNS) malformations commonly observed with compounds of the same chemical class known as the triazoles (PMRA# 3594790, PMRA# 3504788). In rodents, zebrafish, and xenopus, various triazoles induce CNS malformations similar to those induced by excess RA. Craniofacial abnormalities induced by triazole pesticides are postulated to occur through the inhibition of CYP26 activity leading to altered RA metabolism, abnormal homeobox (HOX) gene expression and branchial arch disorganization as described in a recently published adverse outcome pathway (AOP) (PMRA# 3594790, PMRA# 3504788). Data were available in the published literature for various triazole pesticides in support of this AOP, with effects noted on RA levels, gene expression and branchial arch morphology, indicating a broader class effect.

Specifically, enzymatic assays and in silico approaches indicate that the triazole pesticides triadimefon, cyproconazole, and flusilazole act as competitive inhibitors of CYP26 isoenzymes (PMRA# 3594792). Additionally, in surrogate vertebrate models such as zebrafish, exposure to cyproconazole, flusilazole and triadimefon resulted in differential expression of Cyp26a1, Cyp26b1 and hoxb1a genes (PMRA# 3594287). Disruption of RA metabolism by triazole pesticides is further supported by gene expression profiling experiments in rat whole embryo cultures illustrating that the triazoles flusilazole, cyproconazole and triadimefon alter the expression of key genes involved in RA metabolism. In this study, effects on the gene expression signature were similar to those observed following excess RA exposure (PMRA# 3594798). Additionally, propiconazole, triadimefon, and myclobutanil were shown to decrease the level of hepatic RA in mouse studies (PMRA# 3594106).

Although no data were available to illustrate that tebuconazole is an inhibitor of CYP26 isoenzyme activity, tebuconazole was shown to disrupt branchial arch morphology in vitro; albeit at higher concentrations than other triazole pesticides (in other words, triadimefon, fluconazole, triadimenol, cyproconazole and flusilazole) (PMRA# 3594789).

Overall, the weight of evidence (WoE) that considered the available information from the published scientific literature as well as summaries from other regulators/international bodies for tebuconazole and other registered triazole pesticides, supports a role for the disruption of RA metabolism resulting in craniofacial malformations for some compounds of this chemical class. Further, Health Canada determined that examining incidences of individual craniofacial malformations (exencephaly and open eyes) separately, as was done in the original assessment, was no longer considered appropriate. At 10 mg/kg bw/day, the fetal and litter incidence of exencephaly and partial acrania exceeded incidences in the concurrent controls as well as the upper range of the provided historical control data. Craniofacial malformations, including protruding tongue, palatoschisis and eye abnormalities, were also increased above concurrent controls at 10 mg/kg bw/day. Although a dose-response relationship for these malformations was not always present, in the absence of historical control information and in consideration of the available WoE, these findings were attributed to treatment. Moreover, when the combined incidence of craniofacial/CNS malformations (eye, head or skull) in this study were considered, an increased incidence when compared to concurrent controls was noted at 10 mg/kg bw/day, albeit in the absence of a clear dose response. Given the rare nature of these effects and their presence in exceedance of controls, the increased incidences of craniofacial/CNS malformations at 10 mg/kg bw/day were considered treatment related. In summary, based on the available WoE, Health Canada reinterpreted the developmental findings from the 1995 developmental toxicity study in mice (PMRA# 1038120–1038123) and concluded that the increased incidence of craniofacial/CNS malformations occurring at 10 mg/kg bw/day in the absence of maternal toxicity were treatment-related and the developmental NOAEL for this study was revised from 10 mg/kg bw/day to 3 mg/kg bw/day.

This revised developmental NOAEL for the gavage developmental toxicity study in mice is consistent with the point of departure established by the USEPA for this study. Based on the revised conclusion from the mouse developmental toxicity study, there was concern for prenatal toxicity and sensitivity of the young as these malformations were considered serious endpoints and occurred in the absence of maternal toxicity. Therefore, the 10-fold PCPA factor was retained for scenarios in which this endpoint was used to establish the point of departure for assessing risk to women of reproductive age. Consequently, Health Canada has revised the acute reference dose for females 13 to 49 years of age as well as the reference values for the short-, intermediate-, and long-term inhalation risk assessments based on the developmental toxicity NOAEL of 3 mg/kg bw/day from the gavage developmental toxicity study in mice. In addition to the 10-fold PCPA factor, standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied, resulting in a composite assessment factor or target margin of exposure of 1000. The resulting acute reference dose for females 13–49 years of age is 0.003 mg/kg bw.

As noted above, the dietary DNT study was used to establish the reference value for short-, intermediate-, and long-term dermal assessments. A dermal developmental toxicity study in mice was available for tebuconazole and craniofacial malformations were noted in this study; however, this study was not considered appropriate for risk assessment as the NOAEL

established in this study was not protective of the effects observed in the dietary DNT study. A dermal DNT study was not available, thus necessitating the use of an oral study for risk assessment.

## 1.2 Comments related to occupational and non-occupational exposure

### 1.2.1 Comments related to the agricultural and turf postapplication exposure and risk assessment

**Comment:** On page 22, the proposed re-evaluation decision refers to short rotation intensive culture for spruce and willow. The single reference to "spruce" on this page is incorrect and should be replaced with "poplar". In all other instances throughout the proposed re-evaluation decision, the document correctly indicates short rotation intensive culture for poplar and willow.

**Health Canada's response:**

Health Canada agrees with this comment.

### 1.2.2 Comments related to the non-occupational and occupational exposure and risk assessment

**Comment:** PMRA has not included the exposure and risk calculations for applicators making aerial applications in Table 4, Mixer/Loader/Applicator Commercial Agriculture Exposure and Risk Assessment (p. 47 of the proposed re-evaluation decision). The aerial applicator calculations should be included in the proposed re-evaluation decision for completeness.

**Health Canada's response:**

Health Canada agrees with this comment. Table 2 in Appendix VI has been amended to include the aerial applicator scenario.

**Comment:** Incorrect unit exposure values were used in a few seed treatment risk assessments, resulting in incorrect margins of exposure.

**Health Canada's response:**

Health Canada agrees with this comment. Unit exposure values used in the seed treatment risk assessments have been corrected to reflect current inputs and updated tables can be found in Appendix VI, Tables 5–7.

### 1.2.3 Comments related to label statements

**Comment:** Clarification was requested regarding the intent of the statement regarding "unless more protective personal protective equipment statements already present" on a label. If a registrant label for a product that contains only tebuconazole currently lists more protective personal protective equipment than what is required based on the risk conclusions in the proposed re-evaluation decision, the registrant should be free to align their product labels with the personal protective equipment requirements and mitigation conclusions of the proposed re-evaluation decision and should not be required to retain personal protective equipment that is not warranted based on exposure assessment considerations.

**Health Canada's response:**

Personal protective equipment could be on end-use product labels for a variety of reasons.

- To address acute hazards identified in the acute toxicology studies conducted for each end-use product (for example, protective eyewear for products identified as eye irritants).
- To address risks identified as part of the exposure and risk assessment.
- The registrant may also choose to include more personal protective equipment than required by Health Canada on the label.

Review by Health Canada is required to determine why certain personal protective equipment are on the label and whether this personal protective equipment need to be retained on the label or can be reduced. Prior to adjusting personal protective equipment on an end-use product label, registrants are required to submit an application to Health Canada.

## 2.0 Comments related to the environmental risk assessment

In response to the consultation for PRVD2021-08, comment related to the environmental assessment was received from Bayer CropScience Inc. and the public.

### 2.1 Comments related to water modelling

**Comment:** The estimated environmental concentration (EEC) resulting from refined modelling (228 µg a.i./L) is the same as that from the screening level modelling. Health Canada should clarify what refinements were made for water modelling.

**Health Canada's response:**

The EEC of 228 µg a.i./L is not a refined value, as the modelling for tebuconazole considered two cases: Level 1 modelling at the highest crop use rate (for asparagus, maximum seasonal rate of 504 g a.i./ha) and Level 2 for the use on turf (maximum seasonal rate of 3100 g a.i./ha). Level 2 modelling for uses of tebuconazole on turf separately consider the labelled diseases on turf to further inform the acute dietary risk assessment (in other words, Level 2, for use on turf – snow mould: 1 application of 1440 g a.i./ha and Level 2, for use on turf: 3 applications totalling 3100 g a.i./ha, at 14-day interval). It was not possible to refine the Level 2 EECs for turf use because of limitations of the available environmental fate data for tebuconazole.

### 2.2 Comments related to use of field-based tebuconazole half-life values

**Comment:** Consider using field-based tebuconazole half-life values to refine modelled drinking water concentrations.

The registrant requested that Health Canada consider amending values for the laboratory aerobic soil biotransformation half-life inputs for drinking water modelling with terrestrial field dissipation half-life values for tebuconazole. The registrant suggested that this could be considered as a refinement of the EECs as the field data would represent more real-life conditions. The registrant provided four terrestrial field dissipation (TFD) studies conducted in the United States (US) that would be considered as representative of Canadian conditions in addition to a single Canadian TFD study.

It was suggested to Health Canada that the 90% upper confidence bound on the mean of the TFD half-lives could provide an alternative model input, which would result in an approximation of the soil biodegradation half-life of 200 days.

The registrant indicated that the United States Environmental Protection Agency (USEPA) is currently conducting re-registration of tebuconazole, and in their preliminary risk assessment, they recognized the conservative nature of the Pesticide Water Calculator (PWC) model for groundwater concentration estimates. One of the options explored by the USEPA was to use soil dissipation half-lives from TFD studies rather than laboratory soil biodegradation half-lives. The Environmental Fate and Effects Division (EFED) of the Office of Pesticide Programs (OPP) has completed a drinking water assessment as part of the registration review of tebuconazole. The modelling input refinement included the TFD dissipation half-lives (Tebuconazole – Drinking water Assessment for Registration Review, January 26, 2021. USEPA 2021). Input from the Antimicrobial Division (AD) on drinking water impacts from antimicrobial uses of tebuconazole has also been characterized in this assessment. The registrant also added that tebuconazole is a known antimicrobial compound, which means that there could be uncertainty regarding the viability of microbial biomass in the test soils throughout a year-long laboratory study.

When considering all currently registered tebuconazole uses in Canada, the highest estimated drinking water concentrations resulted from modelled turf scenarios. The registrant argued that Health Canada's estimated tebuconazole exposure (228 $\mu g\ L^{-1}$) from the Pesticide Water Calculator (PWC) model is overly conservative considering that the maximum tebuconazole concentration detected in 7000+ groundwater monitoring samples is less than 0.1 $\mu g\ L^{-1}$.

**Health Canada's response:**

**Uncertainty of the results of the laboratory study**

Health Canada typically requires that laboratory aerobic soil biotransformation trials for an active ingredient be performed on a minimum of four soils with varying characteristics to be submitted during an assessment. In this case, one aerobic biotransformation study from 1987 was available to Health Canada, which examined the biotransformation of tebuconazole in a sandy loam soil (PMRA# 1229603). The study showed that tebuconazole is persistent under the test conditions with a $DT_{50}$ value of 883 days (slower rate of the Double First Order in Parallel kinetic model, DFOP), which was used for the environmental and drinking water modelling and in risk assessment. It should be noted that the microbial activity of the soil was not reported, therefore, it is not clear if the soil was microbially active. To investigate further, Health Canada considered additional studies on the degradation of tebuconazole in soil, with different rates and different incubation intervals submitted to the European Food and Safety Association (EFSA, PMRA# 3093536). The EFSA report indicates that either it was not possible to measure the decrease of tebuconazole concentrations as a function of time in a reliable way, due to concentrations declining quite slowly, and calculated half-lives being too great to be determined under laboratory conditions, or the study was not reliable because of an uncommon application technology. The lack of aerobic soil data limits the ability of Health Canada to assess this pesticide; therefore, conservative assumptions were made to ensure the protection of Canadians. With only a single value, Health Canada has assumed that this study represents the upper 90% confidence interval bound on the mean for aerobic soil transformation.

**USEPA approach and field study data**

The approach used by the USEPA cited in, "Tebuconazole – Drinking Water Assessment for Registration Review" (USEPA, 2021), which provides the option to use selected TFD study values to represent the laboratory aerobic soil biotransformation half-lives, is not considered at Health Canada. Even when considering this approach, the USEPA did not accept all of the registrant-submitted field studies due to deficiencies.

Health Canada disagrees with a statement made by the registrant suggesting that the use of multiple TFD-based half-life values by the USEPA is more realistic as these studies represent real world use conditions. Although "real world data" has value, it is not appropriate as a modelling input as it represents a different process (dynamic versus static) and includes the effects of other undefined factors acting on the active ingredient (for example, water movement, photolysis). If the regulatory model requires inputs that minimize the effects of the other confounding factors, then field data does not meet this requirement and could produce incongruous results. In the natural environment, dissipation, which is a function of multiple processes, is not equivalent to any single transformation process.

The environmental fate field study protocols do not provide sufficient detailed information or the appropriate parameters to be used as inputs when performing modelling for regulatory decision-making purposes. Field studies measure the dissipation of the parent compound and not the specific processes (in other words, transport and degradation) of the parent compound and its transformation products individually. Mass balance is not possible in field studies and accounting for the fate of the parent compound and its transformation products for each process cannot be verified, and therefore, results are not appropriate as modelling inputs. Sampling at the time of application to represent the applied concentration is challenging given the large variability typically observed under field conditions and the differences often observed between the soil samples taken at application compared to the amounts determined during application verification.

The variability of the conditions experienced in field studies combined with the uncertainty of the dynamic processes concerning transport and degradation, would prohibit the direct use of this data in the modelling process. Given that radiolabelling of the active ingredient (in other words, test substance) is used in laboratory studies, there exists the ability to account for transformations of the applied substance, mass balance, degradation and transport, which are required for regulatory decision-making purposes; this information is not available in field studies. Field dissipation endpoints are usually shorter than those from laboratory soil biotransformation studies as dissipation in field studies represents multiple processes.

Typically, the purpose of a field dissipation study is to put into practice the proposed use pattern and monitor the response to determine if the laboratory data is sufficient. When field dissipation studies result in longer endpoints than the laboratory, further investigations should be considered as this suggests the laboratory data is not adequate to describe the fate of the pesticide. Further, it suggests that the inputs for water modelling are resulting in EECs that might not be protective of Canadians.

**Field data provided by registrant**

Studies evaluated prior to 2015 may not use the appropriate degradation kinetics and will, therefore, require re-assessment. In older studies, the transformation rate of pesticides in the environment is commonly described using first-order kinetics, often referred to as Single First-Order (SFO). More recently, two additional models are considered when determining degradation kinetics, the DFOP and the Indeterminate Order Rate Equation (IORE), along with a set of criteria for selecting parameters (Standard Operating Procedure for Using the North American Free Trade Agreement (NAFTA) Guidance to Calculate Representative Half-life Values and Characterizing Pesticide Degradation, Bohaty et. al. 2015).

In the data presented by the registrant, $DT_{50}$ (the time required for the concentration to decline to half of the initial value) values represent the SFO model curve fit, which was the accepted methodology at the time of conducting the studies.

The NAFTA guidance introduces a representative half-life ($t_{rep}$) to estimate an SFO half-life for model input from a degradation curve that does not follow the SFO equation. The procedure takes into consideration the frequent observation that concentrations of pesticide can decline fast initially and then become slower as time passes, to a greater degree than a first-order representation could predict. The $t_{rep}$ is the time required to reduce the concentration by 50% from any concentration point in time. The $t_{rep}$ considers both the initial and the slower portions of the transformation curve and is not necessarily numerically similar to the value of the $DT_{50}$.

Following current NAFTA guidance, one of the three approved models that best fits the data will be selected, whereas the selection was limited to the SFO model in older studies. When using the SFO model as best fit, the $DT_{50}$ is equivalent to the representative half-life ($t_{rep}$) as a modelling input. If the IORE or the DFOP model is determined to be the best fit, it is necessary to use the calculated $t_{rep}$ values and not use the $DT_{50}$ values as modelling inputs. The representative half-lives for these models may differ greatly from the determined $DT_{50}$ values, which is often the case with tebuconazole.

A summary of each field study provided by the registrant, using NAFTA guidance, is presented in Table 1 below.

**Table 1 Comparison of the registrant-calculated $DT_{50}$ values and the Health Canada-calculated representative half-lives for field studies conducted with tebuconazole**

| Field study site | Registrant-calculated $DT_{50}$ | Representative half-life ($t_{rep}$) as calculated by Health Canada (upper 15 cm depth) | Comments | PMRA document number |
|---|---|---|---|---|
| Waseca, Minnesota, USA (Turf) | $DT_{50}$ = 80.6 days | $t_{rep}$ = indeterminate not included (zero slope) | No decline in parent compound concentration was observed when considering the data for the soil component. Registrant analysis appears to use combined soil and turf data | 2456673 |
| Glenmark, New York, USA (Turf) | $DT_{50}$ = 305 days | $t_{rep}$ = 1404 days | Entire data set used in determination<br><br>SFO half-life* | 2456683 |
| Belleville, Wisconsin, USA (Turf) | $DT_{50}$ = 163.2 days | $t_{rep}$ = 149.3 days | DFOP representative half-life | 3282140 |
| Belleville, Wisconsin, USA (Bare ground, but planted to grass seed after application) | $DT_{50}$ = 216 days | $t_{rep}$ = 333.1 days | DFOP representative half-life | 3282140 |
| Canada – EcoRegion 9.2: Minto, Manitoba (Bare soil) | Bare soil<br>Year 1 $DT_{50}$ = 157 days<br>Year 2 $DT_{50}$ = 52.1 days<br>Year 3 $DT_{50}$ = 88.5 days | Bare soil<br>Year 1 $t_{rep}$ = 2903 days<br>Year 2 $t_{rep}$ = 298.5 days<br>Year 3 $t_{rep}$ = 211.7 days | DFOP representative half-lives | 1522419 |
| Canada – EcoRegion 9.2: Minto, Manitoba | Cropped soil<br>Year 1 $DT_{50}$ not provided<br>Year 2 $DT_{50}$ not provided | Cropped soil<br>Year 1 $t_{rep}$ = indeterminate<br>Year 2 $t_{rep}$ = 1650 days | SFO half life* DFOP representative half-life | 1522419 |

| Field study site | Registrant-calculated $DT_{50}$ | Representative half-life ($t_{rep}$) as calculated by Health Canada (upper 15 cm depth) | Comments | PMRA document number |
|---|---|---|---|---|
| (Cropped soil) | Year 3 $DT_{50}$ not provided | Year 3 $t_{rep}$ = 1244 days | | |
| mean | 151.8 days | 1024 days | N/A | N/A |
| 90% upper confidence bound on the mean | 199.8 days | 1508 days | N/A | N/A |

* $t_{rep}$ is equivalent to the $DT_{50}$ for the SFO model

The registrant's calculations were solely $DT_{50}$ values determined through SFO modelling, which produces lower determinations and may not be the best fit for the data given that other models are now available. Re-evaluation using current NAFTA guidance shows that some of the studies are better represented by the DFOP model and since both the initial and the slower portions of the transformation curve are considered with this model, the $t_{rep}$ determinations may vary significantly from the SFO $DT_{50}$ values.

As seen in Table 1, even if the process proposed by the registrant was considered, the 90% upper confidence bound on the mean $t_{rep}$ (used as the modelling input) proposed as a surrogate for the laboratory aerobic soil biotransformation would be 1508 days. The submitted laboratory aerobic soil biotransformation study $DT_{50}$ was 883 days. The USEPA calculated a $DT_{50}$ of 783 days from the same laboratory study, although three times this value was used in the initial USEPA modelling, which follows their policy when only one study is submitted. The refined assessment value reported in, "Tebuconazole – Drinking Water Assessment for Registration Review" (USEPA, 2021), which includes soils that are not applicable to Canada, produced a mean $DT_{50}$ value of 532 days. The details of the NAFTA degradation kinetics of the submitted studies are presented in Appendix VIII.

The replicate variability observed and the different processes represented within the field studies presented by the registrant indicate that these data cannot be used as inputs in the models used in the PMRA's Environmental Assessment Directorate. This combined with the uncertainty in determining the contributions from all processes involved in field dissipation, means that effectively applying the current field data, and the required determination of the soil aerobic biotransformation kinetics necessary as modelling input, would not be possible.

**Monitoring data**

A concern was raised by the registrant that the modelling results do not seem to be representative of the monitoring results addressed in the PRVD2021-08 and "Tebuconazole – Drinking Water Assessment for Registration Review" (USEPA, 2021, cited by the registrant). In general, there are multiple factors that contribute to the large differences between monitoring and local-scale modelling values in both surface water and groundwater. While the available monitoring data provide some characterization of regional tebuconazole concentrations (lower values due to

sampling distance from application), it is expected that higher monitoring values would be found if site selection and timing of sample collection were targeted to areas at the application site, especially in areas of high tebuconazole usage, accompanied by increased monitoring frequency.

The fact that Health Canada uses the 90$^{th}$ percentile of the modelling results in determining the EECs means that the model determinations will likely be more conservative than determinations from most field studies.

**Conclusion**

Considering this information, Health Canada has determined that laboratory soil aerobic biotransformation results, and not terrestrial field dissipation study values, are to be used as conservative estimates in the determination of modelled EECs for the acute and chronic dietary risk assessment of tebuconazole in drinking water.

## 3.0 Comments related to the value assessment

In response to the consultation for PRVD2021-08, comment related to the value assessment was received from Bayer CropScience Inc. and the public.

### 3.1 Comment on the proposed reduction of use rates for turf

**Comment:** Bayer CropScience Inc. commented that tebuconazole is a highly effective four season utility fungicide. Based on efficacy review of all registered fungicides in the United States, tebuconazole provides consistently good to excellent control of dollar spot, and anthracnose, brown patch, and good to excellent control of summer patch. No other standalone demethylation inhibitor ranks better than tebuconazole for any of those summer diseases except Maxtima Fungicide (mefentrifluconazole) which provides consistently good to excellent control of anthracnose. All of those aforementioned diseases are quite common in Canada and often involve several fungicide applications per year to provide acceptable control. Another important aspect is the strength of tebuconazole for managing gray snow mould in Canada. No other standalone fungicide for any mode of action ranks higher than tebuconazole. Under severe snow mould pressure, higher rates are absolutely needed to provide 150 day protection against gray snow mould. Essentially a high labelled rate of tebuconazole is needed for snow mould control and a minimum of one application of tebuconazole is needed to control the full spectrum of labelled diseases during the summer months. The proposed rates of tebuconazole provided by the PMRA do not provide the superintendents with the needed tools to provide an exceptional playing experience for their golfing community. In addition, trials conducted in Ontario and Quebec with tebuconazole provided commercial level of dollar spot control.

**Health Canada's response:**

Health Canada acknowledges the value of tebuconazole for managing turf diseases. However, health risks of concern remain and the uses of tebuconazole for managing turf diseases are cancelled.

# Appendix IV Toxicology information for health risk assessment

**Table 1 Revised toxicology reference values for use in health risk assessment of tebuconazole**

| Exposure scenario | Study | Point of Departure (POD) and endpoint | CAF or target MOE[1] |
|---|---|---|---|
| **Acute Dietary Gen. population** | **Dietary Developmental Neurotoxicity (DNT) Study - rat** | **Developmental no observed adverse effect level (NOAEL) = 22 mg/kg bw/day ↑ motor activity, ↓ auditory startle response, ↓ brain wt and altered brain morphometrics in the presence of maternal toxicity** | **300** |
| **Acute Reference Dose (ARfD) = 0.07 mg/kg bw/day** | | | |
| **Acute dietary females 13–49 years of age** | **Oral Developmental Toxicity Study - mice** | **Developmental NOAEL = 3 mg/kg bw/day ↑ incidence of craniofacial malformations in the absence of maternal toxicity** | **1000** |
| **ARfD = 0.003 mg/kg bw/day** | | | |
| Repeated Dietary General population | 1-year oral toxicity study - dog | NOAEL = 3 mg/kg bw/day ↑ hypertrophy in the adrenal zona fasciculata, presence of fatty vacuoles in the adrenal zona glomerulosa cells | 100 |
| Acceptable Daily Intake (ADI) = 0.03 mg/kg bw/day | | | |
| **Repeated Dietary females 13–49 years of age** | **Oral Developmental Toxicity Study - mice** | **Developmental NOAEL = 3 mg/kg bw/day ↑ incidence of craniofacial malformations in the absence of maternal toxicity** | **1000** |
| **ADI = 0.003 mg/kg bw/day** | | | |
| **Incidental oral short-to intermediate-term** | **Dietary DNT Study - rat** | **Developmental NOAEL = 22 mg/kg bw/day ↑ motor activity, ↓ auditory startle response, ↓ brain wt and altered brain morphometrics in the presence of maternal toxicity** | **300** |
| **Dermal, All durations[2]** | **Dietary DNT Study - rat** | **Developmental NOAEL = 22 mg/kg bw/day ↑ motor activity, ↓ auditory startle response, ↓ brain wt and altered brain morphometrics in the presence of maternal toxicity** | **300** |

| Exposure scenario | Study | Point of Departure (POD) and endpoint | CAF or target MOE[1] |
|---|---|---|---|
| **Inhalation, All durations[3]** | **Oral Developmental Toxicity Study - mice** | **Developmental NOAEL = 3 mg/kg bw/day<br>↑ incidence of craniofacial malformations in the absence of maternal toxicity** | **1000** |
| **Oral and Dermal[2] Short- and Intermediate-term aggregate assessments, General population** | **Dietary DNT Study - rat** | **Common endpoint:↑ motor activity, ↓ auditory startle response, ↓ brain wt and altered brain morphometrics in the presence of maternal toxicity<br><br>Oral and dermal Developmental NOAEL = 22 mg/kg bw/day** | **300** |
| **Oral and Dermal Short- and Intermediate-term aggregate assessments, Females 13-49** | **oral:<br>Oral Developmental Toxicity Study - mice<br><br>dermal:<br>Dermal Developmental Toxicity Study - mice** | **Common Endpoint:<br>↑ incidence of craniofacial malformations<br>oral NOAEL = 3 mg/kg bw/day<br><br>dermal NOAEL = 275 mg/kg bw/day** | **1000<br><br>300** |
| Cancer | Evidence of liver tumours in mice, for which a mode of action was accepted and a threshold approach for risk assessment was considered appropriate. Equivocal increase in histiocytic sarcomas in mice. Toxicology reference values selected for non-cancer risk assessment are protective of any residual concerns regarding carcinogenic potential. | | |

**Bolded** cells indicate exposure scenarios that have been modified by Health Canada following consideration of the comments received on PRVD2021-08.

[1]CAF (composite assessment factor) refers to a total of uncertainty and PCPA factors for dietary assessments; MOE refers to a target margin of exposure for occupational and residential assessments.

[2]Since an oral NOAEL was selected, a dermal absorption factor of 13% was used in a route-to-route extrapolation

[3]Since an oral NOAEL was selected, an inhalation absorption factor of 100% (default value) was used in route-to route extrapolation.

**Table 2 Summary of toxicology studies considered or revisited following PRVD2021-08**

| Study type/ Animal/PMRA No. | Study results |
|---|---|
| **Short-Term Toxicity Studies** | |
| 90-day oral toxicity (Dietary)<br><br>Bor:WISW Spf-cpb rats<br><br>PMRA No. 1229432 | **No Observed Adverse Effect Level (NOAEL) = 35/11 mg/kg bw/day (♂/♀)**<br>**Lowest Observed Adverse Effect Level (LOAEL) = 172/47 mg/kg bw/day (♂/♀)**<br><br>**≥35/47 mg/kg bw/day:** ↓ abs liver wt (not adverse) (♂); ↑ vacuole formation in adrenals (♀)<br><br>**172/232 mg/kg bw/day**: Two deaths (1♂, 1♀), ↓ terminal bw, ↓ bwg (♂/♀); ↓ abs liver wt, ↑ N-DEM and CYP450, ↑ kidney hydronephrosis (♂); ↑ rel liver wt, ↑ hemosiderin accumulation in spleen (♀) |
| One-year oral toxicity (Dietary)<br><br>Beagle dog<br><br>PMRA No. 1227396 | **NOAEL = 1.1 mg/kg bw/day (♂/♀)**<br>**LOAEL = 6.4 mg/kg bw/day (♂/♀)**<br><br>**≥6.4/6.4 mg/kg bw/day:** 2♀ with vacuoles in adrenal zona fasciculata – moderate to severe. Lens alteration noted in two animals with no impairment of vision.<br><br>**40/43 mg/kg bw/day**: ↑ hemosiderin accumulation in spleen, ↑ N-DEM activity in liver, ↑ TGs in liver, liver lobulation (♂/♀); 2♀ with vacuoles in adrenal zona fasciculata – slight to moderate. Lens alteration noted in one animal with no impairment of vision. |
| One-year oral toxicity (Dietary)<br><br>Beagle dog<br><br>PMRA No. 1136272 | **NOAEL = 3.0 mg/kg bw/day (♂/♀)**<br>**LOAEL = 4.4 mg/kg bw/day (♂/♀)**<br><br>**≥4.4 mg/kg bw/day:** Hypertrophy of adrenal zona fasciculata (in 8 HD animals, 1 control animal), fatty vacuoles in adrenal zona glomerulosa cells (3♂, 2♀ in HD group, 1♂ and 1♀ in control and low dose groups) - severity of effect was minimal in control, minimal to mild in the low dose group, and minimal to moderate in the HD group. |
| **Chronic Toxicity/Oncogenicity Studies** | |
| 21-month oncogenicity (Dietary)<br><br>NMRI mice<br><br>PMRA No. 1229498; 1038116; 1038117 | **NOAEL = 18/26 mg/kg bw/day (♂/♀)**<br>**LOAEL = 53/81 mg/kg bw/day (♂/♀)**<br><br>**≥ 5.9/9.0 mg/kg bw/day**: ↑ plasma bilirubin (non-adverse at this dose level) (♀)<br><br>**≥ 18/26mg/kg bw/day**: ↑ periportal vacuolation at 12 months only (♀) (non-adverse)<br><br>**53/81 mg/kg bw/day**: ↓ cholesterol at 12 months (♂/♀); ↑ rel liver wt at 21 months, ↑ minimal periportal vacuolation (focal and diffuse lipid deposition) |

| Study type/ Animal/PMRA No. | Study results |
|---|---|
| | at 12 months, ↑ periportal vacuolation at 21 months, centrilobular fine vacuolation at 21 months. Vacuoles were attributed to lipid deposition in the liver (♂); ↑ plasma bilirubin at 12 and 21 months, ↑ liver wt, periportal vacuolation was observed at 12 months but not at 21 months (with non-significant ↑ liver wt at 12 and 21 months) (♀).<br><br>**No evidence of tumourigenicity; however, the MTD was considered not to have been reached in this study.** |
| 21-month oncogenicity (Dietary)<br><br>NMRI mice<br><br>PMRA No. 1145666 | **NOAEL not established**<br>**LOAEL = 85/103 mg/kg bw/day (♂/♀)**<br><br>**≥85/103 mg/kg bw/day**: ↓ bw, ↑ liver wt, ↑ ALT, ALP and AST (slight at this dose level), ↓ cholesterol, ↓ albumin (slight) ↑ incidence of pale and large livers, panacinar fine fatty vacuolation and hyperkeratosis and acanthosis in the forestomach at interim sacrifice (♂/♀); ↑ incidence of pigment laden Kupffer cells in the liver at interim sacrifice, ↓ bilirubin at 12 months, ↓ hematocrit, ↑ MCH and MCHC (slight at this dose level) (♂); ↑ centriacinar fatty vacuolation at interim sacrifice, ↑ thrombocyte count (termination) (♀)<br><br>**279/357 mg/kg bw/day**: ↑ distended abdomen, ↑ inorganic phosphate, ↑ leucocyte count, ↓ clotting time (termination only), ↑ incidence of bile duct hyperplasia at interim sacrifice, ↑ incidence of pigment laden Kupffer cells in the liver at termination, ↑ incidence of focal hyperplasia of hepatocytes, panacinar fine fatty vacuolation, oval cell proliferation at interim and terminal sacrifice, ↑ hepatocellular carcinomas, ↑ histiocytic sarcoma (equivocal) (♂/♀); ↓ bw, ↓ erythrocyte count (termination only), ↑ hepatocellular adenomas (♂); ↑ creatinine (12 months only) (♀)<br><br>**Neoplastic findings:**<br>Liver tumour incidences in ♂:<br>Adenomas: 3/47, 2/48, 17/48**<br>Carcinomas: 0/47, 0/48, 10/48**<br>** significantly different from controls $p < 0.001$<br><br>Liver tumour incidences in ♀<br>Adenomas: 0/47, 0/45, 2/46<br>Carcinomas: 1/47, 0/45, 12/46**<br>** significantly different from controls $p < 0.001$<br><br>Histiocytic sarcomas ♂<br>1/48 2/49 and 3/48<br>Histiocytic sarcomas ♀<br>1/47, 3/45, and 5/46<br><br>**Evidence of carcinogenicity (liver tumors)**<br>**Equivocal evidence of carcinogenicity (histiocytic sarcomas)** |

| Study type/ Animal/PMRA No. | Study results |
|---|---|
| 2-year chronic toxicity/oncogenicity (Dietary)<br><br>Wistar (Bor:WISW Spf Cpb) rats<br><br>PMRA No. 1229439; 1227392; 1227395; 1038118; 2758955 | **NOAEL = 55/7.4 mg/kg bw/day (♂/♀)**<br>**LOAEL = not established/23 mg/kg bw/day (♂/♀)**<br><br>**≥ 5.3/7.4 mg/kg bw/day:** ↓ adrenal wt (♀) (non-adverse)<br><br>**≥ 16/23 mg/kg bw/day:** ↓ bw (♀)<br><br>**55/86 mg/kg bw/day**: ↓ testes wt (♂); ↑ fc, ↑ hemosiderin content in the spleen, ↑ rel. liver wt, ↑ liver enzyme induction (non-significant ↑ in hepatic hemosiderin content), ↑ Kupffer cell pigmentation, ↓ water intake (slight) (♀)<br><br>**No evidence of tumourigenicity** |
| **Developmental/Reproductive Toxicity Studies** | |
| Two-generation reproductive toxicity (Dietary)<br><br>Wistar (Bor:WISW Spf Cpb) rats<br><br>PMRA No. 1227397 | **Parental Toxicity**<br>**NOAEL = 22/28 mg/kg bw/day (♂/♀)**<br>**LOAEL = 72/95 mg/kg bw/day (♂/♀)**<br><br>**72/95 mg/kg bw/day:** ↓ bw (♂/♀); ↓ bwg of P and $F_{1b}$ parents during the period of 2 gestations/generation (♀)<br><br>**Offspring Toxicity**<br>**NOAEL = 28 mg/kg bw/day (♂/♀)**<br>**LOAEL = 95 mg/kg bw/day (♂/♀)**<br><br>**72/95 mg/kg bw/day:** ↓ viability and lactation index in 2 litters of P parents, ↓ pup bw during lactation in all litters. **(♂/♀)**<br><br>**Reproductive Toxicity**<br>**NOAEL = 22/28 mg/kg bw/day (♂/♀)**<br>**LOAEL = 72/95 mg/kg bw/day (♂/♀)**<br><br>**72/95 mg/kg bw/day:** ↓ litter size $F_{1a}$ and $F_{1b}$ only, ↓ pup birth wt (♂/♀)<br><br>Limitations: Sperm parameters (motility and morphology), estrous cycle length and periodicity, ovarian follicle counts as well as measurements of puberty onset were not examined |
| Developmental toxicity (Gavage)<br><br>NMRI mice<br><br>PMRA No. 1227400; 1038124; 1038125; 1145301; | **Maternal Toxicity**<br>**NOAEL = 30 mg/kg bw/day**<br>**LOAEL = 100 mg/kg bw/day**<br><br>**100 mg/kg bw/day:** ↑ resorptions, post-implantation loss<br>Note: no histopathology or clinical chemistry analysis were conducted in dams.<br><br>**Developmental Toxicity** |

| Study type/ Animal/PMRA No. | Study results |
|---|---|
| 1230727; 1145682 | **NOAEL = 10 mg/kg bw/day**<br>**LOAEL = 30 mg/kg bw/day**<br><br>**≥30 mg/kg bw/day** ↑ number of runts<br><br>**100 mg/kg bw/day**: ↑ placental wt, ↑ malformations, ↑ resorption, post-implantation loss<br><br>**Evidence of treatment-related malformations; occurrence at non-maternally toxic doses is questionable given the limited maternal parameters examined.** |
| Developmental toxicity (Gavage)<br><br>NMRI mice<br><br>PMRA No. 1038158<br><br>This study was conducted since previous study (PMRA No. 1227400) indicated no maternal toxicity up to 100 mg/kg bw/day | **Supplemental**<br>Small number of animals used to examine individual parameters impedes data interpretation.<br><br>**Maternal Toxicity**<br>**≥10 mg/kg bw/day**: ↑ AST, ↑ ALT, ↑ abs liver wt (no evidence of dose response), (all findings non-adverse)<br><br>**100 mg/kg bw/day**: ↓ bw, ↑ liver TG, ↑ pale liver, liver lobular pattern, ↑ liver vacuolation<br><br>**Developmental Toxicity**<br>Not assessed |
| Developmental toxicity (Gavage)<br><br>NMRI mice<br><br>PMRA No. 1038120–1038123<br><br>This study was conducted as a follow-up to PMRA No. 1227400, to confirm the results from this previous study and included a more comprehensive skeletal evaluation. | **Maternal Toxicity**<br>**NOAEL = 10 mg/kg bw/day**<br>**LOAEL = 30 mg/kg bw/day**<br><br>**≥10 mg/kg bw/day**: liver vacuolization, ↑ liver enzyme (CYP450 O-DEM, N-DEM) (all changes considered non adverse at this dose level)<br><br>**≥ 30 mg/kg bw/day:** ↑ post-implantation loss, ↑ liver TG, ↑ rel liver wt,↑ lipid storage (↑ severity but not incidence), ↑ mononuclear cells in the liver and kidneys, ↑ ALP<br><br>**100 mg/kg bw/day:** ↓ bwg, ↓ bw ,↑ liver wt ↑ rel spleen wt, ↑ early resorption<br><br>**Developmental Toxicity**<br>**REVISED NOAEL = 3 mg/kg bw/day**<br>**LOAEL = 10 mg/kg bw/day**<br><br>**10 mg/kg bw/day**: ↑ incidence of CNS/craniofacial malformations (protruding tongue, fissure in palate), ↑ wart-like growths on forepaw |

| Study type/ Animal/PMRA No. | Study results |
|---|---|
| | **30 mg/kg bw/day**: ↑ post-implantation loss, ↑ incidence of acrania, ↑ incidence of runts<br><br>**100 mg/kg bw/day:** ↓ live fetuses, ↑ external, visceral, and skeletal malformations (exencephaly, palatoschisis, cleft palate, absent/dysplastic/abnormally ossified vertebrae, lordosis and/or scoliosis), ↑ incidence of occipital, parietal or frontal bones missing, ↓ ossification in the fore and hindlimb<br><br>**Evidence of treatment-related malformations**<br>**Evidence of sensitivity of the young** |
| Developmental toxicity (Gavage)<br><br>Chinchilla rabbits PMRA No. 1227393 | **Maternal Toxicity**<br>**NOAEL = 30 mg/kg bw/day**<br>**LOAEL = 100 mg/kg bw/day**<br><br>**100 mg/kg bw/day**: ↓ bwg during treatment, ↑ post-implantation loss<br><br>**Developmental Toxicity**<br>**NOAEL = 30 mg/kg bw/day**<br>**LOAEL = 100 mg/kg bw/day**<br><br>**100 mg/kg bw/day**: ↑ post-implantation loss, ↑ skeletal malformations (malformation included peromelia, agenesis of hindlimb claws with an enlarged fontanelle, palatoschisis and perodactylia)<br><br>**Evidence of treatment-related malformations**<br>**No evidence of sensitivity of the young** |
| Developmental toxicity (Gavage)<br><br>Chinchilla rabbits PMRA No. 1038126; 1038127 | **Maternal Toxicity**<br>**NOAEL = 30 mg/kg bw/day**<br>**LOAEL = 100 mg/kg bw/day**<br><br>**100 mg/kg bw/day**: ↓ fc, ↑ post-implantation loss<br><br>**Developmental Toxicity**<br>**NOAEL = 30 mg/kg bw/day**<br>**LOAEL = 100 mg/kg bw/day**<br><br>**100 mg/kg bw/day**: ↑ post-implantation loss, ↓ mean fetal wt, multiple malformations including spina bifida, malposition of limbs, skull indentation, meningocele, omphalocele, acephaly and incomplete/non-ossification<br><br>**Evidence of treatment-related malformations**<br>**No evidence of sensitivity of the young** |

| Study type/ Animal/PMRA No. | Study results |
|---|---|
| **Neurotoxicity studies** | |
| Acute neurotoxicity study<br>(Gavage)<br><br>Fischer 344 rats<br><br>PMRA No. 1038133–1038135 | **NOAEL = 100 mg/kg bw (♂/♀)**<br>**LOAEL = 500/250 mg/kg bw (♂/♀)**<br><br>**Main Study (Doses: 0, 100/100, 250/500 or 1000/500 mg/kg bw (♂/♀))**<br>**≥100 mg/kg bw**: ↑ arousal (open field) on day 0, ↑ motor activity on day 0 (this dose only) (♂/♀); ↓ landing foot splay (♀). All findings not considered adverse at this dose level.<br><br>**≥250 mg/kg bw (♀ only)**: uncoordinated gait, red nasal stain, oral stain, ↓ motor/locomotor activity on day 0 (recovered on day 7), diminished approach, touch and auditory responses, slightly impaired aerial righting, slightly lower body temp.<br><br>**500 mg/kg bw**: ↓ hindlimb grip strength (♂/♀); 1/12 male died on day 1, uncoordinated gait, ↓ activity, salivation, cool-touch body, lacrimation, staining (urine, red nasal, red lacrimal, oral), ↓ motor/locomotor activity on day 0 (recovered on day 7), diminished approach, touch, auditory and tail pinch responses, impaired aerial righting, lower body temp. (♂)<br><br>**1000 mg/kg bw (♂ only):** 6/12 died day 1–2. Clinical signs appeared on day 0 and persisted until 3–5 days post-treatment.<br><br>**Follow-up study (Doses: 0, 20 or 50 mg/kg bw ♂/♀)**<br>No treatment-related effects observed.<br><br>**Evidence of neurotoxicity** |
| Developmental neurotoxicity study<br>(Dietary)<br><br>Sprague Dawley rats<br><br>PMRA No. 1038136–1038141; 1038142–1038150 | **Maternal Toxicity**<br>**NOAEL = 22 mg/kg bw/day**<br>**LOAEL = 65 mg/kg bw/day**<br><br>**65 mg/kg bw/day:** ↑ mortality (2♀ died due to prolonged gestation), ↑ localized alopecia, ↓ bw and bwg during gestation and lactation, ↓ fc during gestation and up to day 12 of lactation, ↑ duration of gestation, ↑ no. of stillborn pups (♀)<br><br>**Offspring Toxicity**<br>**Revised: $BMDL_5$ of 9.25 mg/kg bw/day for effect on pre-weaning offspring bodyweight**<br>**Developmental neurotoxicity NOAEL = 22 mg/kg bw/day**<br><br>**≥22 mg/kg bw/day**: ↓ pre-weaning pup bw (♂/♀); equivocal decrease in brain wt (♂)<br><br>**65 mg/kg bw/day:** ↓ viability index (PND 5), delay in eye-opening, ↓ auditory |

| Study type/ Animal/PMRA No. | Study results |
|---|---|
| | startle response at PND 23, ↓ brain wt, ↓ cerebellum length at PND 12 and 83, delayed pinna unfolding ↑ no. of stillborn pups (♂/♀); ↑ motor activity at PND 22, ↑ external germinal layer (♂); delayed vaginal patency (♀)<br><br>**Evidence of sensitivity of the young**<br>**Evidence of developmental neurotoxicity** |
| **Supplemental studies from the published scientific literature** | |
| Developmental toxicity (in vitro)<br><br>Rat embryos (CD:Crl)<br><br>PMRA No. 3594789 | E9.5 embryos were explanted from pregnant CD rats and cultured in glass bottles and exposed to the test substance. After 48 hrs in culture, embryos were examined morphologically.<br><br>Tebuconazole NOAEL = 31.3 µM<br>Tebuconazole LOEL = 62.5 µM<br><br>Dysmorphogenic effect was observed at the level of the branchial arches after exposure |
| Developmental toxicity (in vitro)<br><br>Rat and Xenopus laevis embryos<br><br>PMRA No. 3594112 | Rat whole embryo culture (WEC)<br>E9.5 embryos were explanted from pregnant CD rats and cultured in glass bottles and exposed to the test substance. After 48 hrs in culture, embryos were examined morphologically.<br><br>62.5–250 µM: dose-dependent ↑ in branchial arches malformations<br><br>Xenopus WEC<br>Embryos at stage 13 were obtained from natural breeding pairs of X. laevis. Embryos were cultured in the presence of the test substance until stage 17, then culture until stage 47. Larvae were morphologically examined and stained with alcyan blue in order to stain cartilaginous elements and were flat mounted for examination.<br><br>No effect observed on external examination. After cartilage staining and flat mount, the fusion between ceratohyal-quadrate and between quadrate and Meckel cartilages was visible in the totality of larvae exposed to tebuconazle at concentration of 62.5–250 µM. At 250 µM reduction of the cartilaginous |

| Study type/ Animal/PMRA No. | Study results |
|---|---|
| | elements were observed.<br><br>Effects observed with tebuconazole were similar to those noted with triadimefon, with a clear specificity of these molecules in affecting the branchial arch morphogenesis. Triadimefon was more potent than tebuconazole. |
| Neurotoxicity (in vitro)<br>Non-guideline<br><br>Primary rat cortical culture and human neural progenitor cells<br><br>PMRA No. 3594115<br><br><br><br>PMRA No. 3594116<br><br><br><br><br><br><br><br>PMRA No. 3594105 | For all publications primary rat cortical cultures were prepared from one day old Long Evans rat pups. Culture consists of excitatory and inhibitory neurons and glia. After harvesting, cells were plated directly in 48-well microelectrode array (MEA) plates (Axion M768-KAP-48) pre-coated with 0.05% polyethylenimine. The test substance was tested at 7 concentrations in 3 replicates. Test substance was applied 2 hrs after cell attached and exposure continued for 12 days. The medica containing the test substance was exchanged on Days 5 and 9. Spontaneous electrical activity of cortical cultures were measured on days 2, 5, 7, 9 and 12. On day 12, following the last recording cell viability was assessed using 2 commercially available kits. This assay is included in the OECD DNT IVB (PMRA No. 3599976)<br><br>PMRA No. 3594115<br>In addition to the result from the MEA neural network formation assay, which was performed as detailed above, this publication characterized the cell types contained within cortical network was characterized via immunostaining for the presence of dendrites, astrocytes, excitatory and inhibitory neurons as well as microglia. Tebuconazole activity on network parameters occurred at non-cytotoxic concentration<br>$EC_{50\ Minimum}$ 0.35 µM<br>$EC_{50\ Maximum}$ 27.04 µM<br>Tebuconazole was considered to have potent and selective effect on network parameters. No cytotoxicity observed at the highest dose tested.<br><br>PMRA No. 3594116<br>Toxicological “tipping points” are defined as dose-dependent transitions in cells based on their inability to recover to normal (or basal) functions. Tipping points were derived using computational tools based on the results from the MEA neural network formation assay recordings previously captured. Critical concentration or tipping point for TEU was 1.341 µM (95% CI= 0.122-4.382 µM).<br><br>PMRA No. 3594105<br>In addition to the MEA neural network formation assay, this publication examined the findings from other DNT in vitro new approach methodologies that use high content imaging in human neural progenitor cells to evaluate proliferation, apoptosis, neurite outgrowth and synaptogenesis. These assays are included in the OECD DNT IVB (PMRA No. 3599976)<br><br>Tebuconazole was cytotoxic to neurons at concentration that demonstrate little |

| Study type/ Animal/PMRA No. | Study results |
|---|---|
| | or no bioactivity in other cell-types and/or assay platforms. Tebuconazole was active in multiple assays in human neural progenitor cells. See PMRA No. 3594118 for additional details. |
| Neurotoxicity (in vitro)<br>Non-guideline<br><br>Rat primary cortical cells<br><br>Human neuroprogenitor cells<br><br>PMRA No. 3594118 | Compounds were tested in some assays from the OECD DNT IVB (PMRA No. 3599976). Specifically, high content imaging in human neural progenitor cells was used to evaluate proliferation, apoptosis, neurite outgrowth and synaptogenesis. Additionally, neurite outgrowth, as well as neurite maturation and synaptogenesis was assessed in primary rat cortical cells isolated from one day old Long Evans rat pups.<br><br>Chemicals were considered to selectively affect the measured neurodevelopmental endpoint when the potency ($EC_{30}$) for the neurodevelopmental endpoint was at least threefold greater than the potency ($EC_{30}$) for cytotoxicity $EC_{30}$ (µM).<br><br>The assays and $EC_{30}$ concentrations where Tebuconazole induced a selective effect on the neurodevelopmental endpoint of interest are listed below.<br><br>Apoptosis human neural progenitor cells: 28.1 µM<br>Rat cortical neurite maturation: 17.0 µM<br>Rat cortical Synaptogenesis: 37.3 µM |
| Neurotoxicity (in vitro)<br>Non-guideline<br><br>PC12 Cell<br><br>PMRA No. 3594287 | Rat dopaminergic pheochromocytoma (PC12) were grown for 10 passages. Measured using a combined alamar Blue/CFDA-AM (aB/CFDA) assay. Reactive oxygen species (ROS) was used as a measure of oxidative stress and investigated using the fluorescent dye H2-DCFDA. Fluorescence was measured spectrophotometrically. Changes in the [Ca2+] were measured on a single-cell level using the Ca2+-sensitive fluorescent ratio dye Fura-2 AM.<br><br>TEU did not induce overt toxicity after 24 hrs exposure or ↑ ROS production<br>TEU inhibited voltage-gated calcium channels in a dose-dependent manner<br>$IC_{10}$ = 3.4 µM<br>$IC_{50}$ = 11.0 µM<br><br>In vivo, maintenance of intracellular calcium homeostasis is critical for neurodevelopment. Additionally, inhibition of voltage gated calcium channels in vivo would likely result in reduced dopaminergic transmission. Effects of TEU on dopamine levels have not been assessed in vivo. |

# Appendix V Revised dietary exposure and risk estimates for tebuconazole

**Table 1 Summary of dietary acute exposure and risk from tebuconazole with all maximum residue limits (MRLs) on grape commodities revoked and residues set at the general maximum residue limit (GMRL) (0.1 ppm)**

| Population subgroup | Food only with MRLs on all grape commodities revoked and residues set at GMRL[1] | | Drinking water alone using refined EECs[2] | | Food and drinking water | |
|---|---|---|---|---|---|---|
| | Exposure (mg/kg bw/day) | %ARfD[3] | Exposure (mg/kg bw/day) | %ARfD[3] | Exposure (mg/kg bw/day) | %ARfD[3] |
| All Infants (< 1 year old) | 0.009600 | 13.7 | 0.004746 | 6.8 | 0.011033 | 15.8 |
| Children 1–2 years old | 0.010878 | 15.5 | 0.001998 | 2.9 | 0.011621 | 16.6 |
| Children 3–5 years old | 0.007403 | 10.6 | 0.001573 | 2.2 | 0.008275 | 11.8 |
| Children 6–12 years old | 0.003496 | 5.0 | 0.001234 | 1.8 | 0.004127 | 5.9 |
| Males 13–19 years old | 0.001621 | 2.3 | 0.001082 | 1.6 | 0.002355 | 3.4 |
| Male 20+ | 0.002167 | 3.1 | 0.001198 | 1.7 | 0.002922 | 4.2 |
| Females 13–49 years old | 0.001806 | 60.2 | 0.001367 | 45.6 | 0.002816 | 93.9 |
| Adults 16+ | 0.002297 | 7.66 | 0.001278 | 4.26 | 0.003048 | 10.16 |
| Adults 50–99 years old | 0.002874 | 4.1 | 0.001178 | 1.7 | 0.003487 | 5.0 |

[1]GMRL of 0.1 ppm was used for all grape commodities.
[2]Based on estimated environmental concentration (EEC) in drinking water of 26 µg/L for a combination of 5.2 g tebuconazole/ha seed treatment and 136 g tebuconazole/ha foliar spray per annum.
[3]Acute Reference Dose (ARfD) of 0.07 mg/kg bw for all subpopulations except female 13–49 yr old; and ARfD of 0.003 mg/kg bw for females 13–49 yr old.

**Table 2 Summary of dietary chronic exposure and risk from tebuconazole with all maximum residue limits (MRLs) on grape commodities revoked and residues set at the general maximum residue limit (GMRL) (0.1 ppm)**

| Population subgroup | Food alone with MRLs on all grape commodities revoked and residues set at GMRL[1] | | Drinking water alone using refined EECs[2] | | Food and drinking water | |
|---|---|---|---|---|---|---|
| | Exposure (mg/kg bw/day) | %ADI[3] | Exposure (mg/kg bw/day) | %ADI[3] | Exposure (mg/kg bw/day) | %ADI[3] |
| All Infants (< 1 year old) | 0.000460 | 1.5 | 0.001887 | 6.3 | 0.002347 | 7.8 |
| Children 1–2 years old | 0.001135 | 3.8 | 0.000695 | 2.3 | 0.001829 | 6.1 |
| Children 3–5 years old | 0.000679 | 2.3 | 0.000565 | 1.9 | 0.001244 | 4.1 |
| Children 6–12 years old | 0.000362 | 1.2 | 0.000420 | 1.4 | 0.000782 | 2.6 |
| Males 13–19 years old | 0.000195 | 0.7 | 0.000332 | 1.1 | 0.000527 | 1.8 |
| Male 20+ | 0.000190 | 0.6 | 0.000469 | 1.6 | 0.000659 | 2.2 |
| Females 13–49 years old | 0.000174 | 5.8 | 0.000493 | 16.4 | 0.000667 | 22.2 |
| Adults 16+ | 0.000183 | 0.6 | 0.000503 | 1.7 | 0.000669 | 2.2 |
| Adults 50–99 years old | 0.000183 | 0.6 | 0.000493 | 1.6 | 0.000672 | 2.2 |

[1]GMRL of 0.1 ppm was used for all grape commodities.
[2]Based on estimated environmental concentration (EEC) in drinking water of 25 µg/L for a combination of 5.2 g tebuconazole/ha seed treatment and 136 g tebuconazole/ha foliar spray per annum.
[3]Acceptable daily intake (ADI) of 0.03 mg/kg bw/day for all subpopulations except female 13–49 yr old; and ADI of 0.003 mg/kg bw/day for females 13–49 yr old.

# Appendix VI Revised occupational and non-occupational exposure and risk assessment for tebuconazole

Details for the revised risk assessment are included in this appendix. Please refer to PRVD2021-08 for additional information.

There were no changes to the dermal absorption value from PRVD2021-08. No additional dermal absorption data were submitted. Based on the data available, the dermal absorption value of 13% continues to be appropriate to estimate dermal absorption for tebuconazole for pesticide application and postapplication scenarios.

**Occupational exposure and risk assessment**

The occupational mixer, loader, applicator and postapplication assessments were revised to incorporate the updated toxicology reference values and address comments received during the proposed re-evaluation decision consultation period.

See Table 1 for a summary of mitigation required as a result of the revised occupational risk assessment. Mitigation measures for some scenarios were changed from what was proposed in PRVD2021-08. See discussion below for more information.

**Agriculture exposure and risk assessment**

In the updated agricultural handler assessment (see Table 2), margin of exposures (MOE) were greater than the target MOE and risks were shown to be acceptable for all of the occupational scenarios at single layer personal protective equipment (PPE) and chemical resistant (CR) gloves except for:

- Mixing, loading, and application of liquids using a mechanically pressurized handgun (MPHG)
- Application of liquid formulations using a handheld airblast/mistblower (HH AB/MB)

To mitigate risk for the MPHG scenario, a respirator will also be required for all mixing, loading and application activities. For the HH AB/MB scenario, MOEs did not reach the target MOE at maximum PPE, CR hood, CR gloves, and a respirator. MOEs met the target MOE and risks were shown to be acceptable at the amount handled per day of 0.06 kg a.i.. To mitigate risk, CR coveralls, CR footwear, a CR hood and a respirator are also required and the amount of active ingredient (kg a.i.) that can be handled will be limited to 0.06 kg a.i. per day per person.

In the updated postapplication assessment, calculated MOEs for all postapplication scenarios exceeded the target MOE on the day of application (day zero) and risks were shown to be acceptable (see Table 3). The standard minimum restricted-entry interval (REI) of 12 hours will be required for all agricultural postapplication activities, except for golf course turf where the required REI of “until sprays have dried” would have been required. As all turf uses have been cancelled to reduce exposure from drinking water, the REIs for turf and sod farm postapplication activities are not required. Due to the updated toxicological reference values, the REI of 1 day proposed in PRVD2021-08 for the short rotation intensive culture (poplar and willow) harvesting activity has decreased to 12 hours.

**Heavy duty wood preservatives exposure and risk assessment**

In the updated wood treatment assessment (see Table 4), MOEs for industrial workers were greater than the target MOEs and risks were shown to be acceptable at single layer PPE (long-sleeved shirt, long pants) and CR gloves. As proposed in PRVD2021-08, additional PPE is required for personnel who work with preservatives as per the "Recommendations for Design and Operation of Wood Preservation Facilities, 2013 Technical Recommendations Document (TRD)" (ECCC, 2013), which is enforced by Environment and Climate Change Canada. The PPE requirements in the TRD are task-based and are dependent on whether workers are working under dry conditions, when there is risk of getting wet from the preservative, or in an enclosed environment with pesticides.

**Seed treatment exposure and risk assessment**

For the commercial treatment of wheat, barley, oat, rye, and triticale seed, calculated dermal and inhalation MOEs exceeded the target MOEs and risks were shown to be acceptable for the PPE in the underlying exposure studies. For treater activities (with open or closed M/L) and bagger/sewer/stacker activities, this was single layer PPE (long pants, long-sleeved shirt, CR gloves) and maximum PPE (CR coveralls over a long-sleeved shirt, long pants, CR gloves) for cleaning activities.

For the commercial treatment of corn seed, calculated dermal MOEs exceeded the target MOE and risks were shown to be acceptable at the PPE and engineering controls in the underlying exposure studies (closed M/L, closed transfer). This was single layer PPE (long pants, long-sleeved shirt, CR gloves) for all activities. Calculated inhalation MOEs were below the target MOE for bagger/sewer/stackers and cleaners and risks were not shown to be acceptable. To mitigate these risks, a filtering facepiece respirator (dust mask) will be required for all bagging, sewing, and stacking activities and a respirator will be required for cleaning activities. When these mitigation measures are applied, target MOEs are met and risks are shown to be acceptable. Calculated inhalation MOEs for treaters (mixer/loader/applicator) activities exceeded the target MOE and risks were shown to be acceptable without additional mitigation.

For the on-farm seed treatment and planting risk assessment (wheat, barley, oat, rye, and triticale), calculated dermal and inhalation MOEs exceeded the target MOEs and risks were shown to be acceptable at the PPE and engineering controls (closed cab) in the underlying exposure studies. This was single layer PPE (long pants, long-sleeved shirt) and CR gloves with an open mix/load system for all activities. PRVD2021-08 had proposed that the closed cab for planting requirement be waived as the calculated MOEs well exceeded the target MOE, thus providing a sufficient margin to address the protection that would be provided by a closed cab. Due to the updated toxicological reference values, the inhalation MOE is smaller and no longer meets the requirement for the waiver. Therefore, the requirement of a closed cab could not be waived. A closed cab for on-farm planting of wheat, barley, oat, rye and triticale will be required.

For loading/planting of commercially treated or imported corn seed, dermal and inhalation MOEs exceeded the target MOE and risks were shown to be acceptable at the PPE (long-sleeved shirt, long pants, CR gloves) and engineering controls (closed cab planter) in the underlying exposure study. For the loading/planting of commercially treated or imported wheat, barley, oat, rye, and triticale seeds, the dermal MOE exceeded the target MOE and risk was shown to be

acceptable at the PPE (coveralls over a long-sleeved shirt, long pants, CR gloves) and engineering controls (closed cab planter) in the underlying exposure study. The inhalation MOE was below the target MOE and risk was not shown to be acceptable. To mitigate risk, a filtering facepiece respirator (dust mask) will be required for loading and handling (not during planting using a closed cab) of treated wheat, barley, oat, rye, and triticale.

PRVD2021-08 had proposed that the closed cab for planting requirement be waived due to the calculated MOEs well exceeding the target MOEs, thus providing a sufficient margin to address the protection that would be provided by a closed cab. Due to the updated toxicological reference values, the inhalation MOE no longer meets the criteria for a waiver. Therefore, the requirement of a closed cab could not be waived. A closed cab for the commercial planting of all registered seed types will be required.

**Non-occupational exposure and risk assessment**

There are no domestic-class products containing tebuconazole registered for use in Canada. Therefore, a non-occupational handler exposure and risk assessment was not required.

The non-occupational postapplication exposure and risk assessments were revised to incorporate the updated toxicology reference values.

As presented in PRVD2021-08, exposures to vapours via the inhalation route meets the NAFTA criteria for a qualitative inhalation risk assessment based on low volatility due to a vapour pressure of $< 7.5 \times 10^{-4}$ mmHg outdoors (NAFTA, 1999). Therefore, based on a qualitative assessment, postapplication inhalation exposure is considered to be minimal.

**Golf course turf**

The updated risk assessment for postapplication dermal exposure for golfing is summarized in Table 8. MOEs exceed the target MOE for all index life stages and risks were shown to be acceptable however, all turf uses have been cancelled to reduce exposure from drinking water.

**Treated wood**

The updated postapplication risk assessment for exposure to treated wood is summarized in Table 9. MOEs exceeded the target MOE for all index life stages and risks were shown to be acceptable.

A specific dermal exposure assessment for females (13–49 years) was included in the treated wood assessment to support the aggregate risk assessment. Typically, this sub-population is addressed by other index populations; however, a specific assessment was required for this life stage as an aggregate toxicological reference value was determined for females (13–49 years) based on a different toxicology study than used for the other index life stages. No dermal absorption value was required for this calculation as the dermal aggregate toxicology reference value was based on a dermal toxicity study. The surface area/body weight (SA/BW) ratio was maintained at 280 for the females (13–49 years) life stage as this value is representative of the standard value for adults and youth (11<16 years).

A dermal postapplication MOE was not calculated for females (13–49 years) as only an exposure value was required for input into the aggregate risk assessment. For the dermal postapplication assessment, females of any life stage would be addressed by the adult and children (1<2 years) assessments.

The updated risk assessment for incidental oral exposure is summarized in Table 10. The MOE exceeds the target MOE and risks were shown to be acceptable.

**Table 1 Summary of mitigation requirements based on the updated risk assessment**

| Scenario | Required mitigation |
|---|---|
| Commercial M/L/A, unless specified below (agricultural crops) | Single layer, CR gloves |
| Commercial liquid M/L/A using MPHG (agricultural crops) | Single layer, CR gloves, and a NIOSH-approved organic-vapour removing cartridge with a prefilter approved for pesticides, or a NIOSH-approved canister approved for pesticides. |
| Commercial liquid application using a HH AB/MB (agricultural crops) | CR coveralls over long pants and long-sleeved shirt, CR gloves, socks, CR footwear and a NIOSH-approved organic-vapour removing cartridge with a prefilter approved for pesticides, or a NIOSH-approved canister approved for pesticides.<br><br>Restrict the amount handler per day to 0.06 kg a.i. per person, per day. |
| Postapplication workers (agricultural crops) | 12 hour REI, except for golf courses where the REI is “until sprays have dried” |
| Heavy duty wood preservatives | Additional PPE required for personnel who work with preservatives as per the “Recommendations for Design and Operation of Wood Preservation Facilities, 2013 Technical Recommendations Document”. |
| Seed treatment (Corn) | Use in commercial seed treatment facilities (and mobile treaters) with closed transfer including closed mixing, loading, calibrating, and closed treatment equipment only. No open transfer is permitted.<br>Treating (M/L/A) activities: Single layer PPE.<br>Bagger/sewer/stacker activities: Single layer PPE, CR gloves, and a NIOSH-approved N95 (minimum) filtering facepiece respirator (dust mask).<br>Cleaning and repair activities: Single layer PPE, CR gloves and a NIOSH-approved organic-vapour removing cartridge with a prefilter approved for pesticides, or a NIOSH- |

| Scenario | Required mitigation |
|---|---|
| | approved canister approved for pesticides.<br><br>Planting: Single layer PPE, CR gloves and use of a closed-cab tractor. |
| Seed Treatment<br>(Wheat, Barley, Oat, Rye, Triticale) | Use in commercial seed treatment facilities (and mobile treaters) with open or closed mixing, loading, calibrating, and transfer treatment equipment.<br>Treating (M/L/A) and baggers/sewer/stacker activities during commercial seed treatment: Single layer PPE, CR gloves.<br>Cleaning and repair activities: CR coveralls over long pants, long-sleeved shirt, CR gloves.<br><br>Planting commercially-treated or imported seed: Coveralls over single layer PPE, CR gloves and use of a closed-cab tractor.<br><br>On-farm seed treatment: Single layer PPE and CR gloves and use of a closed-cab tractor. |

M/L/A = mixer/loader/applicator; MPHG = mechanically pressurized hand gun; HH AB/MB = handheld airblast/mistblower; PPE = personal protective equipment; CR = chemical resistant; REI = restricted-entry interval
Single layer PPE = long-sleeved shirt, long pants

**Table 2 Short- to intermediate-term exposure and risk estimates for agricultural and turf scenarios**

| Site(s) | Equipment | Maximum application rate | ATPD | Dermal Exposure[a] (µg/kg bw/day) | Inhalation exposure[b] (µg/kg bw/day) | Dermal MOE[c] | Inhalation MOE[d] |
|---|---|---|---|---|---|---|---|
| **PPE: Single Layer PPE, CR gloves** | | | | | | | |
| SRIC (poplar and willow) | Airblast | 0.126 kg a.i./ha | 20 ha/day | 15.675 | 0.306 | 1400 | 9800 |
| | Aerial (M/L) | | 400 ha/day | 4.791 | 0.397 | 4600 | 7600 |
| | Aerial (A) | | | 0.219 | 0.006 | 100 000 | 490 000 |
| | Backpack | 1.26 g a.i./L | 150 L/day | 1.673 | 0.147 | 13 000 | 20 000 |
| | MPHW | | | 0.290 | 0.107 | 76 000 | 28 000 |
| | MPHG | | 3800 L/day | 43.458 | 9.037 | 510 | **330** |
| Asparagus | Groundboom (vegetable) | 0.126 kg a.i./ha | 26 ha/day | 0.447 | 0.095 | 49 000 | 32 000 |
| | Backpack | 0.63 g a.i./L | 150 L | 0.836 | 0.073 | 26 000 | 41 000 |
| | MPHW | | | 0.145 | 0.053 | 150 000 | 46 000 |
| | MPHG | | 3800 L | 21.729 | 4.519 | 1000 | **664** |
| Barley, Wheat | Groundboom (custom)[e] | 0.126 kg a.i./ha | 360 ha/day | 6.184 | 1.310 | 3600 | 2300 |
| | Aerial (M/L) | | | 4.791 | 0.397 | 4600 | 7600 |

**Table 2 Short- to intermediate-term exposure and risk estimates for agricultural and turf scenarios**

| Site(s) | Equipment | Maximum application rate | ATPD | Dermal Exposure[a] (µg/kg bw/day) | Inhalation exposure[b] (µg/kg bw/day) | Dermal MOE[c] | Inhalation MOE[d] |
|---|---|---|---|---|---|---|---|
| | Aerial (A) | | 400 ha/day | 0.219 | 0.006 | 100 000 | 490 000 |
| Oats, Triticale | Groundboom (custom)[e] | 0.125 kg a.i./ha | 360 ha/day | 6.135 | 1.299 | 3600 | 2300 |
| | Aerial (M/L) | | 400 ha/day | 4.753 | 0.394 | 4600 | 7600 |
| | Aerial (A) | | | 0.217 | 0.006 | 100 000 | 500 000 |
| Soybean | Groundboom (custom)[e] | 0.136 kg a.i./ha | 360 ha/day | 6.675 | 1.414 | 3300 | 2100 |
| | Aerial (M/L) | | 400 ha/day | 5.171 | 0.428 | 4300 | 7000 |
| | Aerial (A) | | | 0.236 | 0.007 | 93 000 | 460 000 |
| Spring Barley | Groundboom (custom)[e] | 0.06525 kg a.i./ha | 360 ha/day | 3.203 | 0.678 | 6900 | 4400 |
| | Aerial (M/L) | | 400 ha/day | 2.481 | 0.206 | 8900 | 15 000 |
| | Aerial (A) | | | 0.113 | 0.003 | 190 000 | 950 000 |
| Turf (sod farm and golf course) | Groundboom (small area) | 1.536 kg a.i./ha | 26 ha/day | 5.445 | 1.153 | 4000 | 2600 |
| | Turf Gun Sprayer | | 2 ha/day | 3.919 | 0.154 | 5600 | 20 000 |
| | Backpack | 2.56 g a.i./L | 150 L/day | 3.398 | 0.298 | 6500 | 10 000 |
| **PPE: (M/L) Single layer, CR gloves; (A) Maximum PPE + CR hood + Respirator** | | | | | | | |
| SRIC (poplar and willow) | HH AB/MB | 1.26 g a.i./L | 150 L/day | 10.018 | 9.310 | 2200 | **320** |
| **Mitigation required for MPHG (M/L/A): Single Layer PPE, CR gloves + Respirator** | | | | | | | |
| SRIC (poplar and willow) | MPHG | 1.26 g a.i./L | 3800 L/day | 43.458 | 0.904 | 510 | 3300 |
| Asparagus | | 0.63 g a.i./L | | 21.729 | 0.452 | 1000 | 6600 |
| **Mitigation required for HH AB/MB PPE: (M/L) Single layer, CR gloves; (A) Maximum PPE, CR hood + Respirator + Restricted amount handled per day** | | | | | | | |
| SRIC (poplar and willow) | HH AB/MB | 0.06 kg a.i./day[f] | | 0.003 | 0.003 | 7100 | 1000 |

M/L/A = mix/load/apply; ATPD = area treated per day; MOE = margin of exposure; PPE = personal protective equipment; SRIC: short rotation intensive culture; MPHG = mechanically pressurized handgun; MPHW = manually pressurized handwand; CR = chemical-resistant; HH AB/MB = handheld airblast/mistblower; NOAEL = no observed adverse effect level

Single Layer PPE = long-sleeved shirt, long pants

Maximum PPE = CR coveralls over long-sleeved shirt, long pants, socks and CR footwear, CR gloves

Respirator = NIOSH-approved organic-vapour-removing cartridge with a prefilter approved for pesticides OR a NIOSH-approved canister approved for pesticides.

**Bolded** cells indicate where MOE is below the target MOE and risks were not shown to be acceptable.

[a] Dermal exposure (mg/kg bw/day) = (dermal unit exposure × ATPD × maximum application rate × 13% dermal absorption)/80 kg body weight
[b] Inhalation exposure (mg/kg bw/day) = (inhalation unit exposure x ATPD x maximum application rate)/80 kg body weight
[c] Dermal MOE = Dermal NOAEL/Dermal Exposure. Based on a NOAEL of 22 mg/kg bw/day from an oral rat developmental neurotoxicity study; target MOE = 300.
[d] Inhalation MOE = Inhalation NOAEL/Inhalation Exposure. Based on a NOAEL of 3 mg/kg bw/day from an oral mouse developmental neurotoxicity study; target MOE = 1000.
[e] Groundboom application assessed as custom (360 ha/day) as a Tier 1 assessment. This addresses application by farmers.
[f] Maximum kg a.i. handled per day to reach target MOE = maximum application rate (1.26 g a.i./L) × amount handled per day (150 L/day) × MOE (320)/Target MOE (1000)

## Table 3 Short- to intermediate-term postapplication exposure and risk assessment for agricultural crops

| Crop | Activity | TC[a] ($cm^2$/hr) | Rate (kg a.i./ha) | Number of Applications per year | Min intervals between applications (Days) | MOE[b] (Day 0) | REI[c] (hrs) |
|---|---|---|---|---|---|---|---|
| SRIC (poplar and willow) | Harvest (seedling production) | 6700 | 0.126 | 2 | 14 | 650 | 12 |
| | Irrigation (hand set) | 1750 | | | | 2500 | |
| | Harvest | 1400 | | | | 3100 | |
| | Hand Pruning, Scouting | 580 | | | | 7500 | |
| | Transplanting, Hand Weeding | 230 | | | | 19 000 | |
| Asparagus | Irrigation (hand set) | 1750 | 0.126 | 4 | 14 | 2400 | 12 |
| | Harvesting | 1100 | | | | 3800 | |
| | Transplanting | 230 | | | | 18 000 | |
| | Scouting | 210 | | | | 20 000 | |
| | Hand Weeding | 70 | | | | 59 000 | |
| Barley | Scouting | 1100 | 0.126 | 1 | - | 4900 | 12 |
| Spring Barley | Scouting | 1100 | 0.066 | 2 | 14 | 7700 | 12 |
| Oats | Scouting | 1100 | 0.125 | 2 | 14 | 4000 | 12 |
| | Hand Weeding | 70 | | | | 63 000 | |
| Soybean | Scouting | 1100 | 0.136 | 2 | 10 | 3400 | 12 |
| | Hand Weeding | 70 | | | | 53 000 | |
| Triticale | Scouting | 1100 | 0.125 | 1 | - | 4900 | 12 |
| | Hand Weeding | 70 | | | | 77 000 | |
| Wheat | Scouting | 1100 | 0.126 | 1 | - | 4000 | 12 |
| | Hand Weeding | 70 | | | - | 62 000 | |
| Turf – Sod Farms[d] | Harvesting (Slab), Transplanting/Planting | 6700 | 1.536 | 2 | 14 | 1300 | 12 |
| | Irrigation, Mowing, Watering | 3500 | | | | 2600 | |

| Crop | Activity | TC[a] ($cm^2$/hr) | Rate (kg a.i./ha) | Number of Applications per year | Min intervals between applications (Days) | MOE[b] (Day 0) | REI[c] (hrs) |
|---|---|---|---|---|---|---|---|
| | Aerating, Fertilizing, Hand Pruning, Mechanical Weeding, Scouting, Seeding | 1000 | | | | 9000 | |
| Turf – Golf Courses[d] | Transplanting/ Planting, Cup Changing, Irrigation Repair, Mowing, Watering, Grooming | 3500 | 1.536 | 2[e] | 14 | 2600 | Sprays have dried[f] |
| | Aerating, Fertilizing, Hand Pruning, Mechanical Weeding, Scouting, Seeding | 1000 | | | | 9000 | |

MOE = margin of exposure; REI = restricted-entry interval; TC = transfer coefficient; Min = minimum; SRIC = short rotation intensive culture; NOAEL = no observed adverse effect level; DFR = Dislodgeable foliar residue; TTR = turf transferable residue.

There were no chemical-specific DFR or TTR studies submitted. Therefore, a standard peak DFR value of 25%, with a 10% dissipation per day and a standard peak TTR value of 1% of the application rate with a 10% dissipation per day were used.

[a] Values from PMRA memo (PMRA, 2012a), Surrogate TCs were used (Spring barley for barley, wheat [winter/spring] for oats and forestry for SRIC)

[b] MOE = NOAEL/Exposure Based on a NOAEL of 22 mg/kg bw/day from an oral rat developmental neurotoxicity study; target MOE = 300.

[c] Day at which dermal exposure results in an MOE greater than the target MOE.

[d] The maximum rate (2 applications; 14 day interval) was used as this addresses the lower rate (5 applications; 14 day interval) scenarios.

[e] Not stated on label (based on max product rate: 2 applications at high rate).

[f] Golf courses: re-entry statement of "DO NOT enter, or allow entry until sprays have dried". However, all turf uses have been cancelled to reduce exposure from drinking water.

## Table 4 Short- to long-term occupational exposure and risk assessment for heavy duty wood preservatives

| Application method | Worker category | Absorbed dermal exposure (mg/kg bw/day)[a] | Inhalation exposure (mg/kg bw/day)[b] | Dermal MOE[c] | Inhalation MOE[d] |
|---|---|---|---|---|---|
| **PPE = Single layer, CR gloves[e]** | | | | | |
| Pressure Retort | TO | $2.08 \times 10^{-3}$ | $3.65 \times 10^{-4}$ | 11 000 | 8200 |
| | WH | $8.97 \times 10^{-3}$ | $1.73 \times 10^{-3}$ | 2500 | 1700 |

TO = Treatment Operators; WH = Wood Handlers; MOE = margin of exposure; DA = dermal absorption; bw = body weight; NOAEL = no observed adverse effect level; PPE = personal protection equipment; CR = chemical-resistant

Single layer = long-sleeved shirt, long pants

[a] Calculated using unit exposure values from Bookbinder (2014). Dermal Exposure (mg/kg bw/day) = Unit Exposure (µg/%a.i.) × concentration of treating solution (1% a.i.) × DA (13%)/bw (80 kg)

[b] Calculated using unit exposure values from Bookbinder (2014). Inhalation Exposure (mg/kg bw/day) = Unit Exposure (µg/%a.i.) × concentration of treating solution (1% a.i.)/bw (80 kg)

[c] Dermal MOE = Dermal NOAEL/Dermal Exposure. Based on a NOAEL of 22 mg/kg bw/day from an oral rat developmental neurotoxicity study; target MOE = 300.
[d] Inhalation MOE = Inhalation NOAEL/Inhalation Exposure. Based on a NOAEL of 3 mg/kg bw/day from an oral mouse developmental neurotoxicity study; target MOE = 1000.
[e] Additional PPE is required for personnel who work with preservatives as per the "Recommendations for Design and Operation of Wood Preservation Facilities, 2013 Technical Recommendations Document (TRD)" (ECCC, 2013), which is enforced by Environment and Climate Change Canada.

## Table 5 Short- to intermediate-term commercial seed treatment exposure and risk assessment

| Crop | Study formulation[a] | Activity[b] | Application rate (g a.i./kg seed)[c] | Throughput (kg seed/day) | Dermal MOE[d] | Inhalation MOE[e] |
|---|---|---|---|---|---|---|
| **PPE: Single Layer, CR gloves; Open M/L (Krolski, 2006)** | | | | | | |
| Wheat, Barley, Oats, Rye, Triticale | Liquid | Treating | 0.03 | 325700 | 5200 | 9900 |
| **PPE: Single Layer, CR gloves (Wilson, 2009)** | | | | | | |
| Wheat, Barley, Oats, Rye, Triticale | Liquid | Bagging/Sewing/Stacking | 0.03 | 325700 | 78000 | 28000 |
| **PPE: CR coveralls over single layer, CR gloves (Wilson, 2009)** | | | | | | |
| Wheat, Barley, Oats, Rye, Triticale | Liquid | Cleaning and Repairing | 0.03 | - | 240000 | 130000 |
| **PPE: Single Layer, CR gloves; Closed M/L, Closed Transfer (Krolski, 2010)** | | | | | | |
| Corn | Liquid | Treating | 0.15 | 125000 | 2800 | 3400 |
| | | Bagging/Sewing/Stacking | | | 6300 | **684** |
| | | Cleaning and Repairing | | - | 7100 | **664** |
| **PPE: Single Layer, CR gloves + FFR (as mitigation) (Krolski, 2010)** | | | | | | |
| Corn | Liquid | Bagging/Sewing/Stacking | 0.15 | 125000 | 6300 | 3400 |
| **PPE: Single Layer, CR gloves + Respirator (as mitigation) (Krolski, 2010)** | | | | | | |
| Corn | Liquid | Cleaning and Repairing | 0.15 | - | 7100 | 6600 |

MOE = margin of exposure; MLA = Mixer/Loader/Applicator; NOAEL = No observed adverse effects level; PPE = personal protection equipment; CR = chemical-resistant; DA = dermal absorption; bw = body weight; FFR = filtering facepiece respirator
**Bolded** cells indicate target MOE not met.
Single layer = long-sleeved shirt, long pants, CR gloves
FFR = NIOSH-approved N95 (minimum) filtering facepiece respirator (dust mask) that is properly fit tested.
Respirator = NIOSH-approved organic-vapour-removing cartridge with a prefilter approved for pesticides OR a NIOSH-approved canister approved for pesticides.
[a] Liquid formulation addresses exposure to wettable powders in water soluble packaging.
[b] Activities are based on what was monitored in the surrogate exposure studies.
[c] Maximum application rates were used in the assessment. Cleaning activities were normalized to the application rate rather than the amount handled.

[d] Where: MOE = NOAEL/Exposure, based on a NOAEL of 22 mg/kg bw/day from an oral rat developmental neurotoxicity study. Exposure (mg/kg bw/day) = (Unit exposure (µg/kg a.i.) × Application Rate (g a.i./kg seed) × Throughput (kg seed/day) × DA (13%) × 0.001 mg/µg/bw (80 kg). Target MOE = 300.
[e] Where: MOE = NOAEL/Exposure, based on a NOAEL of 3 mg/kg bw/day from an oral mouse developmental neurotoxicity study. Exposure (mg/kg bw/day) = (Unit exposure (µg/kg a.i.) × Application Rate (g a.i./kg seed) × Throughput (kg seed/day) × DA (13%) × 0.001 mg/µg/bw (80 kg). Target MOE = 1000.

## Table 6 Short- to intermediate-term on-farm seed treatment and planting exposure and risk assessment

| Crop | Formulation[a] | Activity | Application Rate (g a.i./kg seed)[b] | Throughput (kg seed/day)[c] | Dermal MOE[d] | Inhalation MOE[e] |
|---|---|---|---|---|---|---|
| **PPE: Single Layer, CR gloves; Open M/L, Closed Cab Planter (Krolski, 2006)** | | | | | | |
| Wheat, Barley, Oats, Rye, Triticale | Liquid | All Tasks (loading/treating/planting) | 0.03 | 60000 | 52000 | 18000 |

MOE = margin of exposure; PPE = personal protection equipment; NOAEL = no observed adverse effect level; CR = chemical-resistant; M/L = mixer/loader; DA = dermal absorption; bw = body weight
Single layer PPE = long pants, long-sleeved shirt
[a] Liquid formulation includes suspensions and wettable powder in water soluble packages.
[b] Maximum application rates were used in the assessment.
[c] Farm throughput data are based on areas planted per day and high-end seeding rates.
[d] Where: MOE = NOAEL/Exposure, based on a NOAEL of 22mg/kg bw/day from an oral rat developmental neurotoxicity study. Exposure (mg/kg bw/day) = (Unit exposure (µg/kg a.i.) × Application Rate (g a.i./kg seed) × Throughput (kg seed/day) × DA (13%) × 0.001 mg/µg/bw (80 kg). Target MOE = 300.
[e] Where: MOE = NOAEL/Exposure, based on a NOAEL of 3 mg/kg bw/day from an oral mouse developmental neurotoxicity study. Exposure (mg/kg bw/day) = (Unit exposure (µg/kg a.i.) × Application Rate (g a.i./kg seed) × Throughput (kg seed/day) × DA (13%) × 0.001 mg/µg/bw (80 kg). Target MOE = 1000.

## Table 7 Short- to intermediate-term planting exposure and risk assessment for commercially treated and bagged seed[a]

| Crop | Formulation | Application rate (g a.i./kg seed)[b] | Seeding rate (kg seed/ha) | Farm size planted per day (ha/day) | Dermal MOE[c] | Inhalation MOE[d] |
|---|---|---|---|---|---|---|
| **PPE: Single Layer, CR gloves; Open Loading, Closed Cab Planter (Zeitz, 2007)[e]** | | | | | | |
| Corn | Liquid | 0.150 | 31.5 | 100 | 18 000 | 6300 |
| **PPE: Coveralls over single layer, CR gloves; Open Loading, Closed Cab Planter (Krainz, 2013)** | | | | | | |
| Wheat, Barley, Oats, Rye, Triticale | Liquid | 0.03 | 209.88[f] | 162 | 11 000 | **652** |

| Crop | Formulation | Application rate (g a.i./kg seed)[b] | Seeding rate (kg seed/ha) | Farm size planted per day (ha/day) | Dermal MOE[c] | Inhalation MOE[d] |
|---|---|---|---|---|---|---|
| **PPE: Coveralls over single layer, CR gloves, FFR (dust mask) during loading /handling of treated seed (NOT during planting in a closed cab); Open Loading, Closed Cab Planter (Krainz, 2013)** | | | | | | |
| Wheat, Barley, Oats, Rye, Triticale | Liquid | 0.03 | 209.88[f] | 162 | 11 000 | 3300 |

PPE = personal protective equipment; MOE = margin of exposure; CR = chemical-resistant; bw = body weight; NOAEL = no observed adverse effect level; FFR = filtering facepiece respirator
Single layer PPE = long-sleeved shirt, long pants
FFR (dust mask) = NIOSH-approved N95 (minimum) filtering facepiece respirator (dust mask) that is properly fit tested.
**Bolded** cells indicate where MOEs are below the target MOE and risks were not shown to be acceptable.
[a] Planting on-farm treated seed was covered in the on-farm exposure studies. Planting commercial bulk seed is considered to be addressed by on-farm treating and planting of seed as there is no additional exposure from loading seed from bags.
[b] Maximum application rates were used in the assessment.
[c] Where: MOE = NOAEL/Exposure, based on a NOAEL of 22 mg/kg bw/day from an oral rat developmental neurotoxicity study. Exposure (mg/kg bw/day) = (Unit exposure (µg/kg a.i.) × Application Rate (g a.i./kg seed) × Throughput (kg seed/day) × DA (13%) × 0.001 mg/µg/bw (80 kg). Target MOE = 300. Combined MOE = 1/[1/dermal MOE + 1/inhalation MOE], Target = 300
[d] Where: MOE = NOAEL/Exposure, based on a NOAEL of 3 mg/kg bw/day from an oral mouse developmental neurotoxicity study. Exposure (mg/kg bw/day) = (Unit exposure (µg/kg a.i.) × Application Rate (g a.i./kg seed) × Throughput (kg seed/day) × DA (13%) × 0.001 mg/µg/bw (80 kg). Target MOE = 1000.
[e] The dermal unit exposure value of 1606.9 µg/kg a.i. and the inhalation unit exposure value of 80.88 µg/kg a.i. were used in the assessment. These values were recently updated following a secondary review of this study to reflect current policies.
[f] Maximum value from triticale. Addresses seeding rate from barley, oats, rye, and wheat.

## Table 8 Short-term postapplication dermal exposure and risk assessment on golf course turf

| Scenario | TC[a] ($cm^2$/hr) | TTR[b] (ug/$cm^2$) | Dermal exposure[c] (mg/kg bw/day) | Dermal MOE[d] |
|---|---|---|---|---|
| **Postapplication Exposure to Golf Course Turf** | | | | |
| Adult | 5300 | 0.19 | 0.0065 | 3400 |
| Youth (11<16 years) | 4400 | | 0.0076 | 2900 |
| Children (6<11 years) | 2900 | | 0.0089 | 2500 |

TC = transfer coefficient; TTR = turf transferable residue; MOE = margin of exposure; NOAEL = no observed adverse effect level; bw = body weight
[a] Transfer coefficient standard values from the USEPA Residential SOPs (USEPA, 2012) were used.
[b] Turf transferable residues were calculated based on a standard peak value of 1% of the maximum application rate (1536 g a.i./ha) and a daily dissipation rate of 10% per day. Two applications at the maximum application rate with a 14 day interval were considered in the calculation as it addresses the lower application rate (608 g a.i./ha; 5 applications, 14 day interval) scenario.
[c] Dermal exposure (mg/kg bw/day) = TTR (µg/$cm^2$) × TC ($cm^2$/hr) × Duration (4 hrs) × Dermal Absorption (13%)/bw (80 kg for adults, 57 kg for youth (11<16 years) and 32 kg for children (6<11 years)).
[d] MOE = NOAEL/Exposure. Adult, youth (11<16 years), and children (6<11 years) MOEs are based on a NOAEL of 22 mg/kg bw/day from an oral rat developmental neurotoxicity study; Target MOE = 300.

## Table 9 Short-term postapplication dermal exposure from treated wood

| Life stage | Transferable residue ($mg/cm^2$)[a] | SA/BW ($cm^2/kg$) | $F_{body}$ | Dermal exposure (mg/kg bw/day)[b] | Dermal MOE[c] |
|---|---|---|---|---|---|
| Adult | 0.000858 | 280 | 0.31 | 0.0097 | 2300 |
| Children (1<2 years) | | 640 | | 0.0221 | 990 |
| Females (13–49 years) | | 280 | | 0.0745 | Not applicable [d] |

SA/BW = surface area to body weight ratio; $F_{body}$ = fraction of body exposed; MOE = margin of exposure; DA = Dermal Absorption; NOAEL = no observed adverse effect level; bw = body weight

[a] Transferable residue = 0.858 µg/$cm^2$ (Minchin and Morris, 2014) (Day 0 average).

[b] Dermal Exposure (mg/kg bw/day) = Transferable Residue ($mg/cm^2$) × SA/BW ($cm^2/kg$) × $F_{body}$ × DA (13%) (DA value not required for female (13–49 years) exposure calculation as the dermal aggregate toxicological reference value is based on a dermal toxicology study).

[c] MOE = NOAEL/Exposure. Based on an oral NOAEL of 22 mg/kg bw/day from a rat developmental neurotoxicity study; Target MOE = 300.

[d] This index life stage was only calculated to support the aggregate risk assessment. A female (13–49 years) dermal postapplication MOE was not calculated in this table as the exposure value is representative of exposure for comparison to a dermal toxicological reference value. The exposure calculation for females (13–49 years) does not include the dermal absorption value used for the exposure calculations used for the other index life stages in this table, which is part of the standard equation when comparing to a toxicological reference values based on an oral study. For the dermal postapplication assessment, females of any life stage would be address by the adult and children (1<2 years) assessment.

## Table 10 Short-term postapplication hand-to-mouth exposure and risk assessment for children (1<2 years) [a]

| Exposure scenario | Hand residue ($mg/cm^2$)[a] | ET (hours) | Oral dose (mg/kg bw/day)[b] | MOE[c] |
|---|---|---|---|---|
| Residues from treated wood | 0.000858 | 1.5 | 0.0082 | 2700 |

ET = exposure time; MOE = margin of exposure; NOAEL = no observed adverse effect level

[a] Transferable residue = 0.858 µg/$cm^2$ (Day 0 average) (Minchin and Morris, 2014).

[b] Where Oral Dose (mg/kg bw/day) = [Hand Residue ($mg/cm^2$) × Fraction of hand mouthed/event (0.13) × Surface Area of one hand (150 $cm^2$)) × ET (hr) × Replenishment Intervals (4/hr) × (1 – (1 – Saliva Extraction Factor (0.48)) Number events per hour (14)/Replenishment Intervals (4/hr))]/ Body Weight (11 kg).

[c] MOE = NOAEL/Exposure. Based on a NOAEL of 22 mg/kg bw/day from an oral rat developmental neurotoxicity study; Target MOE = 300.

# Appendix VII Revised aggregate exposure and risk assessment

The aggregate assessments were updated due to the updated toxicology points of departure. Results are summarized in Tables 1 and 2.

For tebuconazole, the following scenarios that were expected to co-occur are:

- Postapplication dermal exposure (adult) from postapplication activities with and on treated wood + chronic dietary (food and drinking water).
- Postapplication dermal exposure (females (13–49 years)) from postapplication activities with and on treated wood + chronic dietary (food and drinking water).
- Postapplication dermal exposure (children (1 < 2 years)) + incidental oral exposure from postapplication activities on treated wood + chronic dietary (food and drinking water).

Typically the adults and children (1 < 2 years) index life stages address all other life stages. However, an aggregate toxicological reference value was determined for females (13–49 years) based on a dermal toxicology study. As the toxicology reference values for adults and children (1 < 2 years) were based on oral studies, they could not be used to address this life stage and a specific risk assessment was required for females (13–49 years). Refer to Appendix VI for more information.

As all uses on turf are required to be cancelled to reduce exposure from drinking water, an aggregate assessment for the turf scenario was not required. For treated wood, aggregate margin of exposures were greater than the target margin of exposure and risks were shown to be acceptable for all index life stages. No additional risk mitigation measures are required.

**Table 1 Short-term aggregate exposure and risk assessment**

| Population | PA scenario | PA dermal exposure[a] (mg/kg bw/day) | Incidental oral exposure[b] (mg/kg bw/day) | Dietary exposure[c] (mg/kg bw/day) | Total exposure[d] (mg/kg bw/day) | Aggregate MOE[e] |
|---|---|---|---|---|---|---|
| **Treated wood** | | | | | | |
| Adult 16+ | Contact with Treated Wood | 0.0097 | N/A | 0.00067 | 0.0104 | 2100 |
| Children (1<2 years) | | 0.0221 | 0.0082 | 0.00183 | 0.0321 | 680 |

PA = postapplication; MOE = margin of exposure; NOAEL = no observed adverse effect level

[a] Postapplication dermal exposures from Appendix VI, Table 9)

[b] Value taken from Appendix VI, Table 10.

[c] Based on the dietary risk assessment (Appendix V, Table 2)

[d] Total Exposure (mg/kg bw/day) = Total Dermal Exposure + Chronic Dietary Exposure + Incidental oral Exposure (if applicable)

[e] Aggregate MOE = Aggregate NOAEL/Total Exposure. NOAEL of 22 mg/kg bw/day based on an oral rat developmental neurotoxicity study; target MOE = 300.

**Table 2 Short-term aggregate exposure and risk assessment (females (13–49 years))**

| Population | PA scenario | PA dermal exposure[a] (mg/kg bw/day) | Dermal aggregate MOE[b] | Dietary exposure[c] (mg/kg bw/day) | Oral MOE[d] | Aggregate ARI[e] |
|---|---|---|---|---|---|---|
| **Treated Wood** | | | | | | |
| Females (13–49 years) | Contact with Treated Wood | 0.0745 | 3700 | 0.00067 | 4500 | 3.29 |

PA = postapplication; MOE = margin of exposure; NOAEL = no observed adverse effect level; ARI = aggregate risk index

[a] Postapplication dermal exposures from Appendix VI, Table 9.

[b] Dermal Aggregate MOE = NOAEL/Dermal Exposure. NOAEL of 275 mg/kg bw/day based on a dermal developmental toxicity study in mice; target MOE = 300.

[c] Based on the dietary risk assessment (Appendix V, Table 2)

[d] Oral MOE = NOAEL/Oral Exposure. NOAEL of 3 mg/kg bw/day based on an oral developmental toxicity study in mice; target MOE = 1000.

[e] Aggregate ARI = $1/((\text{Target MOE}_{dermal}/\text{MOE}_{dermal}) + (\text{Target MOE}_{oral}/\text{MOE}_{oral}))$. Target ARI = 1.

# Appendix VIII Details of the NAFTA degradation kinetics of the submitted studies, as calculated by Health Canada

**Waseca, Minnesota, USA (Turf) (PMRA# 2456673)**
The dissipation kinetics calculated by the registrant were based on the entire system (turf and soil), which is not acceptable as a modelling input. The turf grass portion dominates the soil contribution when considering the entire system, producing a half-life nearly identical to the turf grass alone. This study was not included in the USEPA "Tebuconazole – Drinking Water Assessment for Registration Review" (USEPA, 2021) reanalysis using field dissipation studies.

When only the soil data is considered, the observed degradation is stable indicating no effect over the duration of the study; therefore, looking at the soil-only system, Health Canada determined that a representative half-life cannot be determined from this soil.

**Table 1 Dissipation kinetics of Waseca, Minnesota, USA (Turf, PMRA# 3282138)**

| System | Re-evaluated dissipation kinetics (to the 15 cm depth) | |
|---|---|---|
| Total system (turf grass and soil) | Model: | SFO |
| | k: | 0.01047 $day^{-1}$ |
| | $DT_{50}$ | 66.04 days |
| | $t_{rep}$ | 66.04 days |
| Turf grass | model: | SFO |
| | k: | 0.01053 $day^{-1}$ |
| | $DT_{50}$ | 65.84 days |
| | $t_{rep}$ | 66.04 days |
| soil | Model: | zero slope line (all models) |
| | k: | 0 $day^{-1}$ |
| | $DT_{50}$ | indeterminate |
| | $t_{rep}$ | indeterminate |

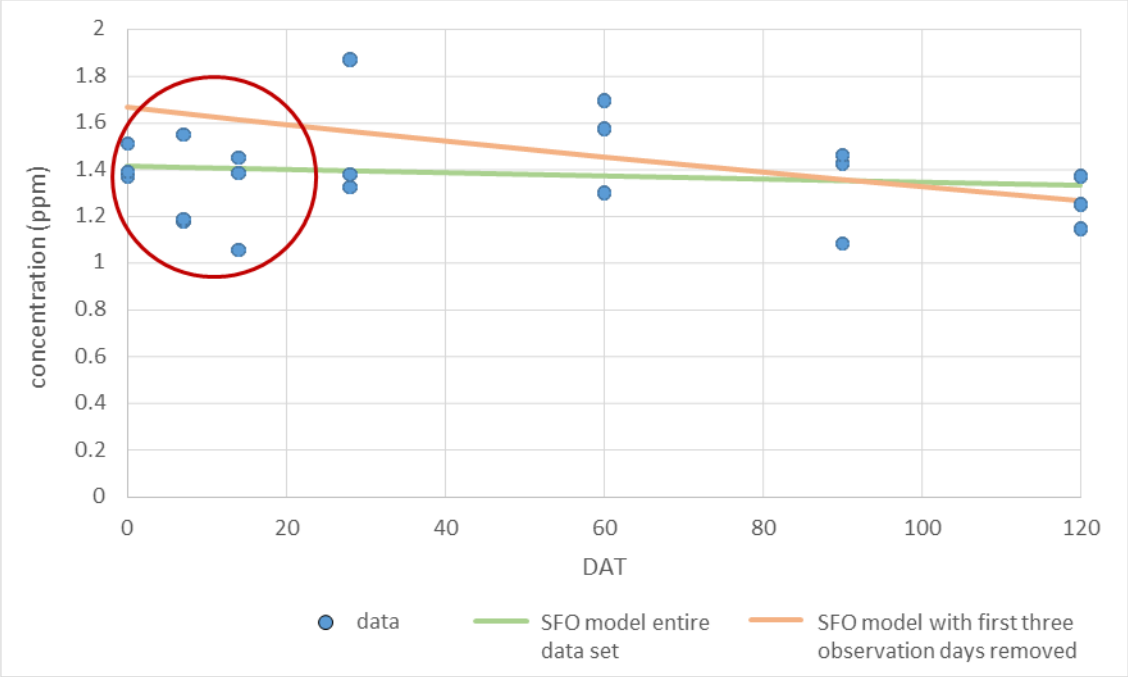
**Glenmark, New York, USA (Turf) (PMRA# 3282139)**
The registrant calculated dissipation kinetics using the day of the highest observed concentration, but eliminated the first three observations (0, 7 and 14 days after last application) without proper scientific justification and left only four observations used in the kinetic evaluation, which is also not acceptable. This approach also left the data analysis from this study treated differently from the remaining studies, which creates problems when including it in the distribution of studies considered in the dissipation assessment. This study was not included in the USEPA "Tebuconazole – Drinking Water Assessment for Registration Review" (USEPA, 2021) reanalysis using field dissipation studies.

Health Canada determined that the SFO model was the best fit and the resulting $DT_{50}$ is 1404 days.

**Table 2 Dissipation kinetics of Glenmark, New York, USA (Turf)**

| System | Re-evaluated dissipation kinetics (to the 15 cm depth) |
|---|---|
| Soil<br>(all data) | Model: SFO<br>k: 0.0004936 $day^{-1}$<br>$DT_{50}$ 1404 days<br>$t_{rep}$ 1404 days |
| Soil<br>(truncated data set)<br>(as a comparison only) | Model: SFO<br>k: 0.002305 $day^{-1}$<br>$DT_{50}$ 300.8 days<br>$t_{rep}$ 300.8 days |

**Figure 1 Data Set Differences for Glenmark, New York, USA (Turf)**




**Belleville, Wisconsin, USA (Turf) (PMRA# 3282140)**

Health Canada confirmed that, using prior methodology, the $DT_{50}$ for a SFO determination was 163.3 days (thus the study $t_{rep}$ is 163.3 days); however, using procedures from the NAFTA guidance it was found that a DFOP model was the most appropriate fit to the data. This study was included in the USEPA "Tebuconazole – Drinking Water Assessment for Registration Review" (USEPA, 2021) reanalysis using field dissipation studies.

Health Canada determined that the $t_{rep}$ is 149.3 days (DFOP $DT_{50}$ 87.26 days).

**Table 3 Dissipation Kinetics of Belleville, Wisconsin, USA (Turf)**

| System | Re-evaluated dissipation kinetics (to the 15 cm depth) | |
|---|---|---|
| Soil | Model: | DFOP |
| | $k_0$: | 0.3182 $day^{-1}$ |
| | $k_1$: | 0.004642 $day^{-1}$ |
| | $DT_{50}$ | 87.26 days |
| | $t_{rep}$ | 149.3 days |

**Belleville, Wisconsin, USA (Bare ground, but planted to grass seed after application) (PMRA# 3282141)**

Health Canada confirmed that using prior methodology the $DT_{50}$ for a SFO determination was 216.3 days (thus the $t_{rep}$ is 216.3 days). Using procedures from the NAFTA guidance it was found that the DFOP model was the most appropriate fit to the data. This study was included in the USEPA "Tebuconazole – Drinking Water Assessment for Registration Review" (USEPA, 2021) reanalysis using field dissipation studies.

Health Canada determined that the $t_{rep}$ is 333.1 days (DFOP $DT_{50}$ 135.9 days).

**Table 4 Dissipation Kinetics of Belleville, Wisconsin, USA (Bare ground)**

| System | Re-evaluated dissipation kinetics (to the 15 cm depth) | |
|---|---|---|
| Soil | Model: | DFOP |
| | $k_0$: | 0.05890 $day^{-1}$ |
| | $k_1$: | 0.002081 $day^{-1}$ |
| | $DT_{50}$ | 135.9 days |
| | $t_{rep}$ | 333.1 days |

**Canada – EcoRegion 9.2: Minto, Manitoba (bare soil and cropped system) (PMRA# 1522419)**

Health Canada confirmed through re-assessment the values presented in the study report (within acceptable error) for the upper 15-cm layer; however, only the $DT_{50}$ values for the DFOP fitted models are presented in the study report whereas the $t_{rep}$ values are required for modelling. This study was not included in the USEPA "Tebuconazole – Drinking Water Assessment for Registration Review" (USEPA, 2021) reanalysis using field dissipation studies.

Health Canada determined that the $t_{rep}$ values for bare soil for Years 1, 2, and 3 of the study are 2903, 298.5, and 211.7 days, respectively. For the cropped system, Health Canada could not determine a representative half-life for Year 1; however, for Years 2 and 3, the $t_{rep}$ values are 1650 and 1244 days, respectively.

**Table 5 Dissipation Kinetics of Minto, Manitoba, Canada (Bare soil)**

| System | Re-evaluated dissipation kinetics (to the 15 cm depth) | |
|---|---|---|
| Bare soil (year 1) | Model: | DFOP |
| | $k_0$: | 0.05739 $day^{-1}$ |
| | $k_1$: | 0.0002387 $day^{-1}$ |
| | $DT_{50}$ | 59.94 days (study report 57.5 days) |
| | $t_{rep}$ | 2903 days |
| Bare soil (year 2) | Model: | DFOP |
| | $k_0$: | 0.6185 $day^{-1}$ |
| | $k_1$: | 0.002322 $day^{-1}$ |
| | $DT_{50}$ | 37.13 days (study report 37.5 days) |
| | $t_{rep}$ | 298.5 days |
| Bare soil (year 3) | Model: | DFOP |
| | $k_0$: | 0.4717 $day^{-1}$ |
| | $k_1$: | 0.003274 $day^{-1}$ |
| | $DT_{50}$ | 87.28 days (study report 77.2 days) |
| | $t_{rep}$ | 211.7 days |
| Cropped system (year 1) | Data produced an indeterminate evaluation (slope = 0) | |
| Cropped system (year 2) | Model: | SFO |
| | k: | 0.004201 $day^{-1}$ |
| | $DT_{50}$ | 1650 days |
| | $t_{rep}$ | 1650 days |
| Cropped system (year 3) | Model: | DFOP |
| | $k_0$: | 0.4717 $day^{-1}$ |
| | $k_1$: | 0.003274 $day^{-1}$ |
| | $DT_{50}$ | 87.28 days (study report 77.2 days) |
| | $t_{rep}$ | 1244 days |

# Appendix IX Label amendments for products containing tebuconazole

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

## 1.1 General directions for use

For labels with asparagus, and short rotation intensive culture Poplar and Willow use, in the Disease/Use Rate table:

- The number of foliar applications per year for asparagus, and short rotation intensive culture Poplar and Willow are reduced to 1 application at 126 g a.i./ha.

For labels with soybean use, in the Disease/Use Rate table:

- The number of foliar applications per year for soybean are reduced to either 1 application at 136 g a.i./ha or 2 applications at 65 g a.i./ha at a minimum 10-day interval.

Note: No label changes are required for the following uses: foliar application uses on barley, oats and wheat, as well as seed treatment uses on barley, corn, rye, oats, triticale and wheat (as the maximum yearly total rates of these uses are all at or below 136 g a.i./ha).

The following statement is required on all end-use products with agricultural uses, unless the current label directions are more restrictive.

- Under a “Crop Rotation” sub header: “A rotational plantback interval of 120 days must be observed for crops not listed on the label.”

A summary of accepted tebuconazole uses is specified in the table below.

| Crop | Maximum single application rate (g a.i./ha) | Maximum number of applications per year | Maximum total rate per year (g a.i./ha) | Retreatment interval (days) | Application methods |
|---|---|---|---|---|---|
| Asparagus | 126 | 1 | 126 | N/A | Foliar |
| Barley | 126 | 1 | 126* | N/A | Foliar |
| | 65 | 2 | 130* | 14 | Foliar |
| Oats | 125 | 1 | 125* | N/A | Foliar |
| | 65 | 2 | 130* | 14 | Foliar |
| Short Rotation Intensive Culture (Poplar and | 126 | 1 | 126 | N/A | Foliar |

| Crop | Maximum single application rate (g a.i./ha) | Maximum number of applications per year | Maximum total rate per year (g a.i./ha) | Retreatment interval (days) | Application methods |
|---|---|---|---|---|---|
| Willow) | | | | | |
| Soybean | 136 | 1 | 136* | N/A | Foliar |
| | 65 | 2 | 130* | 10 | Foliar |
| Wheat | 126 | 1 | 126* | N/A | Foliar |
| | 65 | 2 | 130* | 14 | Foliar |
| Barley | 3 g a.i. /100 kg seed | 1 | N/A | N/A | Seed treatment |
| Corn (all types) | 15 g a.i. /100 kg seed | 1 | N/A | N/A | Seed treatment |
| Oats | 3 g a.i. /100 kg seed | 1 | N/A | N/A | Seed treatment |
| Rye | 1.5 g a.i. /100 kg seed | 1 | N/A | N/A | Seed treatment |
| Triticale | 1.5 g a.i. /100 kg seed | 1 | N/A | N/A | Seed treatment |
| Wheat | 3 g a.i. /100 kg seed | 1 | N/A | N/A | Seed treatment |

N/A - Not applicable
* Maximum total rate per year is calculated based on the maximum number of applications (1 or 2) permitted per year.

The maximum seasonal rate permitted for any product or combination of products containing tebuconazole is 136 g a.i./ha. Therefore the sequential application tables from the following tebuconazole product labels must be removed: FOLICUR 432 F Foliar Fungicide (Registration No. 25940), PROSARO 421 SC Foliar Fungicide (Registration No. 29819), PROSARO 250 EC Fungicide (Registration No. 29821), PALLISER Foliar Fungicide (Registration No. 30491), HORNET 432 F Foliar Fungicide (Registration No. 32500), PROSARO XTR Fungicide (Registration No. 32824), TILMOR 240 EC Fungicide (Registration No. 33825), TEBBIE Foliar Fungicide (Registration No. 33901), PROSARO PRO Foliar Fungicide (Registration No. 34093), Shalimar Fungicide (Registration No. 34357), TEBUSTAR 432 Foliar Fungicide (Registration No. 34372), FBN ProTEB 250 EC (Registration No. 34868) and Advantage Prothio + Teb 250 EC (Registration No. 34975).

**Precautions:**

Drift statement

In order to promote best practices, and to minimize human exposure from spray drift or from spray residues resulting from drift due to the agriculture and turf use of tebuconazole, 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."

Personal protection equipment and equipment restrictions

For mixing, loading, and application using all other application equipment, the following label statements are required on all commercial-class product labels, unless more protective statements are already present:

> "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."

For application using a handheld airblast/mistblower, the following label statement is required:

> "For application using handheld airblast/mistblower equipment, wear chemical-resistant coveralls with a chemical-resistant hood over long-sleeved shirt, long pants, chemical-resistant gloves, socks, chemical-resistant footwear and a respirator with a NIOSH-approved organic-vapour-removing cartridge with a prefilter approved for pesticides OR a NOSH-approved canister approved for pesticides."
>
> "**DO NOT** handle more than [*0.06 kg a.i. to be reported in product equivalent value*] per person, per day when using a handheld airblast/mistblower. These restrictions are in place to minimize exposure to individual applicators. Application may need to be performed over multiple days or using multiple applicators."

For mixing, loading, and application of liquid products to agricultural crops using a mechanically-pressurized handgun, the following label statement is required:

"When mixing, loading and applying using a mechanically-pressurized handgun, wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes, 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 during mixing, loading, application, clean-up and repair."

Restricted-entry intervals

The following statement is required to be added to all commercial-class end-use products that have uses for agricultural crops, unless more protective statements are already present:

> "**DO NOT** enter or allow worker entry into treated areas during the restricted-entry interval of 12 hours."

### 1.2 Seed treatment end-use products

**On the principal panel:**

In order to promote best practices, and to minimize human exposure from spray drift or from spray residues resulting from drift due to the use of tebuconazole, the following label statement is required:

> "Apply only in a way that this product will not contact workers or other persons, either directly or through drift. Only workers wearing personal protective equipment may be in the area when seed is being treated or bagged."

The following statements are required to be added to all commercial-class seed treatment end-use products:

For corn:

> "For corn, only permitted for use in commercial seed treatment (facilities and mobile treaters) with closed transfer including closed mixing, loading, calibrating, and closed treatment equipment only. No open transfer is permitted."

For wheat, barley, rye, triticale, and oats:

"For [wheat, barley, rye, triticale, and oats, *as per label*], only permitted for use in commercial and on-farm seed treatment (facilities and mobile treaters) with open or closed transfer treatment equipment."

**Under precautions:**

Label statements must be amended (or added to) unless the current label mitigation is more restrictive.

| Seed types | Tasks | Personal protective equipment/Engineering controls |
|---|---|---|
| **For commercial seed treatment** | | |
| Corn | Mixing, loading, treating and calibrating | Closed transfer only. Closed transfer includes closed mixing, loading, calibrating, and closed treatment. No open transfer is permitted.<br><br>Wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes. |
| | Bagging, sewing, stacking | Wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes, and a NIOSH-approved N95 (minimum) filtering facepiece respirator (dust mask) that is properly fit tested. |
| | Cleaning and repairing | Wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes, 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. |
| Wheat, Barley, Oat, Rye, | Mixing, loading, treating, calibrating, | Open or closed transfer. |

| Seed types | Tasks | Personal protective equipment/Engineering controls |
|---|---|---|
| **For commercial seed treatment** | | |
| Triticale | bagging, sewing, stacking, and any other activities involving handling treated seed | Wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes. |
| | Cleaning and repairing | Wear chemical-resistant coveralls over a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes. |
| **For on-farm seed treatment** | | |
| Wheat, Barley, Oat, Rye, Triticale | Mixing, loading, treatment, calibration, cleaning, repairing and any other activities involving handling treated seeds | Open or closed transfer<br><br>Wear a long-sleeved shirt, long pants, shoes and chemical-resistant gloves.<br><br>Use a closed-cab tractor when planting. Gloves are not required with a closed cab. |
| **For planting treated seeds (also include on seed tags)** | | |
| Corn | Handling and planting | Wear a long-sleeved shirt, long pants, socks, shoes and chemical-resistant gloves.<br><br>Use a closed-cab tractor when planting. Gloves are not required with a closed cab. |
| Wheat, Barley, Oat, Rye, Triticale | | Wear coveralls over a long-sleeved shirt, long pants, socks, shoes and chemical-resistant gloves.<br><br>During handling of treated seeds, wear a NIOSH-approved N95 (minimum) filtering facepiece respirator (dust mask) that is properly fit tested.<br><br>Use a closed-cab tractor when planting. Gloves and respiratory protection are not required with a closed cab. |

**Under directions for use:**

For all end-use products that are in water soluble packaging the following label statements are required:

> 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 personal protective equipment.
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.

It is unlawful to use any registered pesticide, including WSPs, in a manner inconsistent with its label.

**For seed tags:**

It is required that the following statements be added to all seed tags containing direction for imported treated seed for sale or use in Canada:

> "Keep treated seed out of reach of children and animals."
>
> "**DO NOT** use for food, feed and oil processing."

For corn seed tags, the following is required:

> "During handling and planting treated seed, wear a long-sleeved shirt, long pants, socks, shoes and chemical-resistant gloves. Use a closed-cab tractor when planting. Gloves are not required with a closed cab."

For wheat, barley, oat, soybean and triticale seed tags, the following is required:

> "During handling and planting treated seed, wear coveralls over a long-sleeved shirt, long pants, socks, shoes and chemical-resistant gloves. During handling of treated seeds, wear a NIOSH-approved N95 (minimum) filtering facepiece respirator (dust mask) that is properly fit tested. Use a closed-cab tractor when planting. Gloves and respiratory protection are not required with a closed cab."

### 1.3 Heavy duty wood preservative end-use products:

Label statements, including personal protective equipment, consistent with the Recommendations for Design and Operation of Wood Preservation Facilities, 2013 Technical Recommendations Document" (ECCC, 2013) are required to be added to all commercial-class heavy duty wood preservative end-use products.

### 1.4 Technical grade products and manufacturing concentrates

The following statement is required to be added under ENVIRONMENTAL PRECAUTIONS for all technical grade products:

"Toxic to aquatic organisms."

## 1.5 Commercial class products–Agricultural uses

The following statements are required to be added under ENVIRONMENTAL PRECAUTIONS for all commercial class products with agricultural uses:

"Toxic to aquatic organisms and non-target terrestrial plants. Observe spray buffer zones specified under DIRECTION FOR USE."

**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 km/h at the application site as measured outside of the treatment area on the upwind side."

**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, this product cannot be applied by any type of aerial equipment.

Ensure uniform application. To avoid streaked, uneven or overlapped application, use appropriate marking devices."

**Use precautions**

"Apply only when meteorological conditions at the treatment site allow for complete and even crop coverage. Apply only under conditions of good practice specific to aerial application as outlined in the National Aerial Pesticide Application Manual, developed by the Federal/Provincial/Territorial Committee on Pest Management and Pesticides."

## Product specific precautions

"Read and understand the entire label before opening this product. If you have questions, call the manufacturer at 1-(800)-xxx-xxxx or obtain technical advice from the distributor or your provincial agricultural representative. Application of this specific product must meet and/or conform to the following:
Volume: Apply the recommended rate in a minimum spray volume of X litres per hectare."

## Spray buffer zones

A spray buffer zone is NOT required for uses with hand-held application equipment permitted on this label.

The spray buffer zones specified in the table below are required between the point of direct application and the closest downwind edge of sensitive terrestrial habitats (such as grasslands, forested areas, shelter belts, woodlots, hedgerows, riparian areas and shrublands) and sensitive freshwater habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs and wetlands).

| Method of application | Crop | | Spray buffer zones (metres) required for the protection of | | | | |
|---|---|---|---|---|---|---|---|
| | | | Freshwater habitat of depths | | Estuarine/Marine habitat of depth | | Terrestrial habitat |
| | | | Less than 1 m | Greater than 1 m | Less than 1 m | Greater than 1 m | |
| Field sprayer | Barley, Wheat (winter, spring, durum, hard red, Canada prairie, soft white), Spring Barley, Oat, Soybean, Asparagus, SRIC poplar and willow | | 1 | 0 | 0 | 0 | 1 |
| Airblast | SRIC poplar and willow | Early growth stage | 5 | 0 | 0 | 0 | 2 |
| | | Late growth stage | 3 | 0 | 0 | 0 | 1 |

[Note for the re-evaluation decision: The spray buffer zones presented in this table are for tebuconazole. As spray buffer zones are active specific, for co-formulated products (in other words, Reg. Nos. 29819, 29821, and 32824), care must be taken to ensure the correct spray buffer zones remain on the label. For the co-formulated products, the aquatic spray buffer zones should reflect the tebuconazole distances whereas the larger terrestrial spray buffer zones on the labels should remain. For all non-co-formulated products, the spray buffer zones for tebuconazole apply for both aquatic and terrestrial habitats.]
SRIC - Short rotation intensive culture

## Aerial spray buffer zones

### Aerial spray buffer zones for Reg. No. 25940

| Method of application | Crop | | Spray buffer zones (metres) required for the protection of | | | | |
|---|---|---|---|---|---|---|---|
| | | | Freshwater habitat of depths | | Estuarine/Marine habitat of depths | | Terrestrial habitat |
| | | | Less than 1 m | Greater than 1 m | Less than 1 m | Greater than 1 m | |
| Aerial | SRIC poplar and willow, Wheat (winter durum and spring), Barley, Oats, Soybean (2 applications) | Fixed-wing | 5 | 0 | 0 | 0 | 15 |
| | | Rotary-wing | 4 | 0 | 0 | 0 | 15 |
| | Soybean (1 application) | Fixed-wing | 5 | 0 | 0 | 0 | 15 |
| | | Rotary-wing | 5 | 0 | 0 | 0 | 15 |

SRIC - Short rotation intensive culture

### Aerial spray buffer zones for Reg. No. 30491, and 32500

| Method of application | Crop | | Spray buffer zones (metres) required for the protection of | | | | |
|---|---|---|---|---|---|---|---|
| | | | Freshwater habitat of depths | | Estuarine/Marine habitat of depths | | Terrestrial habitat |
| | | | Less than 1 m | Greater than 1 m | Less than 1 m | Greater than 1 m | |
| Aerial | Wheat (winter durum and spring), Barley, Oats | Fixed-wing | 5 | 0 | 0 | 0 | 15 |
| | | Rotary-wing | 4 | 0 | 0 | 0 | 15 |

### Aerial spray buffer zones for Reg. No. 29819

| Method of application | Crop | | Spray buffer zones (metres) required for the protection of | | | | |
|---|---|---|---|---|---|---|---|
| | | | Freshwater habitat of depths | | Estuarine/Marine habitat of depths | | Terrestrial habitat |
| | | | Less than 1 m | Greater than 1 m | Less than 1 m | Greater than 1 m | |
| Aerial | Wheat (winter, durum and spring), Barley, Oats | Fixed-wing | 4 | 0 | 0 | 0 | 15 |
| | | Rotary-wing | 1 | 0 | 0 | 0 | 10 |

[Note for the re-evaluation decision: The spray buffer zones presented in this table are for tebuconazole. As spray buffer zones are active specific, care must be taken with this co-formulated product to ensure the correct spray

buffer zones remain on the label.]

## Aerial spray buffer zones for Reg. No. 29820

| Method of application | Crop | | Spray buffer zones (metres) required for the protection of | | | | |
|---|---|---|---|---|---|---|---|
| | | | Freshwater habitat of depths | | Estuarine/Marine habitat of depths | | Terrestrial habitat |
| | | | Less than 1 m | Greater than 1 m | Less than 1 m | Greater than 1 m | |
| Aerial | Wheat (winter, durum and spring), Barley, Oats, Soybean | Fixed-wing | 5 | 0 | 0 | 0 | 15 |
| | | Rotary-wing | 2 | 0 | 0 | 0 | 15 |

## Aerial spray buffer zones for Reg. No. 29821

| Method of application | Crop | | Spray buffer zones (metres) required for the protection of | | | | |
|---|---|---|---|---|---|---|---|
| | | | Freshwater habitat of depths | | Estuarine/Marine habitat of depths | | Terrestrial habitat |
| | | | Less than 1 m | Greater than 1 m | Less than 1 m | Greater than 1 m | |
| Aerial | Wheat (winter, durum, spring), Barley, Oats | Fixed-wing | 1 | 0 | 0 | 0 | 15 |
| | | Rotary-wing | 1 | 0 | 0 | 0 | 10 |

[Note for the re-evaluation decision: The spray buffer zones presented in this table are for tebuconazole. As spray buffer zones are active specific, care must be taken with these co-formulated products to ensure the correct spray buffer zones remain on the label.]

## Aerial spray buffer zones for Reg. No. 32824

| Method of application | Crop | | Spray buffer zones (metres) required for the protection of | | | | |
|---|---|---|---|---|---|---|---|
| | | | Freshwater habitat of depths | | Estuarine/Marine habitat of depths | | Terrestrial habitat |
| | | | Less than 1 m | Greater than 1 m | Less than 1 m | Greater than 1 m | |
| Aerial | Wheat (winter, durum, spring), Barley, Oats | Fixed-wing | 2 | 0 | 0 | 0 | 15 |
| | | Rotary-wing | 1 | 0 | 0 | 0 | 10 |

[Note for the re-evaluation decision: The spray buffer zones presented in this table are for tebuconazole. As spray buffer zones are active specific, care must be taken with these co-formulated products to ensure the correct spray buffer zones remain on the label.]

When tank mixes are permitted, 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 Pesticides portion of the Canada.ca website.

### 1.6 Commercial class products – Wood treatment uses

The following statements are required to be added under ENVIRONMENTAL PRECAUTIONS for all commercial class products with wood treatment uses:

“Toxic to aquatic organisms.

Drip aprons must be roofed, paved and drained to prevent dilution and loss of treatment solution.

Store treated lumber on a roofed drip pad until dripping has ceased. Slope lumber on the drip pad to expedite drainage and to ensure that no puddles remain on the surface of the wood. Manage drippage and other related wastes to prevent release in the environment.

**DO NOT** expose treated lumber to rains immediately after treatment.

For further information on storage, handling, and disposal of treated wood, contact the manufacturer of this product or the provincial regulatory agency.

This registration is granted under the Pest Control Products Act and does not exempt the user from any other legislative requirements.

Use of this product and management of any resulting discharge or release of any effluents or runoff containing this product must also be in accordance with the Fisheries Act and with any required provincial legislation.

Consult with provincial regulatory authorities on any authorizations or other requirements for use of this product and management of any resulting discharge or release of any effluents or runoff containing this product.”

# Appendix X References considered following publication of PRVD2021-08

## A. Information Considered in the Updated Toxicological Assessment

### List of Studies/Information Submitted by Registrant

| PMRA Document Number | Title |
|---|---|
| 3282143 | 2021. Memorandum Re: Tebuconazole Toxicity Studies Data Evaluation Records. DACO: 12.5.4 |
| 3282142 | 2005. Bayer CropSciences Response to U.S. EPA Data Evaluation Record for a Developmental Neurotoxicity Study with Technical Grade Tebuconazole in Sprague-Dawley Rats. DACO: 4.8 |

### Additional Information Considered

### Published Information

| PMRA Document Number | Title |
|---|---|
| 3595037 | Wentao Zhu et al. 2007. Stereoselective Degradation Kinetics of Tebuconazole in Rabbits. DACO: 4.8 |
| 3595036 | Yingfen Ying et al. 2021. Tebuconazole exposure disrupts placental function and causes fetal low birth weight in rats. DACO: 4.8 |
| 3595035 | C. Taxvig et al. 2008. Endocrine-disrupting properties in vivo of widely used azole fungicides. DACO: 4.8 |
| 3595034 | Camilla Taxvig et al. 2007. Endocrine-Disrupting Activities In Vivo of the Fungicides Tebuconazole and Epoxiconazole. DACO: 4.8 |
| 3595033 | Kei Tamura et al. 2013. Dose-response involvement of constitutive androstane receptor in mouse liver hypertrophy induced by triazole fungicides. DACO: 4.8 |
| 3595032 | F. Schmidt et al. 2016. Combination effects of azole fungicides in male rats in a broad dose range. DACO: 4.8 |
| 3594799 | Christina L. Sanchez. 2020. Neurotoxicity assessment of triazole fungicides on mitochondrial oxidative respiration and lipids in differentiated human SH-SY5Y neuroblastoma cells. DACO: 4.8 |
| 3594798 | Joshua F. Robinson. 2012. Triazole induced concentration-related gene signatures in rat whole embryo culture. DACO: 4.8 |
| 3594797 | Yosra Ben Othmene et al. 2020. Tebuconazole induced oxidative stress and histopathological alterations in adult rat heart. DACO: 4.8 |
| 3594796 | Yosra Ben Othmene et al. 2020. Tebuconazole induced cardiotoxicity in male adult rat. DACO: 4.8 |
| 3594795 | Yosra Ben Othmene. 2020. Oxidative stress, DNA damage and apoptosis induced by tebuconazole in the kidney of male Wistar rat. DACO: 4.8 |

| PMRA Document Number | Title |
|---|---|
| 3594794 | A. Oerlemans. 2019. Toxicokinetics of a urinary metabolite of tebuconazole following controlled oral and dermal administration in human volunteers. DACO: 4.8 |
| 3594793 | Organisation for Economic Co-operation and Development. 2020. Detailed Review Paper on Retinoid Pathway Signalling. DACO: 4.8 |
| 3594792 | Francesca Metruccio et al. 2020. Development of an adverse outcome pathway for cranio-facial malformations: A contribution from in silico simulations and in vitro data. DACO: 4.8 |
| 3594791 | Zhiyuan Meng et al. 2022. A common fungicide tebuconazole promotes colitis in mice via regulating gut microbiota. DACO: 4.8 |
| 3594790 | Elena Menegola et al. 2021. An adverse outcome pathway on the disruption of retinoic acid metabolism leading to developmental craniofacial defects. DACO: 4.8 |
| 3594789 | Elena Menegola et al. 2013. Effects of mixtures of azole fungicides in postimplantation rat whole-embryo cultures. DACO: 4.8 |
| 3594788 | Elena Menegola et al. 2006. Postulated pathogenic pathway in triazole fungicide induced dysmorphogenic effects. DACO: 4.8 |
| 3594787 | Feifei Ma. 2021. Gestational exposure to tebuconazole affects the development of rat fetal Leydig cells. DACO: 4.8 |
| 3594301 | Jingkun Liu et al. 2021. Gut Flora-Mediated Metabolic Health, the Risk Produced by Dietary Exposure to Acetamiprid and Tebuconazole. DACO: 4.8 |
| 3594300 | Hequn Li et al. 2017. Use of physiologically based kinetic modeling-facilitated reverse dosimetry of in vitro toxicity data for prediction of in vivo developmental toxicity of tebuconazole in rats. DACO: 4.8 |
| 3594297 | Hequn Li et al. 2015. Use of the ES-D3 cell differentiation assay, combined with the BeWo transport model, to predict relative in vivo developmental toxicity of antifungal compounds. DACO: 4.8 |
| 3594296 | Subramaniam Kugathas et al. 2016. Effects of Common Pesticides on Prostaglandin D2 PGD2 Inhibition in SC5 Mouse Sertoli Cells, Evidence of Binding at the COX-2 Active Site, and Implications for Endocrine Disruption. DACO: 4.8 |
| 3594295 | Tingting Ku et al. 2021. Tebuconazole induces liver injury coupled with ROS-mediated hepatic metabolism disorder. DACO: 4.8 |
| 3594294 | Constanze Knebel et al. 2019. The azole fungicide tebuconazole affects human CYP1A1 and CYP1A2 expression by an aryl hydrocarbon receptor-dependent pathway. DACO: 4.8 |
| 3594293 | Constanze Knebel et al. 2019. Pregnane X receptor mediates steatotic effects of propiconazole and tebuconazole in human liver cell lines. DACO: 4.8 |
| 3594292 | Constanze Knebel et al. 2018. Unexpected Effects of Propiconazole, Tebuconazole, and Their Mixture on the Receptors CAR and PXR in Human Liver Cells. DACO: 4.8 |
| 3594291 | Shotaro Kamata et al. 2020. Cytotoxicity comparison of 35 developmental neurotoxicants in human induced pluripotent stem cells iPSC, iPSC-derived neural progenitor cells, and transformed cell lines. DACO: 4.8 |

| PMRA Document Number | Title |
|---|---|
| 3594290 | Pernille Rosenskjold Jacobsen et al. 2012. Persistent developmental toxicity in rat offspring after low dose exposure to a mixture of endocrine disrupting pesticides. DACO: 4.8 |
| 3594289 | Nataliya Ilyushina et al. 2019. Maximum tolerated doses and erythropoiesis effects in the mouse bone marrow by 79 pesticides technical materials assessed with the micronucleus assay. DACO: 4.8 |
| 3594288 | M. Hornychova, E. Frantik, J. Dvorak. 1999. Monitoring of Spontaneous Motor Activity in Rats: Detection of Behavioural Effects of Tiazole Fungicides. DACO: 4.8 |
| 3594287 | Harm J. Heusinkveld et al. 2013. Azole Fungicides Disturb Intracellular Ca2 in an Additive Manner in Dopaminergic PC12 Cells. DACO: 4.8 |
| 3594119 | Ulla Hass et al. 2012. Adverse effects on sexual development in rat offspring after low dose exposure to a mixture of endocrine disrupting pesticides. DACO: 4.8 |
| 3594118 | Joshua A. Harrill, Theresa Freudenrich, Kathleen Wallace, Kenneth Ball, Timothy J. Shafer, William R. Mundy. 2018. Testing for developmental neurotoxicity using a battery of in vitro assays for key cellular events in neurodevelopment. DACO: 4.8 |
| 3594117 | Shahram Habibzadeh, Abbas Yazdanbod, Jafar Mohammadshahi, Nasrollah Maleki, and Sobhan Ataei. 2019. Hepatotoxicity After Exposure to Tebuconazole: A Case Report and Brief Review. DACO: 4.8 |
| 3594116 | Christopher L. Frank, Jasmine P. Brown, Kathleen Wallace, John F. Wambaugh, Imran Shah, Timothy J. Shafer. 2018. Defining toxicological tipping points in neuronal network development. DACO: 4.8 |
| 3594115 | Christopher L. Frank, Jasmine P. Brown, Kathleen Wallace, William R. Mundy, and Timothy J. Shafer. 2017. Developmental Neurotoxicants Disrupt Activity in Cortical Networks on Microelectrode Arrays: Results of Screening 86 Compounds During Neural Network Formation. DACO: 4.8 |
| 3594113 | Stefan Masjosthusmann et al. 2020. Establishment of an a priori protocol for the implementation and interpretation of an in-vitro testing battery for the assessment of developmental neurotoxicity. DACO: 4.8 |
| 3594112 | Francesca Di Renzo, Renato Bacchetta, Andrea Bizzo, Erminio Giavini, Elena Menegola. 2011. Is the amphibian X. laevis WEC a good alternative method to rodent WEC teratogenicity assay? The example of the three triazole derivative fungicides Triadimefon, Tebuconazole, Cyproconazole. DACO: 4.8 |
| 3594108 | Verena Christen, Pierre Crettaz, Karl Fent. 2014. Additive and synergistic antiandrogenic activities of mixtures of azol fungicides and vinclozolin. DACO: 4.8 |
| 3594107 | Xiuxiu Chen, Qiqi Zhu, Xiaoheng li, Tongliang Huang, Songxue Wang, Yiyan Wang, Xianwu Chen, Zhenkun Lin, Ren-shan Ge. 2019. Pubertal exposure to tebuconazole increases testosterone production via inhibiting testicular aromatase activity in rats. DACO: 4.8 |

| PMRA Document Number | Title |
|---|---|
| 3594106 | Pei-Jen Chen, William T. Padgett, Tanya Moore, Witold Winnik, Guy R. Lambert, Sheau-Fung Thai, Susan D. Hester, Stephen Nesnow. 2009. Three conazoles increase hepatic microsomal retinoic acid metabolism and decrease mouse hepatic retinoic acid levels in vivo. DACO: 4.8 |
| 3594105 | KE Carstens, AF Carpenter, MM Martin, JA Harrill, TJ Shafer, K Paul Friedman. 2022. Integrating data from in vitro New Approach Methodologies for Developmental Neurotoxicity. DACO: 4.8 |
| 3594104 | Nurgul Atmaca, Sevket Arikan, Dinc Essiz, Hakan Kalender, Ozkan Simsek, Fatih Sultan Bilmen, Ruhi Kabakci. 2018. Effects of mancozeb, metalaxyl and tebuconazole on steroid production by bovine luteal cells in vitro. DACO: 4.8 |
| 3599976 | Organisation for Economic Co-operation and Development. 2023. Initial Recommendations on Evaluation of Data from the Developmental Neurotoxicity(DNT) In-Vitro Testing Battery. DACO: 4.8 |

## B. Information Considered in the Updated Dietary Assessment

### List of Studies/Information Submitted by Registrant

| PMRA Document Number | Title |
|---|---|
| 3621196 | Pest Management Regulatory Agency. 2023. Tebuconazole (TEU) - Registrant's Recommendations on Priority Uses. DACO: Other XLSX |

### Additional Information Considered

### Published Information

| PMRA Document Number | Title |
|---|---|
| 3566632 | United States Environmental Protection Agency. 2022. Tebuconazole: Acute and Chronic Aggregate Dietary Exposure and Risk Assessments in Support of Registration Review. DACO: 6.4 |

## C. Information Considered in the Updated Environmental Assessment

### List of Studies/Information Submitted by Registrant

| PMRA Document Number | Title |
|---|---|
| 2456673 | 1993. Field Dissipation of Tebuconazole on Minnesota Turf. DACO: 8.3.2 |
| 1522419 | 2007. Terrestrial Field Dissipation of Tebuconazole in Canadian Soil, 2000. DACO: 8.3.2 |
| 1229603 | 1987. The metabolism of Folicur in soil (aerobic and anaerobic). DACO: 8.2.3.4.2 and 8.2.3.4.4 |
| 3282141 | 1996. Terrestrial field dissipation of tebuconazole (LYNX) on Wisconsin soil, 1993. DACO: 8.3.2 |
| 3282140 | 1996. Terrestrial field dissipation of tebuconazole (LYNX) on Wisconsin turf, 1993. DACO: 8.3.2 |
| 2456683 | 1997. Terrestrial Field Dissipation of Tebuconazole (LYNX 25DF) on New York Turf, 1996. DACO: 8.3.2 |
| 3621660 | 2021. Tebuconazole – Drinking Water Assessment for Registration Review. DACO: 12.5.5 |

### Additional Information Considered

### Published Information

| PMRA Document Number | Title |
|---|---|
| 3621667 | Bohaty, R.; W. Eckel; M. Shamim; D. Spatz; K. White; and D. Young. 2015. Standard Operating Procedure for Using the NAFTA Guidance to Calculate Representative Half-Life Values and Characterizing Pesticide Degradation. United States Environmental Protection Agency. DACO: 12.5.8 |
| 3093536 | European Food and Safety Association (EFSA). 2007. Tebuconazole, Volume 3, Annex B8: Fate and behaviour, Draft Assessment Report (DAR). DACO: 12.5.8 |