Health Canada / Santé Canada

Reference No. 2025-0231

August 10, 2026

Bronwyn Roe
Ecojustice
1910-777 Bay Street, PO Box 106
Toronto, ON
M5G 2C8

Dear Bronwyn Roe,

Re: Notice of Objection to Re-evaluation Decision RVD2024-09, *Tebuconazole and Its Associated End-use Products*

The notice of objection (NoO) regarding the re-evaluation decision for tebuconazole, filed under subsection 35(1) of the *Pest Control Products Act* (PCPA), has been reviewed and assessed in accordance with the PCPA and the *Review Panel Regulations*.

The Minister of Health's primary objective under the PCPA 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 PCPA, 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 and the environment, both before and after registration, and applies to the regulation of pest control products throughout Canada; and that pest control products of acceptable risk 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 adverse health impact or pollution of the environments.

Legislative and Regulatory Framework for Decision

The 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 or proposed conditions of registration: subsection 2(2) of the PCPA.

In accordance with the PCPA, only pest control products that are considered to have acceptable risks and value are approved for use in Canada. The value of a pest control product, as defined by subsection 2(1) of the PCPA, refers to the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration. This includes the product's efficacy, effect on host organisms, health, safety, and environmental benefits derived from use of the product and social and economic impacts.

The objections submitted by Ecojustice challenged Health Canada's assessment of health and environmental risks in relation to the re-evaluation decision for tebuconazole.

Health and environmental risks are defined in the PCPA 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.

All registered pesticides must be re-evaluated by Health Canada, on behalf of the Minister of Health, to ensure that their risks and value remain acceptable in line with current health and environmental standards. When evaluating the risks of a pesticide and determining whether those risks are acceptable in the context of a re-evaluation, subsection 19(2) of the PCPA requires Health Canada to apply a scientifically based approach to the evaluation of health and environmental risks. A science-based approach to assessing the risks of pesticides considers both the toxicity of and the level of exposure to a pesticide in order to fully characterize and assess risk. Health Canada uses a comprehensive body of robust scientific methods and evidence to determine the nature as well as the magnitude of potential risks posed by pesticides. The integration of scientific information is an iterative process that is repeated for individual studies as well as across similar studies for a particular line of evidence. Multiple lines of evidence related to hazard and exposure are then integrated into an overall risk assessment conclusion. 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 and the primary objective of the PCPA, set out above.

Health Canada's approach to risk assessment is outlined in: risk-management-pest-control-products-eng.pdf

Before making a final decision, a re-evaluation is subject to public consultation in accordance with section 28 of the PCPA. All stakeholders and the public are encouraged to engage in the consultation process and submit information to inform Health Canada's development of the final regulatory decision. Health Canada considers all comments and information on the proposed decision received during the consultation period, which are addressed in the final decision.

Section 35 of the PCPA provides any member of the public an opportunity to file a Notice of Objection (NoO) within 60 days after the final re-evaluation decision is published. The NoO process permits Health Canada, on behalf of the Minister of Health, to seek the assistance of an external expert review panel in response to the NoO, where necessary, and provides another opportunity for an interested member of the public to participate in the scientific aspects of the re-evaluation process. To this end, a person filing an NoO must identify the aspect(s) of the scientific evaluation supporting the registration or re-evaluation/special review decision to which they object and request that the scientific aspect(s) in question be referred to an external review panel. Where a review panel is established, its role is to review the decision at issue according to the terms of reference set out by the Minister and to recommend whether the decision should be confirmed, reversed, or varied.

The *Review Panel Regulations* ("*Regulations*") support the NoO process under the PCPA. Paragraph 2(c) of the *Regulations* requires an objector to identify a scientific basis for their objection to the evaluations on which the decision was based. Paragraph 2(d) of the *Regulations* requires that the NoO also include the evidence to support the objection, including scientific reports or test data. Since NoOs are filed after a lengthy scientific evaluation and public consultation, they should be precise in identifying the scientific aspect to which objection is taken and should be well-supported by evidence.

Should the criteria in subsection 35(1) of the PCPA and section 2 of the *Regulations* be met, Health Canada reviews the NoO to determine whether it is necessary to establish a review panel pursuant to subsection 35(3) of the PCPA.

Section 3 of the *Regulations* states:

> The Minister shall take the following factors into account in determining whether it is necessary to establish a review panel:
>
> a) whether the information in the notice of objection raises scientifically founded doubt as to the validity of the evaluations, on which the decision was based, of the health and environmental risks and the value of the pest control product; and
> b) whether the advice of expert scientists would assist in addressing the subject matter of the objection.

Health Canada has developed the Notice of Objection Review Panel Criteria to guide its analysis of the two factors in section 3 of the *Regulations* which must be taken into account in determining whether it is necessary to establish an external review panel.

In evaluating an NoO, Health Canada will generally consider the following Notice of Objection Review Panel Criteria**:**

1 - Does the information in the notice of objection raise a scientifically founded doubt as to the validity of the evaluations, on which the decision was based, of the health risks or environmental risks or value of the pest control product? To assess this question Health Canada will consider:

a) Is the scientific basis for the objection directly linked to the evaluation of the pest control product?
b) Was the evidence supporting the objection considered in the evaluation?
    i. Was the information available prior to publishing the decision?
        - If the information was available, was it considered in the assessment?
    ii. If the evidence was not considered, does the information meet the criteria for scientific acceptability for use in the evaluation of a pest control product?
c) Does the scientific basis of the objection and the evidence provided in support of the objection, when considered with all scientifically reliable* information available and considered by Health Canada at the time of decision, present uncertainty in an aspect of the evaluation? (***Reliable Science**: science that is credible and unbiased. Information Note: Determining Study Acceptability for use in Pesticide Risk Assessments.)

Studies are classified for acceptability as “acceptable,” “acceptable with limitations” or “unacceptable.” Examples of limitations may be that the protocol does not fully comply with the specified guideline or that raw data are not available. As indicated in the Information Note - Determining Study Acceptability for use in Pesticide Risk Assessments, Health Canada uses studies that are acceptable (that is, acceptable and acceptable with limitations) in its risk assessments, when they are found to be relevant. As such, all cited references presented in this NoO being classified as either “acceptable” or “acceptable with limitations” were considered as meeting the criteria for scientific acceptability and their potential impact on the evaluation of tebuconazole was assessed if they were considered relevant.

The above criteria are directed at a science-based review of the objection and will inform whether there may be scientifically-founded doubt raised by the objection concerning an aspect of the evaluation on which the final decision was based.

2 - Would the advice of expert scientists assist in addressing the subject matter of the objection? To assess this question, Health Canada will consider the following:

a) Is there is a lack of agreement among federal government regulatory scientists with respect to the evidence presented in the objection, and could it affect the outcome of the evaluation?
b) Is the area of science relatively new and the regulatory approach still under development globally and, in this context, does Health Canada believe that the advice of the panel will aid in the regulatory decision-making process?
c) Is there a lack of uniformity in global regulatory evaluations related to the health or environmental risks, or value, of the pest control product that is the subject matter of the objection?
    i. Does the lack of uniformity concern an aspect of the evaluation that is relevant to the Canadian use pattern?
    ii. Does the lack of uniformity relate to the scientific risk assessment or a legislative requirement in the foreign jurisdiction that is not applicable to the Canadian context?

The above criteria will inform whether the advice of expert scientists would assist in addressing the subject matter of the objection.

Summary of the Notice of Objection under Review

The following information was received and reviewed in support of your NoO:

- Notice of Objection Form
- Notice of Objection Letter, including detailed arguments and a reference list of 134 references, consisting of US EPA reviews, EFSA reports, independent studies, journals, and articles.

The NoO set out four themes under which all the objections and supporting arguments were organized:

1) Cumulative health risk assessment of triazoles – 2 objections
2) Cancer risk assessment and developmental toxicity – 2 objections
3) Impact of fungicide resistance to medical applications – 1 objection
4) Accumulation in the environment – 5 objections

Health Canada's Consideration of the Objections:

The following details Health Canada's response to each of the objections and takes into account the Notice of Objection Review Panel Criteria, set out above, to guide the determination as to whether it is necessary to establish an external review panel for one or more of the objections, based on the factors set out in section 3 of the *Regulations*.

Cumulative health risk assessment of triazoles

Objection 1*:* "PMRA cannot continue the registration of triazole fungicides without conducting a cumulative health assessment that includes food, drinking water and residential uses. The PMRA must address the combined effects of the various triazoles, their transformation products and the conjugates of those transformation products together in a cumulative risk assessment."

Objection 2: "The PMRA must also conduct a cumulative health risk assessment for 1,2,4, triazole and its metabolites."

Health Canada's Response:

As noted in the proposed re-evaluation decision document (PRVD2021-08), tebuconazole is a triazole-based fungicide which belongs to a group of structurally similar pesticides that have common metabolites, including 1,2,4-triazole and triazole conjugates. At the time of the re-evaluation, no clear common mechanism of toxicity had been confirmed on which to base a cumulative risk assessment (CRA), and it was stated in PRVD2021-08 that a CRA for the common triazole metabolites would be addressed in a separate assessment. On October 30, 2024, Health Canada initiated a CRA of triazole pesticides and their common metabolites under submission number 2024-1674 and subsequently published the scoping assessment (REV2026-02). As indicated in the scoping document, this CRA intends to identify potential common mechanisms of toxicity of triazole pesticides and evaluate human health risks associated with co-exposures from all non-occupational sources of exposure.

The resulting Notice of Objection of the re-evaluation decision for tebuconazole was received on January 14, 2025. As noted in above, the CRA for the triazole fungicides and their common metabolites will be assessed under a separate submission (2024-1674), which was already initiated prior to the re-evaluation decision for tebuconazole.

As the CRA for triazole fungicides and their common metabolites has already been initiated, objections 1 and 2 will not be addressed under the current notice of objection, but rather under the CRA (2024-1674). This approach to address the CRA under the ongoing and separate submission is also supported by the fact that no other regulatory authority has cancelled tebuconazole based on cumulative-related risks of concerns.

Consequently, the references submitted by the objector (Appendix I, Table 1), which were identified to be related to the cumulative assessment, will not be considered under the current notice of objection. Rather they will be considered as part of the CRA for triazole fungicides and their common metabolites under submission 2024-1674. Therefore, these objections will not be evaluated against the notice of objection assessment criteria.

Cancer risk assessment and developmental toxicity

Objection 3*:* "In the proposed re-evaluation decision, the PMRA initially acknowledged the carcinogenicity of tebuconazole. However, no cancer endpoint was provided… The PMRA must identify whether there are non-threshold cytotoxic effects or alternatively identify a clear carcinogenic endpoint."

Summary of Objection 3: Ecojustice stated that Health Canada's cancer risk assessment for tebuconazole published in the proposed re-evaluation decision is not acceptable. The objector stated that it is impossible to verify that the endpoints selected for non-cancer risk assessment were protective of carcinogenic potential, as stated in PRVD2021-08, as a specific cancer endpoint was not established. Ecojustice objected to the fact that Health Canada has not established a carcinogenic endpoint, nor has Health Canada identified whether there are non-

threshold cytotoxic effects. Furthermore, the objector stated that Health Canada must revise the cancer risk assessment for triazoles as a group, and for metabolites and their conjugates.

Health Canada's Response:

Criterion 1: Does the information in the notice of objection raise a scientifically founded doubt as to the validity of the evaluations, on which the decision was based, of the health and environmental risks and value of the pest control product? To assess whether there is scientifically founded doubt, Health Canada will consider:

a) Is the scientific basis for the objection directly linked to the evaluation of the pest control product?

Yes, the scientific basis for the objection is directly linked to the evaluation of the pest control product, specifically that there is an objection to Health Canada's cancer risk assessment for tebuconazole. However, the statement that Health Canada must revise the cancer risk assessment for triazoles as a group and for metabolites and their conjugates is not directly linked to the evaluation of the cancer assessment of tebuconazole. Furthermore, it should be noted that most of the cited references were found not to be relevant to addressing the objection. One study (PMRA#3689018) was found to be relevant; however, it was determined to be scientifically unacceptable. In most cases, data was not specific to tebuconazole or not related to cancer.

b) Was the evidence supporting the objection considered in the evaluation?

i. Was the information available prior to publishing the decision?

- **If the information was available, was it considered in the assessment?**

ii. If the evidence was not considered, does the information meet the criteria for scientific acceptability for use in the evaluation of a pest control product?

Several documents were referenced by Ecojustice (PMRA#3688977, 3688981, 3688999, 3689002, 3689018, 3689020, and 3689044) to support their objection related to the cancer risk assessment. All of these references were available prior to the publication of the proposed re-evaluation decision of tebuconazole, and none of them were considered in the re-evaluation. Many of these references were not considered relevant to supporting this objection because the underlying studies were either not conducted with tebuconazole or they assessed endpoints that were not relevant to a cancer assessment. In one case, a study (PMRA#3689018) was found to be relevant to supporting the objection; however, it was determined to be scientifically unacceptable because the data was not specific to tebuconazole, nor related to cancer. Primary references used to address Objection 3 include PMRA#3688977, 3688981, 3688999, 3689002, 3689018, 3689020, and 3689044. The relevance and scientific acceptability of these studies is summarized in Appendix I, Table 1.

Elcombe CR et al. 2014 (PMRA#3688977) evaluated the modes of action (MOAs) of phenobarbital (PB) to activate constitutive androstane receptor (CAR) and pregnane X receptor (PXR) to induce liver tumours in rodents. According to this study, a MOA for PB-induced liver tumours with CAR activation has been established in the literature, while a MOA for PXR activation could not be established due to a lack of data. The MOA was evaluated using the modified Bradford Hill criteria for causality. It was concluded that while PB induces liver tumours in rodents, the MOA identified for tumour formation was not plausible in humans. Furthermore, there is no supporting evidence in the literature that PB exposure leads to increased liver tumour risk in humans. This study was available when RVD2024-09 was published but was not considered in the re-evaluation. This study was not reviewed for scientific acceptability since

it is not relevant to the cancer risk assessment of tebuconazole as it was conducted with PB and not tebuconazole.

EPA (7/27/94). Carcinogenicity Peer Review of Difenoconazole (PMRA#3688981) is a memorandum written by the Health Effects Division of the United States Environmental Protection Agency (US EPA) that discusses the peer review of a different active ingredient, difenoconazole, by the Health Effects Division Carcinogenicity Peer Review Committee. It discusses the meeting held on May 18, 1994, in which it was decided that a margin of exposure (MOE) (or threshold approach) would be taken with the difenoconazole cancer assessment. In this meeting, difenoconazole was classified as a Group C – possible human carcinogen based on the increase in hepatocellular tumours in mice at dose levels considered to be excessively high. Contributing to the weight of evidence, there was a lack of mutagenicity observed, and no increase in tumour formation observed in rats. Included in the memorandum is a reference to tebuconazole having structural similarities to difenoconazole, and tebuconazole is also classified by the US EPA as a group C carcinogen. This memorandum was available when RVD2024-09 was published. This specific memorandum was not considered in the re-evaluation; however, the US EPA conclusions pertaining to cancer classification of tebuconazole were considered at the time. For the purposes of this objection, the memorandum was not reviewed since the majority of its content is not relevant for use in the cancer risk assessment of tebuconazole. That is, the memorandum summarizes a cancer assessment of a different active ingredient, difenoconazole, and the brief mention of tebuconazole does not provide any new information about tebuconazole.

EPA (5/16/18). Tebuconazole: Pesticide Tolerances (PMRA#3688999) is a section of the Federal Register, which is a daily journal from the United States government that publishes presidential updates, new rules and regulations, changes to existing rules, and other similar government updates. The section in question is the published final decision from the US EPA about establishing tolerances for residues of tebuconazole in or on ginseng. In reference to the cancer assessment, the document states that a cancer assessment was not conducted because the reference values established for the chronic risk assessment of tebuconazole are protective of any cancer effects. This publication of the Federal Register was available when RVD2024-09 was published but was not considered in the re-evaluation. This publication was not relevant to the cancer risk assessment of tebuconazole because its only reference to cancer is to indicate that a separate cancer assessment was not required without providing any supporting information.

EPA (1/11/00). Tetraconazole – Report of the Cancer Assessment Review Committee (PMRA#3689002) is another memorandum written by the Health Effects Division of the US EPA that discusses the peer review of tetraconazole by the Health Effects Division Cancer Assessment Review Committee. It discusses a meeting held on November 10, 1999, in which it was decided that tetraconazole was “likely to be carcinogenic to humans” by the oral route of exposure based on liver tumours in mice, and a linear low-dose extrapolation approach was recommended for the cancer assessment. This memorandum was available when RVD2024-09 was published but was not considered in the re-evaluation. This memorandum was not relevant to the cancer risk assessment of tebuconazole because it does not make any reference to tebuconazole.

Ilyushina NA et al., 2020 (PMRA#3689018) is a genotoxicity study conducted with a mixture of imidacloprid, imazalil, and tebuconazole in a ratio of 14.0:1.7:1.0 by weight, respectively. It was reported that the results of the Ames assay and *in vivo* micronucleus test were negative for genotoxicity when the pesticides were tested individually; however, data to support this conclusion were not included in the published report. When all three chemicals were combined, the Ames assay was also negative, and the micronucleus test revealed "weak genotoxicity" according to the study authors. The study authors indicate that due to the mixture of three chemicals, it is unclear whether the weak genotoxic effects were due to mutual influence on each other, their metabolites, or impurities. They concluded that more research is required to determine if there is a synergistic effect. This study was available when RVD2024-09 was published but was not considered in the re-evaluation. While this study was relevant to support the objection, it was determined to be scientifically unacceptable because the testing was conducted with a mixture of chemicals, with tebuconazole representing the smallest ratio by weight. Therefore, this study cannot be used reliably to assess the genotoxic potential of tebuconazole. Additionally, the mention of negative genotoxicity findings with tebuconazole when tested alone does not call into question the validity of the cancer risk assessment of tebuconazole, as it supports Health Canada's conclusion that tebuconazole was negative for genotoxicity.

Jeong JY et al. (2022) (PMRA#3689020) is a repeat-dose dietary toxicity study in pigs conducted with tebuconazole. Twenty pigs were treated with different doses of tebuconazole (up to 25 mg/kg bw/day) for 28 days, and blood biochemistry, histology, and residual levels of tebuconazole were analyzed. According to the results of the study, there were changes to biochemical parameters and histology, and tebuconazole residues were detected in the liver and fat. This study was available when RVD2024-09 was published but was not considered in the re-evaluation. This study was not relevant to the objection regarding the cancer risk assessment of tebuconazole because the study was short-term and did not test for genotoxicity or tumorigenicity.

Nesnow et al. (2009) (PMRA#3689044) compares the transcriptional analyses of mice treated with tumourigenic levels of phenobarbital (PB), propiconazole (Pro), or triadimefon (Tri). The transcriptional analysis examined differentially expressed genes, and analyses were also conducted to compare relevant genes and potential tumourigenic pathways using known databases. The goal of the study was to compare PB to Pro and Tri (two conazole fungicides), all of which are known to cause mouse liver tumours. The results of this study showed that the transcriptional profiles of Pro and Tri were similar to each other, but had greater differences compared to PB. The study author concluded that due to these differences, the mechanism of action between PB and the two conazoles are likely different. This study was available when RVD2024-09 was published but was not considered in the re-evaluation. This study was not relevant to the cancer risk assessment of tebuconazole because it was not conducted with tebuconazole.

c) Does the scientific basis of the objection and the evidence provided in support of the objection, when considered with all scientifically reliable information available and considered by Health Canada at the time of decision, present uncertainty in an aspect of the evaluation?

Not all of the documents cited in the NoO were evaluated for scientific acceptability because many of them were not relevant for use in the Health Canada cancer risk assessment of tebuconazole. Several referenced documents did not provide any quantifiable data about liver tumours or genotoxicity related to the cancer hazard or risk assessment of tebuconazole, and did not provide evidence to support the objection that Health Canada 's cancer risk assessment is unacceptable. One study (PMRA#3689018) was found to be relevant to supporting the objection, however it was found to be scientifically unacceptable for use in the PMRA cancer risk assessment of tebuconazle, as it was primarily conducted with a mixture of chemicals. Neither the scientific basis for the objection nor the evidence provided, when considered with all scientifically reliable information available at the time of the proposed re-evaluation decision, present uncertainty regarding any aspect of the approach to the cancer risk assessment.

Objection 3/Criterion 1 - Overall Conclusion: The scientific basis for Objection #3 is directly linked to the evaluation of tebuconazole. Besides one study that was found to be scientifically unacceptable, the scientific acceptability of the information provided by the objector was not determined because the information was not relevant for use in Health Canada's cancer risk assessment of tebuconazole. The information in the NoO does not raise a scientifically founded doubt as to the validity of the health risks of tebuconazole, on which the decision was based.

Criterion 2: Would the advice of expert scientists assist in addressing the subject matter of the objection? To assess this question Health Canada will consider the following:

a) Is there is a lack of agreement among federal regulatory scientists with respect to the evidence presented in the objection, and could it affect the outcome of the evaluation?

Health Canada applies internationally accepted hazard and risk assessment methods as well as modern risk management approaches and policies to help ensure the safety of each pesticide registered in Canada. Regarding the cancer risk assessment of tebuconazole, there is no disagreement among federal regulatory scientists on issues raised in this objection, and as such it would not affect the outcome of the evaluation. The advice of expert scientists would not assist in addressing the subject matter of this objection, namely that Health Canada's cancer risk assessment for liver tumours in the proposed re-evaluation decision of tebuconazole is not acceptable.

b) Is the area of science relatively new and the regulatory approach still under development globally and, in this context, does the Health Canada believe that the advice of the panel will aid in the regulatory decision-making process?

The area of science covered in this objection is not new and the regulatory approach for the evaluation of this type of pesticide is well established globally. The health risk assessment of tebuconazole was completed according to the standard regulatory and risk assessment frameworks, which have been in place in Canada and other OECD countries for many years. Health Canada's scientific risk-based approach to the regulation of pesticides is consistent with international standards and is similar to Health Canada's regulatory approach for other types of chemicals. This framework provides predictability and transparency to the process used to protect the health of Canadians and their environment and helps ensure risk management decision making considers all relevant criteria in a comprehensive fashion

c) Is there a lack of uniformity in global regulatory evaluations related to the health or environmental risks, or value, of the pest control product that is the subject matter of the objection?

i. Does the lack of uniformity concern an aspect of the evaluation that is relevant to the Canadian use pattern?

ii. Does the lack of uniformity relate to the scientific risk assessment or a legislative requirement in the foreign jurisdiction that is not applicable to the Canadian context?

Health Canada's conclusion on the cancer risk assessment of tebuconazole is consistent with that of independent reviews by multiple scientific experts from other major pesticide regulatory authorities internationally. There are no significant differences in this aspect of the cancer risk assessment of tebuconazole, as informed by recent Health Canada, US EPA, and EU/EFSA publications. In the most recent US EPA proposed documentation (2022), it was concluded that the chronic risk assessment of tebuconazole is considered to be protective of any cancer effects; therefore, a separate quantitative cancer risk assessment was not conducted.
Therefore, the advice of expert scientists will not assist in addressing the subject matter of the objection pertaining to the cancer risk assessment.

Objection 3/Criterion 2 - Overall Conclusion: The objection was reviewed by Health Canada scientists not involved in the original re-evaluation of tebuconazole. There is agreement among federal regulatory scientists in Canada as well as a uniformity in global regulatory evaluations related to the cancer risk assessment of tebuconazole. Therefore, the advice of expert scientists will not assist in addressing the subject matter of the objection pertaining to the cancer risk assessment.

Objection 3 overall conclusion:
Objection 3 did not raise scientifically founded doubt on the approach Health Canada has taken. The references provided for Objection 3 does not raise scientifically founded doubt as to the validity of Health Canada's evaluation and the advice of expert scientists would not assist in addressing the subject matter of this objection.

Objection 4: "We agree with the PMRA's decision to revise the proposed re-evaluation to use the 10 fold PCPA factor for assessing risk to women of reproductive age, however it should be used for developmental toxicity as well."

Summary of Objection 4:
Ecojustice agrees with Health Canada's approach in the final re-evaluation decision to retain the full PCPA factor of 10-fold when assessing risks to women of reproductive age. However, the objector argues that it should also be applied for developmental toxicity as well, specifically effects in the developmental neurotoxicity study, based on several areas of incomplete information. Ecojustice raised several arguments to further support this objection:

a) The objector argues that the European Union classifies tebuconazole as "suspected of damaging the unborn child," and a 2014 review by the European Food Safety Agency suggested that the chemical be classified as one that "may damage the unborn child."
b) The objector argues that the lack of a dermal developmental neurotoxiciy study that evaluates tebuconazole reinforces the need to apply a 10-fold PCPA factor.

c) The objector argues that the PMRA has incomplete information on exposure due to a lack of biomonitoring, water and food residue monitoring and must maintain the 10 fold safety factor.

Health Canada's Response:

Criterion 1: Does the information in the notice of objection raise a scientifically founded doubt as to the validity of the evaluations, on which the decision was based, of the health and environmental risks and value of the pest control product? To assess whether there is scientifically founded doubt, Health Canada will consider:

a) Is the scientific basis for the objection directly linked to the evaluation of the pest control product?

Yes, the scientific basis for the objection is directly linked to the evaluation of the pest control product, specifically that there is an objection to the PCPA factor established by Health Canada in the re-evaluation decision for tebuconazole. However, it should be noted that not all of the cited references were found relevant to addressing the objection. In one case, data from a study had already been considered as part of the re-evaluation decision of tebuconazole. In another instance, a cited study did not measure or make reference to developmental toxicity or effects in the young.

b) Was the evidence supporting the objection considered in the evaluation?

i. Was the information available prior to publishing the decision?

- **If the information was available, was it considered in the assessment?**

ii. If the evidence was not considered, does the information meet the criteria for scientific acceptability for use in the evaluation of a pest control product?

Consideration of arguments 4a) & 4b):

Two documents were referenced by Ecojustice (PMRA#3689020 and 3689037) to support their objection related to changing the magnitude of the PCPA factor to 10-fold when developmental neurotoxicity endpoints are used for the risk assessment. Both of these references were available prior to the publication of the proposed re-evaluation decision of tebuconazole. One of these studies (PMRA#3689037) was already relied upon during the re-evaluation of tebuconazole, and the data has been considered in that review. However, the other study, *Jeong JY et al. (2022)* (PMRA#3689020), was not considered to be relevant for use in Health Canada's risk assessment, because it did not measure any developmental toxicity parameters or effects in the young, and it did not provide information on the dermal developmental neurotoxicity study.

Jeong JY et al. (2022) (PMRA#3689020) is a repeated-dose dietary toxicity study in pigs conducted with tebuconazole. Twenty pigs were treated with different doses of tebuconazole (up to 25 mg/kg bw/day) for 28 days, and blood biochemistry, histology, and residual levels of tebuconazole were analyzed. According to the results of the study, there were changes to biochemical parameters and histology, and tebuconazole residues were detected in the liver and fat. This study was available when RVD2024-09 was published but was not considered in the re-evaluation. This study was not reviewed for scientific acceptability since it is not relevant for use in Health Canada's developmental or reproductive health risk assessment. It is not relevant to the determination of a PCPA factor or in assessing the risk to infants, children, or pregnant people, because it is not a reproductive or developmental toxicity study and did not include multiple generations, or measure any effects in the young animal.

The relevance and scientific acceptability of the primary references used to address objection 4 a) and b), which include references PMRA#3689020 and PMRA#3689037, are summarized in Appendix I, Table 1.

Consideration for argument 4c):
Yes, the evidence provided to support argument 4 c), from a health risk (exposure) perspective, is a reference to Section 19(2)(b)(iii) of the *Pest Control Product Act*, which was available prior to publishing the decision. The assessment supporting the Re-evaluation decision has considered this evidence, i.e., the supported use patterns comply with the requirements of the Act. In other words, re-evaluation decision considered that sufficient data were available to conduct the exposure assessments. Application of the PCPA factor is dependent on availability of sufficient data for the exposure assessment, but not on the availability of specific monitoring data. It is noted that the argument raised is based on a different interpretation of the Act and Health Canada's guidance and risk assessment approaches than how Health Canada interprets them for a health risk assessment.

The NoO cited one peer-reviewed scientific study from published academic literature that was assessed by Health Canada to be relevant, from an environmental risk perspective, for Argument 4 c). Based on the 2022 date of publication, Huang et al. (2022) was available before the final decision for tebuconazole was published. Huang et al. (2022) was not considered in the re-evaluation assessment of tebuconazole. It did not provide scientific evidence that would be applicable to the environmental risk assessment and only measurement values were reported and no other information that would be useful or informative for the risk assessment was provided. The NoO cited various other studies and documents that were not relevant to the active ingredient of concern (tebuconazole) or to the scope of work as to how Health Canada conducts science-based risk assessments. These documents are summarized in Appendix I, Table 1.

c) Does the scientific basis of the objection and the evidence provided in support of the objection, when considered with all scientifically reliable information available and considered by Health Canada at the time of decision, present uncertainty in an aspect of the evaluation?

Consideration of arguments 4a) & 4b):
Jeong JY et al. (2022) (PMRA#3689020) cited in the NoO was not evaluated for scientific acceptability because it was not relevant for use in the Health Canada risk assessment pertaining to developmental toxicity. The referenced study did not provide any quantifiable data about developmental toxicity, and did not provide evidence to support the objection that Health Canada should retain the full PCPA factor of 10-fold when developmental neurotoxicity endpoints are used for risk assessment. Neither the scientific basis for the objection nor the evidence provided, when considered with all scientifically reliable information available at the time of the proposed re-evaluation decision, present uncertainty regarding any aspect of the established PCPA factor.

Consideration for argument 4c):
From a health risk (exposure) perspective, the lack of monitoring data provided as evidence is not relevant as long as sufficient data were available and used in conducting the exposure assessment to address potential health risks.

Specifically, the Act requires considering an additional factor (often referred to as PCPA factor)

to account for potential pre- and post-natal toxicity and completeness of the data with respect to the exposure of, and toxicity to, infants and children. For exposure assessment, it would be making sure that a complete set of exposure data was available to estimate the risk and make a recommendation on the products' safe use. It is important to note that Health Canada uses a tiered approach for risk assessment (SPN 2003-03), i.e., initial risk assessment uses "worst-case" assumptions, and are refined, when required, to represent more realistic scenarios on a case-by-case basis.

Monitoring data, e.g., food residue monitoring, water monitoring or biomonitoring, provide useful real-life information that help to refine the risk, but are not always necessary in the basic or lower tier risk assessments. In other words, data used to refine risk assessments (e.g., monitoring data such as biomonitoring, food residue monitoring, or water monitoring) are not mandatory for registration or continued registration of a pest control product. Therefore, the absence of monitoring data in itself would not warrant retention of the 10-fold PCPA factor.

It is noted that the dietary risk assessment conducted as part of the published re-evaluation decision (RVD) considered that sufficient information was available to assess risk for the supported use pattern. The risk assessment did use available food residue monitoring data from the Canadian Food Inspection Agency (CFIA) and the United States Department of Agriculture Pesticide Data Program (USDA PDP). While water monitoring data were not used in the risk assessment, data available since the publication of the RVD from the Canadian Water Monitoring Program for Pesticides indicate that tebuconazole is detected only in a small proportion of Canadian water samples (5% of the 7701 samples tested) and when detected, it was present at a very low concentration. The maximum concentration detected was 1.4 µg/L in comparison to the estimated environmental concentrations (EEC) of 25 µg/L and 26 µg/L used in chronic and acute dietary risk assessments, respectively. Therefore, the re-evaluation risk assessment using the EEC values, if any, would be overly protective for the consumers.

From an environmental risk perspective, to support the re-evaluation of tebuconazole, an updated summary of available water monitoring information was provided in Appendix VIII of the Proposed Re-evaluation Decision PRVD2021-08. The water monitoring data considered in the re-evaluation were from Canada and the United States (US). The measured concentrations reported in Huang et al. (2022) (PMRA#3689016) were from sampling conducted in Costa Rica, Switzerland, and France. Water monitoring data from outside of Canada and the US are not considered acceptable for use in a Canadian environmental risk assessment for pesticides as use patterns (application rates, crops) of tebuconazole and the weather, climate, and soils in these countries will be different compared to Canada. This scientific policy of considering water monitoring data from Canada and possibly from the US is outlined on page 17 of the document Health Canada's Approach to Environmental Risk Assessment for Pest Control Products.
Consequently, the environmental scientific argument for Objection 4c) does not present uncertainty because either (1) the water monitoring information was not collected in Canada or in the US, or (2) individual data points were presented without the supporting citation (raw data were not available for assessment/verification of endpoints).

Objection 4 a) and b)/Criterion 1 - Overall Conclusion: The scientific basis for Objection 4a) and 4b) is directly linked to the evaluation of tebuconazole. The scientific acceptability of the information provided by the objector was not determined because the new information provided was not relevant for use in Health Canada's risk assessment pertaining to developmental toxicity. The information in the NoO does not raise a scientifically founded doubt as to the validity of the health risks of tebuconazole, on which the decision was based.

Objection 4 c)/Criterion 1 – Overall Conclusion:
In summary, the only health related reference provided for this argument, which is based on a different interpretation of the Act and the guidance, does not support the objection and argument that a full 10-fold PCPA factor for developmental toxicity (DNT) needs to be applied due to an apparent incomplete exposure data package. In the re-evaluation of tebuconazole, a complete data package was available for the exposure assessment of tebuconazole. As a result, there is no need to apply an additional PCPA factor of 10. From an environmental perspective, Objection 4c) is linked to the evaluation of tebuconazole. However, the study by Huang et al. (2022) (PMRA#3689016) provided with the NoO did not meet the criteria for scientific acceptability for use in the evaluation of a pest control product because the information it contained was from countries outside of Canada or the US and not representative of the Canadian use pattern. Therefore, neither the objection nor the supporting information have raised scientific doubt regarding the scientific rigour of the of the risk assessment of tebuconazole.

Criterion 2: Would the advice of expert scientists assist in addressing the subject matter of the objection? To assess this question Health Canada will consider the following:

a) Is there is a lack of agreement among federal regulatory scientists with respect to the evidence presented in the objection, and could it affect the outcome of the evaluation?

Health Canada applies internationally accepted hazard and risk assessment methods as well as modern risk management approaches and policies to help ensure the safety of each pesticide registered in Canada. Regarding the PCPA factor for tebuconazole, there is no disagreement among federal regulatory scientists on issues raised in this objection, and as such it would not affect the outcome of the evaluation. The advice of expert scientists would not assist in addressing the subject matter of this objection. The objections were reviewed by Health Canada scientists not involved in the original re-evaluation of tebuconazole, and these scientists concluded that the exposure assessment conducted is appropriate and indicates no harm to any segment of the population when considering the supported conditions of use on product labels or maximum residue limits (MRLs) on imported commodities that were retained.
Also, there is no lack of agreement among federal government regulatory scientists regarding the consideration of national monitoring data and exclusion of foreign monitoring data.

b) Is the area of science relatively new and the regulatory approach still under development globally and, in this context, does Health Canada believe that the advice of the panel will aid in the regulatory decision-making process?

The area of science covered in this objection is not new and the regulatory approach for the evaluation of this type of pesticide is well established globally. The health risk assessment of tebuconazole was completed according to the standard regulatory and risk assessment frameworks, which have been in place in Canada and other OECD countries for many years. Health Canada's scientific risk-based approach to the regulation of pesticides is consistent with

international standards and is similar to Health Canada's regulatory approach for other types of chemicals. This framework provides predictability and transparency to the process used to protect the health of Canadians and their environment and helps ensure risk management decision making considers all relevant criteria in a comprehensive fashion.
The objection raised (PCPA factor) is, however, a unique provision in the *Pest Control Product Act*. A similar provision exists in the United States Food Quality Protection Act (FQPA), where there is a similar provision of consideration of a safety factor of 10-fold to take into account potential pre- and post-natal toxicity and completeness of the data with respect to exposure and toxicity to infants and children. It is noted that the US EPA in its recent Proposed Interim Registration Review Decision (2022) had determined that an FQPA factor of 1 is appropriate for risk assessment of tebuconazole. This is less conservative than the 3- or 10-fold PCPA factors that Health Canada used in its risk assessments.

Therefore, given that the science and the regulatory framework are not new, and that Health Canada has applied more protective PCPA factors than the FQPA factor applied by the US EPA, it is concluded that the advice of an external review panel will not aid in the regulatory decision-making process for this specific objection. The objection, which focuses on the interpretation of the Act and the guidance, does not raise scientifically founded doubt as to the validity of the evaluations on which the decision was based, and the advice of expert scientists would not further assist in responding to the objection, given the current assessment is protective of the potential concerns raised.

c) Is there a lack of uniformity in global regulatory evaluations related to the health or environmental risks, or value, of the pest control product that is the subject matter of the objection?

i. Does the lack of uniformity concern an aspect of the evaluation that is relevant to the Canadian use pattern?

ii. Does the lack of uniformity relate to the scientific risk assessment or a legislative requirement in the foreign jurisdiction that is not applicable to the Canadian context?

Health Canada's established PCPA factor for tebuconazole is consistent with that of independent reviews by multiple scientific experts from other major pesticide regulatory authorities internationally. Although EU/EFSA classifies tebuconazole as "suspected of damaging the unborn child," in their most recent publication (2014), they have not established an uncertainty factor of 10-fold to address uncertainty around developmental toxicity. Similar to Health Canada, the EU/EFSA is using a 3-fold uncertainty factor when developmental toxicity endpoints are used for risk assessment of tebuconazole. Furthermore, Health Canada's established reference values are more conservative than those established by the EU/EFSA and the US EPA. In the most recent US EPA human health draft risk assessment (2021, PMRA# 3688996), they have not included any additional uncertainty factors to account for developmental or neurodevelopmental effects in the young or the unborn children of females of reproductive age. They do however provide separate reference values for females of reproductive age that are more conservative than those for the general population, similar to Health Canada. Overall, there are no significant differences in the PCPA hazard characterization of tebuconazole, as informed by recent Health Canada, the US EPA, and the EU/EFSA publications. None of these agencies have applied a 10-fold PCPA factor to address uncertainty around developmental neurotoxicity. Having said that, it

is acknowledged that, each country has a specific regulatory framework, and may have different circumstances related to use patterns, monitoring data and food consumption data. This may result in variances in exposure estimates despite using similar assessment strategies and tools.

Objection 4 a), b), and c)/Criterion 2 - Overall Conclusion: The objection was reviewed by Health Canada scientists not involved in the original re-evaluation of tebuconazole. There is agreement among federal regulatory scientists in Canada as well as a uniformity in global regulatory evaluations related to the PCPA hazard characterization of tebuconazole. Therefore, the advice of expert scientists will not assist in addressing the subject matter of the objection pertaining to the PCPA factor.

Objection 4 overall conclusion:
Three arguments were raised in this objection, none of which raised scientifically founded doubt on the approach Health Canada has taken. As such, Objection 4 does not raise scientifically founded doubt as to the validity of Health Canada's evaluation and the advice of expert scientists would not assist in addressing the subject matter of this objection.

Impact of fungicide resistance to medical applications

Objection 5: "PMRA must address the potential indirect health impacts of fungicide resistance to medical applications of fungicides. In order to continue the registration of tebuconazole the PMRA must find that there is reasonable certainty that no harm will occur to human health and the environment from the use of tebuconazole. Harm to health includes harm to the health of humans from fungicide resistance, which may make it extremely challenging to treat a rising tide of fungal infections in humans"

Health Canada's Response:
The re-evaluation of tebuconazole was initiated in 2017 with the PRVD and RVD published in 2021 and 2024, respectively. While the re-evaluation did not include a section on antimicrobial resistance (AMR), Health Canada conducted a scan of the literature during this timeframe to determine whether there were any AMR-related health risks of concern from the approved triazole-based pesticides in Canada.

The scan was conducted in early 2020 and included literature up to January 10, 2020. The findings of the scan were largely consistent with the references cited in the NoO (PMRA#3688942, 3688943, 3689006, 3689007, 3689017, 3689035, 3689061, 3689065, 3689081, 3689082), specifically: i) pesticidal triazoles and triazole drugs are structurally similar and can bind to CYP51 in a similar manner; ii) agricultural environments could play a role in the development of triazole resistance; iii) exposure to triazole pesticides could result in greater tolerance of pathogen species to clinical drugs; and iv) specific environmental and clinical isolates (including those from triazole-naïve individuals) shared similarities in mutations associated with resistance including TR34/L98H or TR46/Y121F/T289A mutations in the CYP51A gene.

The available literature, at the time of the scan, however, did not confirm a direct causal link tracing the flow of triazole resistance from the environment to humans as a result of pesticidal uses of triazoles under Canadian use conditions.

From the references provided (please see Appendix I, Table 1), two references (PMRA#3688975 and 3689023), published after the 2020 scan, are considered relevant to AMR. As Health Canada is actively engaged with AMR-related activities, Health Canada intends to undertake an updated AMR assessment for the triazole class of pesticides. This update will leverage both existing Health Canada work as well as relevant information accessible by national and international partnerships. This updated AMR assessment will consider the two aforementioned references.

Health Canada intends to conduct the updated AMR assessment separately from, but in tandem, with the cumulative health risk assessment (Information Note – Cumulative health risk assessment operational planning framework - Canada.ca). Therefore, Objection 5 and the supporting references provided with the current NoO will be addressed under the updated AMR assessment. As a result, Objection 5 was not further evaluated against the NoO assessment criteria. Health Canada's approach to proceed with an independent AMR assessment is reaffirmed by the fact that no other regulatory authority has cancelled tebuconazole due to AMR concerns.

https://www.canada.ca/en/health-canada/services/consumer-product-safety/reports-publications/pesticides-pest-management/fact-sheets-other-resources/information-note-cumulative-health-risk-assessment-operational-planning-framework.html

Accumulation in the environment

Objection 6: "The PMRA's risk assessment does not address evidence that tebuconazole is resistant to the full range of breakdown processes in operative crop fields and water bodies and will likely accumulate in the environment. The PMRA should add significant additional uncertainty factors to address these significant gaps in environmental fate."

Summary of Objection 6:
The objector raised three *arguments* to further support this objection:

a) The objector argues that "The PMRA's risk assessment does not address evidence that tebuconazole is resistant to the full range of breakdown processes in operative crop fields and water bodies and will likely accumulate in the environment."
b) The objector argues that: "With only a single value, Health Canada has assumed that this study [a single aerobic soil biotransformation study] represents the upper 90% confidence interval bound on the mean for aerobic soil transformation [for water modelling]. This is not a scientifically based approach and cannot result in reasonable certainty that no harm will occur pursuant to s.2(2) of the *Pest Control Products Act*."
c) The objector argues that: "The PMRA should add significant additional uncertainty factors to address these significant gaps in environmental fate."

Health Canada's Response:

Criterion 1: Does the information in the notice of objection raise a scientifically founded doubt as to the validity of the evaluations, on which the decision was based, of the health and environmental risks and value of the pest control product? To assess whether there is scientifically founded doubt, Health Canada will consider:

a) Is the scientific basis for the objection directly linked to the evaluation of the pest control product?

Yes, Objection 6 is directly linked to the evaluation of the pest control product, tebuconazole.

b) Was the evidence supporting the objection considered in the evaluation?

i. Was the information available prior to publishing the decision?

- **If the information was available, was it considered in the assessment?**

ii. If the evidence was not considered, does the information meet the criteria for scientific acceptability for use in the evaluation of a pest control product?

The NoO cited five (PMRA#3688938, 3688971, 3689016, 3688998, 3689000) peer-reviewed scientific studies/documents from published academic literature and other regulatory organizations that were assessed by Health Canada to be relevant for Objection 6. Based on the dates of study publication (or digital signature for USEPA documents), it can be assumed that all five documents were available prior to publication of the final decision for tebuconazole.
Three (PMRA#3688938, 3688971, 3689016) of the citations were not considered in the re-evaluation assessment of tebuconazole (PMRA#3688938, 3688971, 3689016). These studies did not provide scientific evidence that would be applicable to the environmental risk assessment and did not meet criteria for scientific acceptability as only endpoints were reported and no other information that may be useful or informative for the risk assessment was submitted.
Two of the citations were reports of risk assessments conducted for tebuconazole by the USEPA regulatory group for pesticides (PMRA#3688998, 3689000). Information contained in these documents was considered by Health Canada for the re-evaluation assessment of tebuconazole, which cited the original laboratory or field studies for these endpoints. The USEPA (PMRA#3689000) reference was considered in the final re-evaluation decision and is listed in Appendix X, Section C of Re-evaluation Decision RVD2024-09.
The NoO cited various studies and documents that were not relevant to the active ingredient of concern (tebuconazole) or to the scope of work as to how Health Canada conducts science-based risk assessments. See Appendix I, Table 1.

c) Does the scientific basis of the objection and the evidence provided in support of the objection, when considered with all scientifically reliable information available and considered by Health Canada at the time of decision, present uncertainty in an aspect of the evaluation?

When considered with all scientifically reliable information available and considered by Health Canada at the time of the decision, the scientific basis for arguments 6a), b), and c) does not raise scientifically founded doubt as to the validity of the Health Canada re-evaluation of tebuconazole.

Consideration of Argument 6a)

The fate characterization for tebuconazole, published by Health Canada, described tebuconazole as persistent in soil and water matrices. Only two minor transformation products were reported in the studies/information available for the re-evaluation, and mineralization to carbon dioxide was minimal. Adsorption to soil and sediment was also observed as a route of dissipation of

tebuconazole. Under field conditions, however, tebuconazole dissipated more rapidly than was shown in laboratory studies. Also, based on the totality of information from field studies that was available, it was observed that the carryover/accumulation of tebuconazole residues in soil plateaued after a number of years of consecutive use, and that it is unlikely that concentrations of tebuconazole would continue to increase over time. Notwithstanding, a statement explaining that tebuconazole is persistent and will carry over, appears on product labels. The labels also recommend that any products containing tebuconazole not be used in areas treated with a tebuconazole product during the previous season.

Barraclough et al. (2005) (PMRA#3688938) was a general discussion of the topic of bound residues in soil. It did not refer to any specific chemicals in its discussion; therefore, it is not directly related to tebuconazole and does not suggest an uncertainty in the assessment. Health Canada's assessment used environmental fate data (from both laboratory and field studies) that was specific to tebuconazole and considered its persistence and potential for carryover in soil from one year to the next. Precautionary measures based on this assessment were implemented on product labels.

Dong (2024) (PMRA#3688971) was a review of published literature. Individual study details and original citations were not provided and therefore information could not be considered further. Notwithstanding, this literature review focused on various transformation processes that are outside the scope of Health Canada's environmental risk assessment methodology. Therefore, this information would not be used in the environmental risk assessment and does not present uncertainty in the assessment.

The fate half-lives for tebuconazole in water and soil reported by Health Canada (1140 days and 883 days, respectively) were more conservative that those reported in the literature conducted by Huang et al. (2022) (PMRA#3689016) (22 days and 600 days, respectively). The citations themselves were not provided therefore study details were not available and the data could not be assessed. However, as Health Canada used more conservative parameters for the fate characterisation of tebuconazole, this information provided by the objector does not present uncertainty in the risk assessment.

Many of the studies in USEPA (2021a) (PMRA#3688998) draft ecological risk assessment for tebuconazole and USEPA (2021b) (PMRA#3689000) tebuconazole drinking water assessment were available for the fate characterisation of tebuconazole by Health Canada. The reports were not referenced directly in Health Canada's assessment as they did not provide new or different data compared to what was used in the decision. The process/standard practice for parameter selection for water modelling may differ between regulatory agencies in the US and Canada based on respective governmental policies and approaches. The USEPA (2021b) (PMRA#3689000) reference was considered in the final re-evaluation decision and is listed in Appendix X, Section C of Re-evaluation Decision RVD2024-09. However, despite potential differences, USEPA (2021a) (PMRA#3688998) and USEPA (2021b) (PMRA#3689000) did not present uncertainty because the conclusions/fate characterisations of tebuconazole were similar to those of Health Canada.

Consequently, the scientific argument for argument 6a) does not present uncertainty because either (1) information was not directly related to tebuconazole, (2) individual data points were presented without the supporting citation (raw data were not available for assessment/verification of endpoints) or (3) additional data/endpoints would not change the outcome of the assessment (Health Canada's assessment endpoints were more conservative than those provided by the objector). In addition, Health Canada agrees with the classification of tebuconazole as a persistent pesticide in the environment, as this is supported by a review of various laboratory and field studies investigating the fate of tebuconazole in the environment.

Consideration of Argument 6b)
For argument 6b), three studies were assessed and used in a weight of evidence approach to characterize the biotic transformation of tebuconazole in aerobic soil (PMRA# 1229603 and two studies contained in PMRA# 3093536). These studies are referenced in the PRVD2021-08 and RVD2024-09 documents. From all studies, the most reliable endpoint of DT_{50} = 883 days was selected for use in the Health Canada risk assessment.

The objector did not provide any references/citations to be assessed by Health Canada for relevancy to argument 6b). Therefore, no evidence was provided to support the objection as stated. Consequently, the scientific argument for argument 6b) does not present uncertainty.

Consideration of Argument 6c
Uncertainty factors are applied to toxicity effects endpoints used in environmental risk assessments to account for potential differences in species sensitivity as well as varying protection goals such as protecting at the community, population, or individual level; they are not applied to environmental fate inputs used in environmental modelling. Details about ecotoxicity uncertainty factors are outlined in the Guidance Document, A Framework for Risk Assessment and Risk Management of Pest Control Products. The objector did not provide any references/citations to be assessed by Health Canada for relevancy to argument 6c. Therefore, no evidence was provided to support the objection as stated. Consequently, the scientific argument for argument 6c does not present uncertainty.

Objection 6/Criterion 1 – Overall Conclusion:
In summary, Objection 6 is linked to the evaluation of tebuconazole. However, three of the studies/reports provided with the NoO did not meet the criteria for scientific acceptability for use in the evaluation of a pest control product because the original sources for the information that were relevant to this objection were not provided. Barraclough et al. (2005) (PMRA# 3688938) was a general overview of partitioning/adsorption of chemicals in soil and was not specific to tebuconazole. Potentially new endpoints for environmental fate parameters were listed (PMRA#3688971 and 3689016), however, they were also not supported by original citations. The other two US EPA reports (PMRA#3688998 and 3689000) included potentially new endpoints for environmental fate parameters however; they were either similar to parameters used by Health Canada or less conservative estimates of persistence than was already used to support the tebuconazole re-evaluation decision. The USEPA 2021b reference (PMRA#3689000) was considered in the final re-evaluation decision and is listed in Appendix X, Section C of Re-evaluation Decision RVD2024-09. Therefore, neither the objection nor the supporting information have raised scientific doubt regarding the scientific rigour of the fate

assessment or determination of fate parameters describing environmental transformation processes of tebuconazole.

Criterion 2: Would the advice of expert scientists assist in addressing the subject matter of the objection? To assess this question, Health Canada will consider the following:

a) Is there a lack of agreement among federal regulatory scientists with respect to the evidence presented in the objection, and could it affect the outcome of the evaluation?

No, there is no lack of agreement among federal government regulatory scientists regarding the consideration of persistence classifications used to characterise the environmental fate of tebuconazole.

b) Is the area of science relatively new and the regulatory approach still under development globally and, in this context, does Health Canada believe that the advice of the panel will aid in the regulatory decision-making process?

No, the addition of uncertainty factors to address significant data gaps in environmental fate is not new, and the approach is not under development globally. Health Canada does not believe that the advice of a panel would aid in the regulatory decision-making process in this context.

c) Is there a lack of uniformity in global regulatory evaluations related to the health or environmental risks, or value, of the pest control product that is the subject matter of the objection?

i. Does the lack of uniformity concern an aspect of the evaluation that is relevant to the Canadian use pattern?

ii. Does the lack of uniformity relate to the scientific risk assessment or a legislative requirement in the foreign jurisdiction that is not applicable to the Canadian context?

No, there is no lack of uniformity in global regulatory evaluations with respect to the subject matter of this objection. Health Canada applied standard approaches in determining study acceptability and relevancy, consistent with what is done internationally, and applied the same acceptability and relevancy criteria across the wide range of available data sources.

Objection 6/Criterion 2 - Overall Conclusion: Health Canada applies standard approaches in determining study acceptability and relevancy that are consistent with other regulatory authorities for pest control products. The arguments and acceptable evidence provided do not reflect a lack of agreement among regulatory scientists in the case of the accumulation of tebuconazole in the environment.

Objection 6 overall conclusion:

Three arguments were raised in this objection, none of which raised scientifically founded doubt on the approach Health Canada has taken. As such, Objection 6 does not raise scientifically founded doubt as to the validity of Health Canada's evaluation and the advice of expert scientists would not assist in addressing the subject matter of this objection.

Effects on endangered insect and fish

Objection 7: "There is evidence that tebuconazole may affect numerous threatened and endangered species including sturgeon, rusty-patched bumblebees, and monarch butterflies. A jeopardy assessment should be conducted under the Species at Risk Act for all species that are potentially vulnerable to the chronic and acute effects of tebuconazole and other triazoles. The general and acute-only focused

"representative species" assessment does not target the most ecologically or toxicologically vulnerable species and does not address potential ecological-scale impacts as required by the Pest Control Products Act."

Summary of Objection 7:

The objector raised three *arguments* to further support this objection:

a) The objector argues that there is evidence that tebuconazole may affect numerous threatened and endangered species including sturgeon, rusty-patched bumblebees, and monarch butterflies.
b) The objector argues that a jeopardy assessment should be conducted under the Species at Risk Act for all species that are potentially vulnerable to the chronic and acute effects of tebuconazole and other triazoles.
c) The objector argues that the general and acute-only focused "representative species" assessment does not target the most ecologically or toxicologically vulnerable species and does not address potential ecological-scale impacts as required by the Pest Control Products Act.

Health Canada Response:

Criterion 1: Does the information in the notice of objection raise a scientifically founded doubt as to the validity of the evaluations, on which the decision was based, of the health and environmental risks and value of the pest control product? To assess whether there is scientifically founded doubt, Health Canada will consider:

a) Is the scientific basis for the objection directly linked to the evaluation of the pest control product?

Yes, Objection 7 is directly linked to the evaluation of the pest control product, tebuconazole.

b) Was the evidence supporting the objection considered in the evaluation?

i. Was the information available prior to publishing the decision?

- **If the information was available, was it considered in the assessment?**

ii. If the evidence was not considered, does the information meet the criteria for scientific acceptability for use in the evaluation of a pest control product?

The NoO cited 12 (twelve) peer-reviewed scientific studies/documents from published academic literature and other regulatory organizations that were assessed by Health Canada to be relevant for Objection 7. Based on the dates of study publication (or digital signature for USEPA documents), it can be assumed that all 12 documents were available prior to publication of the final decision for tebuconazole.

Ten (10) of the citations were not considered in the re-evaluation assessment of tebuconazole. These were: Chauzat et al. (2009)- PMRA# 3688949, David et al. (2016)- PMRA# 3688965, Dong (2024)- PMRA# 3688971, Huang et al. (2022)- PMRA# 3689016, Li et al. (2019a)- PMRA# 3689031, Li et al. (2019b)- PMRA# 3689032, Li et al. (2020)- PMRA# 3689034, Macirella et al. (2022)- PMRAA# 3689039 , Roszko et al. (2016)- PMRA# 3689057, and Zubrod et al. (2019)- PMRA# 3689085. These studies did not provide scientific evidence that would be applicable to the environmental risk assessment and did not meet criteria for scientific acceptability as only endpoints were reported and no other information that may be useful or informative for the risk assessment was provided.

Tofan et al. (2023) (PMRA#3689070) was not considered in the re-evaluation assessment of tebuconazole. However, the information contained in this document meets the criteria for scientific acceptability for use in the evaluation of a pest control product because it is a primary

literature source reporting results of the original acute toxicity test that generated an ecotoxicity endpoint on fish.

USEPA (2021a) (PMRA#3688995) reported on the *Draft Ecological Risk Assessment for the Registration Review of Tebuconazole* by the USEPA regulatory group for pesticides. Information contained in this document was considered acceptable by Health Canada for the re-evaluation assessment of tebuconazole, which cited the original laboratory or field studies for the endpoints that were reported.

The NoO cited various studies and documents that were not relevant to the active ingredient of concern (tebuconazole) or to the scope of work as to how Health Canada conducts science-based risk assessments.

c) Does the scientific basis of the objection and the evidence provided in support of the objection, when considered with all scientifically reliable information available and considered by Health Canada at the time of decision, present uncertainty in an aspect of the evaluation?

When considered along with all scientifically reliable information available and considered by Health Canada at the time of the decision, the scientific basis for arguments 7a), b), and c) does not raise scientifically founded doubt as to the validity of the Health Canada evaluation of tebuconazole.

Consideration of Argument 7a)

The intent of the framework documented in Health Canada's Approach to Environmental Risk Assessment for Pest Control Products is to outline the standard, internationally accepted test species to investigate the ecotoxicity of pesticides to non-target organisms. The risk assessment using the results from these studies are meant to represent and be protective of all species in the environment. The risk assessment for tebuconazole, published by Health Canada, described the risks to fish, pollinators and terrestrial invertebrates as follows:

- Risks to fish from all uses of tebuconazole are acceptable with the addition of spray buffer zones to mitigate the exposure of aquatic habitats through spray drift, label statements informing users of the potential toxicity of tebuconazole to aquatic organisms and precautionary statements to reduce potential runoff of tebuconazole to adjacent aquatic habitats for sites with characteristics that may be conducive to runoff and when heavy rain is forecasted.
- Risks to pollinators (*Apis* and non-*Apis* bees) from all uses of tebuconazole are acceptable and no mitigation measures are required.
- Risks to terrestrial invertebrates from all uses of tebuconazole are acceptable and no mitigation measures are required.

Dong (2024) (PMRA#3688971), Huang et al. (2022) (PMRA#3689016), Zubrod et al. (2019) (PMRA#3689085), Li et al. (2019a/PMRA#3689031, 2019b/PMRA#3689032 and 2020/PMRA#3689034), and Macirella et al. (2022) (PMRA#3689039) are all review articles that reported effects information on either fish, pollinators, or terrestrial invertebrates. None of the organisms discussed in these articles were species of sturgeon, the rusty-patched bumblebee, the monarch butterfly nor any other species that is listed as threatened or endangered according to the *Species at Risk Act* (SARA) Schedule 1. Huang et al. (2022) (PMRA#3689016) did present a range of LC_{50} values for acute zebrafish ecotoxicity tests with tebuconazole. However, Health

Canada used a more sensitive effect level than the rate range Huang et al. (2022) presented for both the freshwater fish acute risk assessment (LC_{50} = 2.3 mg a.i./L) and the marine fish acute risk assessment (LC_{50} = 5.9 mg a.i./L; Proposed Re-evaluation Decision PRVD2021-08). For all seven of these articles the information presented was obtained from primary literature sources that were not provided in support of the objection. No other details about how, when, or where these studies were conducted were provided in the review articles. This information is a requirement for Health Canada to determine if studies can be used in a pesticide risk assessment as outlined in Information Note – Determining Study Acceptability for use in Pesticide Risk Assessments. Therefore, these review articles did not present uncertainty in the assessment. Many of the studies in USEPA (2021a) (PMRA#3688995) were available for the tebuconazole ecotoxicity characterization conducted by Health Canada. The reports were not referenced directly in Health Canada's assessment as they did not provide new or different data compared to what was used in the decision. A comparison of the endpoints selected and used in the Health Canada and USEPA risk assessments is captured in the table below. Risk assessments are based on surrogate species from organism groups such as freshwater fish and pollinators.

Table 1. Comparison of the freshwater fish and pollinator endpoints selected for use in risk assessments conducted by Health Canada and USEPA

Risk Assessment Organism Group	Exposure	Health Canada Endpoint Value and Description	USEPA Endpoint Value and Description	References and Note
Freshwater fish	Acute	LC_{50} = 2.3 mg a.i./L	LC_{50} = 2.27 mg a.i./L	PMRA# 3131948 MRID# 46919204
Freshwater fish	Chronic	NOEC = 0.012 mg a.i./L	NOAEC = 0.011 mg a.i./L	PMRA# 3131948 MRID# 48109802
Pollinators	Adult acute oral honey bee	LD_{50} = 42.16 µg a.i./bee	LD_{50} = 38.59 µg a.i./bee	PMRA# 2758962 MRID# 50231601 NOTE: The same study was used by both Health Canada and USEPA but the endpoints selected differ.
Pollinators	Adult acute contact honey bee	LD_{50} = 47.8 µg a.i./bee	LD_{50} > 100 µg a.i./bee	PMRA# 2758961 MRID# 50762402 NOTE: Health Canada considered the same reference as USEPA in the risk assessment but did select a more conservative endpoint.
Pollinators	Adult chronic honey bee	NOEL = 4.86 µg a.i./bee/day	NOAEL < 2.13 µg a.i./bee/day	PMRA# 2758967 MRID# 50755103 NOTE: The same study was used by both Health Canada and USEPA but the endpoints selected differ. USEPA also classified this study as supplemental and listed it as a data deficiency.
Pollinators	Larval honey bee	LD_{50} = 11.4 µg a.i./larva	LD_{50} = 7.7 µg a.i./larva	PMRA# 2758966 MRID# 50232101 NOTE: Could not verify USEPA reference details since only the MRID number was listed in the USEPA (2021a) document submitted.

Also, as specified in USEPA (2021a) (PMRA#3688995), US federally listed threatened/endangered species were not evaluated in this document. The process/standard practice for ecotoxicity endpoint selection may differ between regulatory agencies in the US and Canada based on respective governmental policies and approaches. However, despite potential differences, USEPA (2021a) (PMRA#3688995) did not present uncertainty because the ecotoxicity conclusions of tebuconazole were similar to that of Health Canada.
Chauzat et al. (2009) (PMRA#3688949), David et al. (2016) (PMRA#3688965), and Roszko et al. (2016) (PMRA#3689057) are all monitoring studies conducted in European countries that detected tebuconazole in honey bee colony matrices. No direct effects on pollinators were evident in any of these studies after exposure to tebuconazole was confirmed. Therefore, these monitoring studies did not present uncertainty in the risk assessment for pollinators.

Tofan et al. (2023) (PMRA#3689070) contains information on an acute toxicity test that produced an ecotoxicology effect on a marine fish species. The study produced an LC_{50} value of 1.13 mg a.i./L for *Chelon auratus* after being exposed to tebuconazole. For comparison, this is lower than the acute endpoint used in Health Canada's risk assessment for marine fish which was 5.9 mg a.i./L (see Table 12 from the Proposed Re-evaluation Decision PRVD2021-08). However, when the risk assessment calculations were checked using the lower value from Tofan et al. (2023), the level of concern was not exceeded; the risk quotient remained less than a value of 1.0. The table below shows the comparison of the screening-level risk assessment calculations for the soybean and short rotation intensive culture (SRIC) uses based on the PRVD2021-08 endpoint value and those based on the Tofan et al. (2023) value. Of note is that during the consultation process of the proposed decision, additional information was submitted on risks to human health associated with the turf use, which resulted in this use being cancelled (Re-evaluation Decision RVD2024-09):

Table 2. Comparison of the risk quotient calculations for acute marine fish exposed to soybean and SRIC treatments using the endpoint selected by Health Canada and those using the endpoint from the Tofan et al. (2023) reference

Source for the Endpoint	Acute Marine Fish Endpoint (mg a.i./L)	Uncertainty Factor (UF)	Endpoint / UF = Effects Metric	Use Site or Crop	Screening-level EEC (mg a.i./L)	EEC/Effects Metric Value = Risk Quotient (RQ)	Does this exceed the Level of Concern of 1.0?
PRVD 2021-08	5.9	10	0.59	Soybean	0.03	0.03 / 0.59 = 0.05	NO
				SRIC	0.02	0.02 / 0.59 = 0.03[a]	NO
Tofan et al. (2023)	1.13	10	0.113	Soybean	0.03	0.03 / 0.113 = 0.3	NO
				SRIC	0.02	0.02 / 0.113 = 0.2	NO

[a]NOTE: The risk quotient presented here has been corrected from a typo that was present in PRVD2021-08. Neither the typo value of RQ = 0.07 nor the corrected value of RQ = 0.03 show that the risk to marine fish exceeds the level of concern.

Therefore, since this fish is not a species of sturgeon and is not listed as threatened or endangered according to the *Species at Risk Act* (SARA) Schedule 1, and the reported LC_{50} endpoint would not result in a change to the overall fish risk assessment outcome, including mitigation measures, this article did not present uncertainty in the assessment.

Consequently, argument 7a does not present uncertainty because either (1) information presented did not correlate effects of tebuconazole on threatened and endangered species including sturgeon, rusty-patched bumblebees and monarch butterflies, (2) individual data points were presented without the supporting citation (raw data were not available for assessment/verification of endpoints) or (3) additional data/endpoints that were provided would not have changed the outcome of the assessment (Health Canada's assessment endpoints were more conservative or yielded the same risk assessment outcome as those provided by the objector).

Consideration of Argument 7b)
The objector did not provide any references/citations to be assessed by Health Canada for relevancy to argument 7b). Therefore, no evidence was provided to support the objection as stated.

Pesticide use is regulated under the *Pest Control Products Act* (PCPA), which defines the "environment" to encompass biodiversity and wildlife, including species at risk. In protecting species at risk, Health Canada currently takes a tiered approach. Health Canada's current science-based environmental risk assessments are intended to prevent unacceptable risk to non-target plant and animal species in the environment. Additionally, when there are specific concerns for a particular species at risk through use of a pest control product, this is considered and incorporated into the environmental risk assessment and any required mitigation measures. Pest control product users are required to respect provisions of other legislation that are implicated when using pest control products, notably the *Species at Risk Act* (SARA) and the *Fisheries Act*. Consequently, the scientific argument for argument 7b) does not present uncertainty.

Consideration of Argument 7c)
The objector did not provide any references/citations to be assessed by Health Canada for relevancy to argument 7c). Therefore, no evidence was provided to support the objection as stated. Health Canada conducts environmental risk assessments according to the Guidance Document, A Framework for Risk Assessment and Risk Management of Pest Control Products. This framework notes that assessment endpoints are more specific descriptions of taxonomic groups and their attributes that need to be protected and, for pesticides, are defined based on the broader, over-arching protection goals as described under the *Pest Control Products Act*. Under certain circumstances, protection of individuals of threatened or endangered species can be the desired protection goal however, in most studies, effects are measured in individual organisms, even if the entity to be protected is at the population or community level.
The framework also notes that Health Canada assesses environmental risks from both acute and chronic exposures. The fate and behaviour of a pesticide, its chemistry and its use pattern will determine where the pesticide will end up in the environment and for how long. This, in turn, allows Health Canada to decide what types of organisms will most likely be exposed to the chemical and over what period of time. Health Canada uses this information to decide what organisms require toxicity testing and whether short-term (acute) or both acute and chronic (longer-term) studies are required. Consequently, the scientific argument for argument 7c) does not present uncertainty.

Objection 7/Criterion 1 – Overall Conclusion:
In summary, Objection 7 is linked to the evaluation of tebuconazole. However, ten of the studies/reports provided with the NoO did not meet the criteria for scientific acceptability for use in the evaluation of a pest control product because the original sources for the information that was relevant to this objection were not provided (Chauzat et al. 2009-PMRA# 3688949, David et al. 2016- PMRA# 3688965, Dong 2024- PMRA# 3688971, Huang et al. 2022- PMRA# 3689016, Li et al. 2019a- PMRA# 3689031, Li et al. 2019b- PMRA# 3689032, Li et al. 2020- PMRA# 3689034, Macirella et al. 2022- PMRA# 3689039, Roszko et al. 2016- PMRA# 3689057, and Zubrod et al. 2019- PMRA# 3689085).

A potential new acute toxicity endpoint for fish was presented in Tofan et al. (2023) (PMRA#3689070), that met the criteria for scientific acceptability for use in the evaluation of a pest control product. However, it was not relevant to the objection since it was conducted on a fish that is not a species of sturgeon and is not listed as threatened or endangered according to the *Species at Risk Act* (SARA), and the reported LC_{50} endpoint would not result in a change in the fish risk assessment outcome. Therefore, this article did not present uncertainty in the assessment.
The other report (USEPA 2021a) (PMRA#3688995) included potentially new ecotoxicity endpoints; however, they were either similar to values used by Health Canada or less conservative estimates than were already used to support the tebuconazole re-evaluation decision. Therefore, neither the objection nor the supporting information have raised scientific doubt regarding the scientific rigour of the risk assessment of tebuconazole.

Criterion 2: Would the advice of expert scientists assist in addressing the subject matter of the objection? To assess this question Health Canada will consider the following:

a) Is there a lack of agreement among federal regulatory scientists with respect to the evidence presented in the objection, and could it affect the outcome of the evaluation?

No, there is no lack of agreement among federal government regulatory scientists regarding the consideration of ecological-scale impacts to threatened, endangered species or other vulnerable species.

b) Is the area of science relatively new and the regulatory approach still under development globally and, in this context, does Health Canada believe that the advice of the panel will aid in the regulatory decision-making process?

No, Health Canada applies standard approaches in determining study acceptability and relevancy that are consistent with other regulatory authorities for pest control products. As such, Objection 7 does not raise scientifically founded doubt as to the validity of Health Canada evaluation and the advice of expert scientists would not assist in addressing the subject matter of this objection.

c) Is there a lack of uniformity in global regulatory evaluations related to the health or environmental risks, or value, of the pest control product that is the subject matter of the objection?

i. Does the lack of uniformity concern an aspect of the evaluation that is relevant to the Canadian use pattern?

ii. Does the lack of uniformity relate to the scientific risk assessment or a legislative requirement in the foreign jurisdiction that is not applicable to the Canadian context?

No, the arguments and acceptable evidence provided do not reflect a lack of agreement among regulatory scientists in the case of effects of tebuconazole on endangered insects and fish.

<u>Objection 7/Criterion 2 - Overall Conclusion</u>:
Health Canada applies standard approaches in determining study acceptability and relevancy that are consistent with other regulatory authorities for pest control products. The arguments and acceptable evidence provided do not reflect a lack of agreement among regulatory scientists in the case of effects of tebuconazole on endangered insects and fish.

Objection 7 overall conclusion:

Three arguments were raised in this objection, none of which raised scientifically founded doubt on the approach Health Canada has taken. Health Canada applied standard approaches in determining study acceptability and relevancy, consistent with what is done internationally, and applied the same acceptability and relevancy criteria across the wide range of available data sources. As such, Objection 7a), b), and c) does not raise scientifically founded doubt as to the validity of Health Canada evaluation and the advice of expert scientists would not assist in addressing the subject matter of this objection.

Certain uses should be cancelled

Objection 8: "Tables 19 through 24 in the proposed re-evaluation decision confirm high levels of risks to birds, from treated seed uses, which can kill birds after eating only 5 treated corn seeds. These uses are not acceptable."

Health Canada Response:

Criterion 1: Does the information in the notice of objection raise a scientifically founded doubt as to the validity of the evaluations, on which the decision was based, of the health and environmental risks and value of the pest control product? To assess whether there is scientifically founded doubt, Health Canada will consider:

a) Is the scientific basis for the objection directly linked to the evaluation of the pest control product?

Yes, Objection 8 is directly linked to the evaluation of the pest control product, tebuconazole.

b) Was the evidence supporting the objection considered in the evaluation?

i. Was the information available prior to publishing the decision?
If the information was available, was it considered in the assessment?

ii. If the evidence was not considered, does the information meet the criteria for scientific acceptability for use in the evaluation of a pest control product?

The NoO cited two (2) peer-reviewed scientific studies/documents from published academic literature and other regulatory organizations that were assessment by Health Canada to be relevant for Objection 8. Dong (2024) (PMRA# 3688971) was published in January 2024, between the publication of Health Canada's proposed re-evaluation decision for tebuconazole in July 2021 and the publication of the final decision in November 2024. Based on the date of digital signature for the USEPA (2021a) (PMRA#3688995) document, it can be assumed that it was available prior to publication of the final decision for tebuconazole.

Dong (2024) (PMRA# 3688971) was not considered in the re-evaluation assessment of tebuconazole. This study did not provide scientific evidence that would be applicable to the environmental risk assessment and did not meet criteria for scientific acceptability as only endpoints were reported and no other information that may be useful or informative for the risk assessment was submitted.

The other citation was a report containing risk assessments conducted for tebuconazole by the USEPA regulatory group for pesticides (USEPA 2021a) (PMRA#3688995). Information contained in this document was considered by Health Canada for the re-evaluation of tebuconazole, which cited the original laboratory or field studies for these endpoints.

The NoO cited various studies and documents that were not relevant to the active ingredient of concern (tebuconazole) or to the scope of work as to how Health Canada conducts science-based risk assessments.

c) Does the scientific basis of the objection and the evidence provided in support of the objection, when considered with all scientifically reliable information available and considered by Health Canada at the time of decision, present uncertainty in an aspect of the evaluation?

When considered with all scientifically reliable information available and considered by Health Canada at the time of the decision, the scientific basis for Objection 8 does not raise scientifically founded doubt as to the validity of the Health Canada evaluation of tebuconazole.

Many of the studies in USEPA (2021a) (PMRA#3688995) were available for the tebuconazole ecotoxicity characterization conducted by Health Canada. The reports were not referenced directly in Health Canada's assessment as they did not provide new or different data compared to what was used in the decision. A comparison of the bird endpoints selected and used in the Health Canada and USEPA risk assessments is captured in the table below.

Table 3. Comparison of the bird endpoints selected for use in risk assessments conducted by Health Canada and USEPA

Risk Assessment Organism Group	Exposure	Health Canada Endpoint Value and Description	USEPA Endpoint Value and Description	References and Note
Bird	Acute	LD_{50} = 1988 mg a.i./kg bw	LD_{50} = 1988 mg a.i./kg bw	PMRA# 3131948 MRID# 40700905 NOTE: The same study and endpoint value was used by both Health Canada and USEPA.
Bird	Chronic	NOEC < 156 mg a.i./kg diet, equivalent to a NOEL < 12.4 mg a.i./kg bw/d	NOAEC = 73.5 mg a.i./kg diet	PMRA# 3093537[a] MRID# 40700910 and 41624201

[a]NOTE: The PMRA document number presented here has been corrected from a typo that was present in PRVD2021-08.

The objector stated that birds can be killed after eating only 5 corn seeds treated with tebuconazole and that this is not acceptable. To address this objection, more context is provided for how Health Canada conducts environmental risk assessments. As part of the scientific evaluation process, Health Canada scientists conduct an environmental risk assessment that supports the re-evaluation of the registration of pesticides for use in Canada. This assessment is the foundation on which both the proposed re-evaluation decision and the final re-evaluation decision are based, and as per this process, a risk assessment monograph was produced for tebuconazole and its associated end-use products. Below is a summary of the assessment conducted for the seed treatment uses of tebuconazole that explains the approach, how conclusions were reached, and how they were documented in the monograph.
Toxicity values (for example, the LD_{50} – the lethal dose at which 50% of test organisms are affected) are determined under controlled conditions in a laboratory setting, where birds are fed

various doses of the pesticide through a restricted diet or by gavage. These conditions are not representative of how a wild bird may consume the pesticide in a natural setting; therefore, a set of conservative assumptions are made to estimate the potential exposure. For a seed treatment use pattern, at the initial screening level of the risk assessment, it is assumed that the diet of wild birds consists entirely of seeds treated with the pesticide being assessed, and that all of the treated seed that is planted is available for consumption *ad libitum* over an extended period of time. As this is likely to be an over-estimation of the potential exposure, several variables are incorporated into the assessment to lessen the perceived conservatism. Variables, such as feeding preference for various bird species towards different seed types, availability of treated seed on the soil surface after planting or potential avoidance behaviour toward treated seed, are brought into the assessment. In reality, not all seeds planted will be exposed and available for consumption by birds. De Snoo and Luttik (2004) (PMRA#3133554) suggested that the percentage of seeds remaining on the soil surface in fields is dependent on the seeding method (for example, broadcast or drilling) and the time of year in which seeding occurs. The percentages reported in the article ranged from 0.5% of seeds planted for precision drilling, to 3.3% for standard drilling in spring, and 9.2% for standard drilling in autumn. Field corn seeds are seeded in April or early May (Crop profile for field corn in Canada, *http://publications.gc.ca/collections/collection_2009/agr/A118-10-13-2006E.pdf*) and are assumed to be seeded using standard drilling. Additionally, information on typical seeding rates for crops (number of seeds planted per hectare) are used to estimate the minimum and maximum area required for a bird to find enough seeds to reach the toxicity endpoint used in the assessment. In the case of tebuconazole, this was an endpoint for bird reproduction.

To put the exposure and risk assessment into perspective for tebuconazole, an example is used for field corn seeds treated with this fungicide and a chronic toxicity endpoint for reproduction. The analysis in the on-field risk assessment for treated seed showed that the number of treated corn seeds needed to be consumed by a single bird to reach the dose equivalent to the reproductive endpoint, and to not exceed the level of concern (LOC), is lowest for small birds (5 seeds). However, the area that a bird would need to forage to find enough seeds to reach the reproductive endpoint is relatively large (minimum 105 m^2). For medium-sized birds, a relatively higher number of seeds needs to be ingested (25 seeds) requiring an even larger foraging area (524 m^2) to reach the reproductive endpoint. Therefore, for small- and medium-sized birds, chronic risks are considered less likely with tebuconazole-treated field corn seeds because of the relatively large number of seeds needing to be ingested (in case of medium-sized birds) and the large foraging area required for small- and medium-sized birds to acquire enough treated seed to reach the reproductive endpoint.

Additionally, small- and medium-sized birds would have difficulties ingesting a whole corn seed and, as such, it is very unlikely that a significant proportion of their diets would be made up of treated field corn seeds. To further characterise the risks, the assessment was also conducted using wheat seeds, as tebuconazole treatment of this seed crop results in the second highest exposure concentrations for birds and wheat seeds are a more relevant seed type/size for ingestion by small- and medium-sized birds. This assessment showed negligible risk to the reproduction of small- and medium-sized birds as the risk quotients that were calculated (exposure divided by the toxicity) did not exceed the LOC. It can therefore be concluded that potential on-field risks to birds are unlikely from the currently registered rate of application of tebuconazole on seeds.

Objection 8/Criterion 1 – Overall Conclusion:
In summary, Objection 8 is linked to the evaluation of tebuconazole. One study (Dong 2024-PMRA# 3688971) provided with the NoO did not meet the criteria for scientific acceptability for use in the evaluation of a pest control product because the original sources for the information that was relevant to this objection were not provided. Potentially new endpoints for the risk assessment for birds were listed in USEPA 2021a (PMRA#3688995); however, they were similar or less conservative to the endpoints already used by Health Canada to support the tebuconazole re-evaluation decision. Therefore, neither the objection nor the supporting information have raised scientific doubt regarding the scientific rigour of the risk assessment for birds exposed to seeds treated with tebuconazole.

Criterion 2: Would the advice of expert scientists assist in addressing the subject matter of the objection? To assess this question Health Canada will consider the following:

a) **Is there a lack of agreement among federal regulatory scientists with respect to the evidence presented in the objection, and could it affect the outcome of the evaluation**?

No, there is no lack of agreement among federal government regulatory scientists regarding the consideration of the risk to birds from exposure to seeds treated with tebuconazole.

b) **Is the area of science relatively new and the regulatory approach still under development globally and, in this context, does Health Canada believe that the advice of the panel will aid in the regulatory decision-making process?**

No, Health Canada applies standard approaches in determining study acceptability and relevancy that are consistent with other regulatory authorities for pest control products. As such, Objection 8 does not raise scientifically founded doubt as to the validity of Health Canada's evaluation and the advice of expert scientists would not assist in addressing the subject matter of this objection.

c) **Is there a lack of uniformity in global regulatory evaluations related to the health or environmental risks, or value, of the pest control product that is the subject matter of the objection?**
   i. **Does the lack of uniformity concern an aspect of the evaluation that is relevant to the Canadian use pattern?**
   ii. **Does the lack of uniformity relate to the scientific risk assessment or a legislative requirement in the foreign jurisdiction that is not applicable to the Canadian context?**

No, the arguments and evidence provided do not reflect a lack of uniformity among global regulatory scientists in the consideration of the risk to birds from exposure to seeds treated with tebuconazole.

Objection 8/Criterion 2 - Overall Conclusion:
Health Canada applies standard approaches in determining study acceptability and relevancy that are consistent with other regulatory authorities for pest control products. The supporting evidence provided by the objector does not reflect a lack of agreement among regulatory scientists in the case of the risk assessment for birds exposed to seeds treated with tebuconazole.

Objection 8 overall conclusion:
This objection and the supporting evidence provided did not raise scientifically founded doubt on the approach Health Canada has taken. Health Canada applied standard approaches in determining study acceptability and relevancy, consistent with what is done internationally, and

applied the same acceptability and relevancy criteria across the wide range of available data sources. As such, Objection 8 does not raise scientifically founded doubt as to the validity of Health Canada's evaluation and the advice of expert scientists would not assist in addressing the subject matter of this objection.

Objection 9: "The proposed re-evaluation decision includes numerous apparently serious environmental risks for which no clear mitigation measure has been imposed in the final re-evaluation decision."

Summary of Objection 9:
The objector raised six *arguments* to further support this objection:

a) The objector argues that there is unacceptable risk to terrestrial plants from overspray uses, these uses should be cancelled.
b) The objector argues that chronic risks to amphibians are exceeded for amphibians from aerial spraying uses, these uses should be cancelled.
c) The objector argues that soybean uses should be cancelled because they pose unacceptable risks to amphibians.
d) The objector argues that treated wood uses should be cancelled due to unacceptable risks to aquatic organisms.
e) The objector argues that risks to bees from foliar uses are not acceptable.
f) The objector argues that off-field thresholds are exceeded for beneficial arthropods and that the associated uses should be cancelled.

<u>Health Canada Response:</u>

Criterion 1: Does the information in the notice of objection raise a scientifically founded doubt as to the validity of the evaluations, on which the decision was based, of the health and environmental risks and value of the pest control product? To assess whether there is scientifically founded doubt, Health Canada will consider:

a) Is the scientific basis for the objection directly linked to the evaluation of the pest control product?

Yes, Objection 9 is directly linked to the evaluation of the pest control product, tebuconazole.

b) Was the evidence supporting the objection considered in the evaluation?
i. Was the information available prior to publishing the decision? If the information was available, was it considered in the assessment?
ii. If the evidence was not considered, does the information meet the criteria for scientific acceptability for use in the evaluation of a pest control product?

The NoO cited 19 (nineteen) peer-reviewed scientific studies/documents from published academic literature and other regulatory organizations that were assessed by Health Canada to be relevant for Objection 9. Based on the dates of study publication (or digital signature for USEPA documents), it can be assumed that all 19 documents were available prior to publication of the final decision for the re-evaluation of tebuconazole.
Fourteen (14) of the submitted citations were not considered in the re-evaluation assessment of tebuconazole. These were: Bernabo et al. (2020) (PMRA# 3688940), Chauzat et al. (2009) (PMRA# 3688949), David et al. (2016) (PMRA# 3688965), Dong (2024) (PMRA#

3688971), Huang et al. (2022) (PMRA# 3689016), Li et al. (2019a) (PMRA# 3689031), Li et al. (2019b) (PMRA#3689032), Li et al. (2020) (PMRA# 3689034), Macirella et al. (2022) (PMRA# 3689039), Qi et al. (2015) (PMRA# 3689052), Qi et al. (2018) (PMRA# 3689053), Roszko et al. (2016) (PMRA# 3689057), Smalling et al. (2013) (PMRA#3689064), and Zubrod et al. (2019) (PMRA# 3689085). These studies either did not provide scientific evidence that would be applicable to the environmental risk assessment and did not meet criteria for scientific acceptability as only endpoints were reported and no other information that may be useful or informative for the environmental risk assessment was provided. The endpoints that were provided, would not change the outcome of the risk assessment because they were not as conservative as those used in the Health Canada re-evaluation of tebuconazole decision.

Tofan et al. (2023) (PMRA# 3689070), and Ochoa-Acunã et al. (2009) (PMRA# 3689047) were both not considered in the re-evaluation assessment of tebuconazole. However, the information contained in both of these documents meets the criteria for scientific acceptability for use in the evaluation of a pest control product because they are primary literature sources reporting results of original acute toxicity tests that generated endpoints on a marine fish species (LC_{50} = 1.13 mg a.i./L; Tofan et al. 2023) and on *Daphnia magna* (LC_{50} = 0.75 mg a.i./L; Ochoa-Acunã et al. 2009).

USEPA (2021a) (PMRA# 3688995), Bernabo et al. (2016) (PMRA# 3688939) and Wrubleswski et al. (2018) (PMRA# 3689077) were all considered acceptable by Health Canada for use in the re-evaluation assessment of tebuconazole. The USEPA (2021a) (PMRA# 3688995) document reported on the *Draft Ecological Risk Assessment for the Registration Review of Tebuconazole* by the USEPA regulatory agency for pesticides. Bernabo et al. (2016) (PMRA# 3688939) showed a strong correlation between exposure to tebuconazole and the incidence of morphological abnormalities in frogs. This study was reviewed in the Proposed Re-evaluation Decision (PRVD2021-08), and it is listed under Appendix II: Additional References Cited in Health Canada's Response to the NoO section of the references. Health Canada determined that this study did not provide quantitative endpoints that could be used in the risk assessment. Wrubleswski et al. (2018) (PMRA# 3689077) is the same study and endpoint that was used in the Health Canada tebuconazole risk assessment for amphibians (under PMRA# 3133551 as referenced in the Proposed Re-evaluation Decision PRVD2021-08).

The NoO cited various studies and documents that were not relevant to tebuconazole or to the scope of work as to how Health Canada conducts science-based risk assessments.

c) Does the scientific basis of the objection and the evidence provided in support of the objection, when considered with all scientifically reliable information available and considered by Health Canada at the time of decision, present uncertainty in an aspect of the evaluation?

When considered with all scientifically reliable information available and considered by Health Canada at the time of the final decision, the scientific basis for arguments 9a), b), c), d), e), and f) does not raise scientifically founded doubt as to the validity of the Health Canada evaluation of tebuconazole.

General considerations for all arguments under Objective 9

All six of the arguments under Objective 9 are related to how risk is scientifically identified, refined, and mitigated by Health Canada. In general, as these arguments pertain to the process used by Health Canada to conduct risk assessments, consideration must be given to the methodologies used. In the Proposed Re-evaluation Decision PRVD2021-08, the following explanation is available to show how risk characterization evolves as Health Canada scientists go through the process from screening level, to risk refinement, to risk mitigation measures:

> "Initially, a screening-level risk assessment is performed to identify pesticides and/or specific uses that do not pose a risk to non-target organisms, and to identify those groups of organisms for which there may be a potential risk. The screening-level risk assessment uses simple methods, conservative exposure scenarios, and sensitive toxicity endpoints. A risk quotient (RQ) is calculated by dividing the exposure estimate by an appropriate toxicity value (RQ = exposure/toxicity), and the RQ is then compared to the level of concern (LOC = 1 for most species). If the screening-level RQ is below the LOC, the risk is considered negligible, and no further risk characterization is necessary. If the screening-level RQ is equal to or greater than the LOC, then a refined risk assessment is performed to further characterize the risk. A refined assessment takes into consideration more realistic exposure scenarios (such as drift to non-target habitats) and might consider different toxicity endpoints. Refinements may include further characterization of risk based on exposure modelling, monitoring data, results from field or mesocosm studies, and probabilistic risk assessment methods. Refinements to the risk assessment may continue until the risk is adequately characterized or no further refinements are possible. The final phase of the risk assessment framework is the determination of risk management options. When we identify potential environmental risks from pesticides, we consider different measures to reduce or mitigate the risks.
> Mitigation measures generally aim to reduce the potential for exposure to non-target organisms. There are a limited number of circumstances where mitigation is targeted at reducing toxicity (for example, through changes to a formulation resulting in lower toxicity to non-target organisms). These situations are uncommon. Various measures can be employed to reduce risks depending on the type and magnitude of concern. Based on the environmental risk assessment for a pesticide, measures can include:
>
> - label statements to identify hazards and mitigate risks
> - changes to how the pesticide is used, such as application rates, intervals, equipment and timing
> - elimination/cancellation of some or all uses for the pesticide"

The risk management and risk characterization phases are an iterative loop; Health Canada considers the various risk mitigation options when characterizing the risks (Guidance Document, A Framework for Risk Assessment and Risk Management of Pest Control Products 12 April 2024).

Consideration of Argument 9a)

In the Proposed Re-evaluation Decision PRVD2021-08, Table 24 outlines the values used in the screening-level risk assessment for non-target terrestrial plant calculations and Table 25 outlines the values used in the refined risk assessment calculations.

In Table 25, the refined risk assessment for some application methods on turf and short rotation intensive culture (SRIC) of poplar and willow trees exceeded the level of concern for seedling emergence. However, during the consultation process of this proposed decision, additional

information was submitted on risks to human health associated with the turf use, which resulted in this use being cancelled (Re-evaluation Decision RVD2024-09). Therefore, from an environmental standpoint to mitigate the risks from the remaining uses of tebuconazole (i.e. excluding the cancelled turf uses):

- Risks to non-target terrestrial plants from all uses of tebuconazole are acceptable with the addition of precautionary label statements that inform users of the potential toxicity of tebuconazole to non-target terrestrial plants.
- Risks to non-target terrestrial plants from the use of tebuconazole in SRIC are acceptable with the addition of spray buffer zones.

Dong (2024) (PMRA# 3688971) is a review article that reported general ecotoxicity information regarding effects on terrestrial plants. It did not discuss risks to non-target plants from overspray. The information presented was obtained from primary literature sources that were not provided in support of the objection. No other details about how, when, or where these studies were conducted were provided in the review article. This information is a requirement for Health Canada to determine if studies can be used in a pesticide risk assessment as outlined in Information Note – Determining Study Acceptability for use in Pesticide Risk Assessments. Therefore, this review article did not present uncertainty in the assessment. Many of the studies in USEPA (2021a) (PMRA# 3688995) were available for the tebuconazole ecotoxicity characterization conducted by Health Canada. The reports were not referenced directly in Health Canada's assessment as they did not provide new or different data compared to what was used in the decision. A comparison of the terrestrial plant endpoints selected and used in the Health Canada and USEPA risk assessments is captured in the table below.

Table 4. Comparison of the terrestrial plant endpoints selected for use in risk assessments conducted by Health Canada and USEPA

Risk Assessment Organism Group	Exposure	Health Canada Endpoint Value and Description	USEPA Endpoint Value and Description	References and Note
Terrestrial vascular plants	Vegetative vigour	ER_{25} > 453 g a.i./ha	IC_{25} = 0.709 lb a.i./ac (equivalent to 795 g a.i./ha)	PMRA# 1417830 MRID# 50786302
Terrestrial vascular plants	Seedling emergence	ER_{25} = 63.3 g a.i./ha	IC_{25} = 0.045 lb a.i./ac (equivalent to 50.44 g a.i./ha)	PMRA# 1522420 MRID# 47299201 NOTE: The same study was used by both Health Canada and USEPA but the endpoints selected differ.

The process/standard practice for ecotoxicity endpoint selection may differ between regulatory agencies in the US and Canada based on respective governmental policies and approaches. However, despite potential differences, USEPA (2021a) (PMRA# 3688995) did not present uncertainty because the ecotoxicity conclusions of tebuconazole were similar to that of Health Canada.

Consequently, argument 9a) does not present uncertainty because either: (1) individual data points were presented without the supporting citation (raw data were not available for assessment/verification of endpoints) or (2) additional data/endpoints that were provided would not have changed the outcome of the assessment (Health Canada's assessment endpoints were more conservative or yielded the same risk assessment outcome as those provided by the objector).

Consideration of Argument 9b)
In the Proposed Re-evaluation Decision PRVD2021-08, Tables 27 and 28 outline the values and calculations used in the screening-level risk assessment for acute and chronic exposure of amphibians from tebuconazole use on soybeans and SRIC, respectively. Risks to amphibians were further refined for those uses that exceeded the level of concern (i.e. acute and chronic exposure from soybean use, and chronic exposure from SRIC use).

For the refined risk assessment, spray drift data was used to determine the maximum spray deposit into an aquatic habitat located 1-metre downwind from a treated application site. The refined EEC values were calculated for aerial applications to soybean and SRIC poplar, considering a maximum percent drift deposition estimate of 23% (aerial application on crops) for soybean and 60% for SRIC poplar (aerial non-crop application). The values and calculations used in the refined risk assessment for amphibians are presented in Table 27 (for aerial application to soybean) and Table 30 (for SRIC poplar) of PRVD2021-08.

As indicated in Tables 27 and 30 in PRVD021-08, the refined chronic risk assessment for amphibians exceeded the level of concern for aerial application to soybean and SRIC poplar. Therefore, from an environmental standpoint to mitigate this risk:

- Risks to aquatic organisms (including amphibians) from all uses of tebuconazole are acceptable with the addition of precautionary label statements that inform users of the potential toxicity of tebuconazole to aquatic organisms.
- Risks to aquatic organisms from the aerial application of tebuconazole in SRIC poplar/willow and soybean are acceptable with the addition of spray buffer zones.

Bernabo et al. (2016) (PMRA#3688939) was reviewed in the Proposed Re-evaluation Decision PRVD2021-08, and it is listed in the Additional Information Considered section of the references. Therefore, this information does not present uncertainty in the assessment.

Bernabo et al. (2020) (PMRA#368894) looked at sublethal effects on amphibians through histopathological methods. This showed delay in germ cell maturation and changes to reproductive biological structures after exposure to tebuconazole. Quantitative endpoints were not provided in this study and thus, this information does not present uncertainty in the assessment.

Dong (2024) (PMRA#3688971) was a review of published literature. Individual study details and original citations were not provided and therefore information could not be considered further. Notwithstanding, this literature review focused on various transformation processes that are outside the scope of Health Canada and US's environmental risk assessment

methodology. Therefore, this information would not be used in the environmental risk assessment and does not present uncertainty in the assessment.

Many of the studies in USEPA (2021a) (PMRA# 3688995) draft ecological risk assessment for tebuconazole were available for the fate characterisation of tebuconazole by Health Canada. The reports were not referenced directly in Health Canada's assessment as they did not provide new or different data compared to what was used in the decision. A comparison of the amphibian endpoints selected and used in the Health Canada and USEPA risk assessments is captured in the table below.

Table 5. Comparison of the amphibian endpoints selected for use in risk assessments conducted by Health Canada and USEPA

Risk Assessment Organism Group	**Exposure**	**Health Canada Endpoint Value and Description**	**USEPA Endpoint Value and Description**	**References and Note**
Amphibians	Acute	LC_{50} = 0.98 mg a.i./L	LC_{50} = 0.98 mg a.i./L	PMRA# 3133551 MRID# 179653 NOTE: The same study and endpoint value was used by both Health Canada and USEPA.
Amphibians	Chronic	NOEC = 0.012 mg a.i./L	NOAEC = 0.011 mg a.i./L	PMRA# 3131948 MRID# 48109802

The process/standard practice for ecotoxicity endpoint selection may differ between regulatory agencies in the US and Canada based on respective governmental policies and approaches. However, despite potential differences, USEPA (2021a) (PMRA# 3688995) did not present uncertainty because the conclusions/risk characterisations of tebuconazole were similar to that of Health Canada.

Smalling et al. (2013) (PMRA#3689064) is a monitoring study from California that looked at pesticides detected in whole Pacific chorus frog (*Pseudacris regilla*) tissue, water, and sediment. This study did not examine the effects of tebuconazole on frogs, it only confirmed environmental exposure levels of tebuconazole. Since quantitative endpoints were not provided in this study, this information does not present uncertainty in the assessment.

Wrubleswski et al. (2018) (PMRA#3689077) presented a series of acute and chronic pesticide toxicity tests conducted on tadpoles of *Physalaemus cuvieri*. This is the same study and endpoint that was used in the Health Canada tebuconazole risk assessment for amphibians (PMRA#3133551; Proposed Re-evaluation Decision PRVD2021-08). Therefore, this information does not present uncertainty in the assessment.

Consequently, argument 9b) does not present uncertainty because either: (1) the supporting information was already considered in the Health Canada risk assessment, (2) individual data points were presented without the supporting citation (raw data were not available for assessment/verification of endpoints) or (3) additional data/endpoints that were provided would not have changed the outcome of the assessment (Health Canada's assessment endpoints were

more conservative or yielded the same risk assessment outcome as those provided by the objector).

Consideration of Argument 9c)
In the Proposed Re-evaluation Decision PRVD2021-08, Table 27 outlines the values and calculations used in the screening-level risk assessment for acute and chronic exposure of amphibians from tebuconazole use on soybean. As both acute and chronic exposure from soybean use exceeded the level of concern of 1, risks to amphibians were further refined considering spray drift and runoff. The values and calculations used in the refined risk assessment for amphibians as a as result of spray drift from aerial application to soybean are presented in Table 27. Table 32 outlines the values and calculations used in the refined risk assessment that used expected environmental concentrations (EECs) determined for runoff of tebuconazole into water bodies.

In Table 27 and 32, the refined risk assessment for amphibians exceeded the level of concern for spray drift and runoff into water bodies, respectively, as a result of use on soybeans. Therefore, from an environmental standpoint to mitigate this risk:

- Risks to aquatic organisms (including amphibians) from all uses of tebuconazole are acceptable with the addition of precautionary label statements that inform users of the potential toxicity of tebuconazole to aquatic organisms.
- Risks to aquatic organisms from the aerial application of tebuconazole in soybean are acceptable with the addition of spray buffer zones.
- Risks to aquatic habitats (including those that support amphibians) from all outdoor uses of tebuconazole are acceptable with the addition of precautionary label statements that inform users of the potential for runoff to adjacent aquatic habitats for sites with characteristics that may be conducive to runoff and when heavy rain is forecast.

The same 5 studies were submitted to support both argument 9b) and 9c). The relevance and acceptability of these studies is summarized above under argument 9b).
Consequently, argument 9c) does not present uncertainty because either: (1) the supporting information was already considered in the Health Canada risk assessment, (2) individual data points were presented without the supporting citation (raw data were not available for assessment/verification of endpoints) or (3) additional data/endpoints that were provided would not have changed the outcome of the assessment (Health Canada's assessment endpoints were more conservative or yielded the same risk assessment outcome as those provided by the objector).

Consideration of Argument 9d)
In the Proposed Re-evaluation Decision PRVD2021-08, Tables 34–37 outline the values used in the treated wood risk assessment. Default parameter values from the Organisation for Economic Cooperation and Development Emissions Scenario Document (OECD ESD; type and volume of waterbody, wood surface area to water ratios) were used. The screening input values for this assessment are presented in Tables 34 and 35. Fate and ecotoxicity input parameters were the same as those used for the other uses of tebuconazole.

In Table 36, the Tier I assessment indicated potential risk to aquatic invertebrates on a chronic basis, aquatic vascular plants, and freshwater fish on an acute basis with risk quotients (RQ) exceeding the level of concern. In Table 37, the Tier I assessment indicated potential risk to amphibians on an acute and chronic basis where the RQ values exceeded the level of concern. These risks were further refined for aquatic organisms by using the results of a leaching study based on OECD guidance. The refined risk characterization concluded the potential risk identified at Tier I from chronic exposure is not expected to occur, and that the overall impact of potential acute exposure to tebuconazole in the aquatic environment will be limited in scope and magnitude. Therefore, from an environmental standpoint to mitigate these risks:

- Risks to aquatic organisms from treated wood uses of tebuconazole are acceptable with the addition of standard label statements to protect the environment from potential discharge or runoff of tebuconazole from wood preservation facilities.

Many of the studies in USEPA (2021a) (PMRA# 3688995) draft ecological risk assessment for tebuconazole were available for the risk assessment of tebuconazole by Health Canada. The reports were not referenced directly in Health Canada's assessment as they did not provide new or different data compared to what was used in the decision. A comparison of the aquatic organism endpoints selected and used in the Health Canada and USEPA risk assessments is captured in the table below.

Table 6. Comparison of the aquatic organism endpoints selected for use in risk assessments conducted by Health Canada and USEPA

Risk Assessment Organism Group	**Exposure**	**Health Canada Endpoint Value and Description**	**USEPA Endpoint Value and Description**	**References and Note**
Freshwater algae	Acute	EC_{50} = 1.64 mg a.i./L	Not applicable; the USEPA used a surrogate endpoint value in place of the freshwater algae endpoint.	PMRA# 1417830 MRID# 50533002 (PMRA# 1453965) NOTE: The USEPA used a saltwater algae endpoint (EC_{50} = 0.17 mg a.i./L) in the risk assessment in place of an endpoint from a freshwater algae study. This same study was used to support Health Canada's marine algae risk assessment at a Health Canada calculated value of 0.19 mg a.i./L (see Table 12 in PRVD2021-08)
Freshwater invertebrates	Acute	EC_{50} = 2.79 mg a.i./L	EC_{50} = 2.79 mg a.i./L	PMRA# 3131948 MRID# 46919205 NOTE: The same study and endpoint value was used by both Health Canada and USEPA.
Freshwater invertebrates	Chronic	NOEC = 0.01 mg a.i./L	NOEC = 0.12 mg a.i./L	PMRA# 3131948 MRID# 40700915
Freshwater fish	Acute	LC_{50} = 2.3 mg a.i./L	LC_{50} = 2.27 mg a.i./L	PMRA# 3131948 MRID# 46919204
Freshwater fish	Chronic	NOEC = 0.012 mg a.i./L	NOAEC = 0.011 mg a.i./L	PMRA# 3131948 MRID# 48109802

Risk Assessment Organism Group	Exposure	Health Canada Endpoint Value and Description	USEPA Endpoint Value and Description	References and Note
Amphibians	Acute	LC_{50} = 0.98 mg a.i./L	LC_{50} = 0.98 mg a.i./L	PMRA# 3133551 MRID# 179653 NOTE: The same study and endpoint value was used by both Health Canada and USEPA.
Amphibians	Chronic	NOEC = 0.012 mg a.i./L	NOAEC = 0.011 mg a.i./L	PMRA# 3131948 MRID# 48109802

The process/standard practice for ecotoxicity endpoint selection may differ between regulatory agencies in the US and Canada based on respective governmental policies and approaches. However, despite potential differences, USEPA (2021a) (PMRA# 3688995) did not present uncertainty because the conclusions/risk characterisations of tebuconazole were similar to that of Health Canada.

Dong (2024) (PMRA# 3688971), Huang et al. (2022) (PMRA# 3689016), Zubrod et al. (2019) (PMRA# 3689085), Li et al. (2019a/PMRA# 3689031, 2019b/PMRA# 3689032, and 2020/PMRA# 3689034), and Macirella et al. (2022) (PMRA# 3689039) are all review articles that reported effects information on aquatic organisms. Huang et al. (2022) (PMRA# 3689016) did present a range of LC_{50} values for acute zebrafish ecotoxicity tests with tebuconazole. However, Health Canada used a more sensitive toxicity endpoint selected for both the freshwater fish acute risk assessment (LC_{50} = 2.3 mg a.i./L) and the marine fish acute risk assessment (LC_{50} = 5.9 mg a.i./L) in the Proposed Re-evaluation Decision (PRVD2021-08) than the range of endpoints reported in Huang et al. (2022). For all seven of these review articles, the information presented was obtained from primary literature sources that were not provided in support of the objection. No other details about how, when, or where these studies were conducted were provided in the review articles. This information is a requirement for Health Canada to determine if studies can be used in a pesticide risk assessment as outlined in Information Note – Determining Study Acceptability for use in Pesticide Risk Assessments. Therefore, this information would not be used in the environmental risk assessment and does not present uncertainty in the assessment.

Two (2) studies presented information that was both relevant and acceptable to the tebuconazole argument 9d) and the tebuconazole risk assessment. These were Ochoa-Acunã et al. (2009) (PMRA#3689047) and Tofan et al. (2023) (PMRA#3689070).

Tofan et al. (2023) (PMRA#3689070) contains information on an acute toxicity test that produced an effect on a marine fish species. The study produced an LC_{50} value of 1.13 mg a.i./L for *Chelon auratus* after being exposed to tebuconazole. For comparison, this is lower than the acute endpoint selected for use in Health Canada's risk assessment for freshwater fish (2.3 mg a.i./L; see Tables 12, 35 and 36 from the Proposed Re-evaluation Decision PRVD2021-08). According to the OECD guideline scenarios, freshwater organisms are used to assess risks associated with treated wood exposure. Notwithstanding this guidance, when the risk assessment calculations were checked using the lower value from Tofan et al. (2023) for a marine fish

species, the risk quotients (RQs) exceeded the level of concern more than the RQs calculated in the assessment conducted in PRVD2021-08.

The table below shows the comparison of the risk assessment calculations for the treated wood uses based on the PRVD2021-08 endpoint value and those based on the Tofan et al. (2023) value:

Table 7. Comparison of the risk quotient calculations for acute marine fish exposed to treated wood using the endpoint selected by Health Canada's and those using the endpoint from the Tofan et al. (2023) reference

Source of the Endpoint	Acute Marine Fish Endpoint (mg a.i./L)	Uncertainty Factor (UF)	Endpoint/ UF = Effects Metric	Treated Wood OECD Scenario[a]	Screening -level EEC (mg a.i./L)	EEC/Effects Metric = Risk Quotient (RQ)	Does this exceed the Level of Concern of 1.0?
PRVD2001-08	2.3	10	0.23	3a	9.95	9.95 / 0.23 = 43	**YES**
				3b	0.59	0.59 / 0.23 = 3	**YES**
Tofan et al. (2023)	1.13	10	0.113	3a	9.95	9.95 / 0.113 = 88	**YES**
				3b	0.59	0.59 / 0.113 = 5	**YES**

[a]Where freshwater scenarios are: 3a - a generic freshwater, flowing environment, e.g., a bridge, walkway, or dock over a small waterway, and 3b - represents sheet piling in a small waterway.

Ochoa-Acunã et al. (2009) (PMRA#3689047) contains information on an acute toxicity test that produced an ecotoxicology effect on *Daphnia magna*. The study produced an LC_{50} value of 0.75 mg a.i./L after exposure to tebuconazole. For comparison, this is lower than the acute endpoint selected for use in Health Canada's risk assessment (2.79 mg a.i./L; see Tables 12, 35 and 36 from the Proposed Re-evaluation Decision PRVD2021-08). When the risk assessment calculations were checked using the lower value from Ochoa-Acunã et al. (2009), this resulted in an exceedance of the level of concern for both of the OECD scenarios. Numerically, this appears different to the risk previously identified by Health Canada. However, as documented in section 4.2.3.1 Risk to aquatic organisms in the Proposed Re-evaluation Decision PRVD2021-08, the potential for acute risk to certain aquatic organisms will be limited in scope and magnitude, based on the OECD Guidance. The OECD guidance proposes the use of a default assumption where the leachate will reach an area of 10 m^2. Since the proposed area of potential impact for in-service treated wood uses remains 10 m^2 from the source in the waterbody regardless of the endpoint, this suggests that impacts on non-target organisms from uses of treated wood are limited in area. In addition, populations of freshwater aquatic organisms outside the affected area would act as a natural reservoir for immigration, emigration and reproduction of freshwater aquatic populations affected. Thus, neither population nor community level effects are expected, and the overall risk conclusion will not be impacted with a change in effects metric.

The table below shows the comparison of the risk assessment calculations for the treated wood uses based on the PRVD2021-08 endpoint value and those based on the Ochoa-Acunã et al. (2009) value:

Table 8. Comparison of the risk quotient calculations for acute marine fish exposed to treated wood using the endpoint selected by Health Canada's and those using the endpoint from the Ochoa-Acunã et al. (2009) reference

Source for the Endpoint	Acute Daphnia Endpoint (mg a.i./L)	Uncertainty Factor (UF)	Endpoint / UF = Effects Metric	Treated Wood OECD Scenario[a]	Screening-level EEC (mg a.i./L)	EEC/Effects Metric Value = Risk Quotient (RQ)	Does this exceed the Level of Concern of 1.0?
PRVD 2021-08	2.79	2	1.4	3a	9.95	9.95 / 1.4 = 7	**YES**
				3b	0.59	0.59 / 1.4 = 0.42	NO
Ochoa-Acunã et al. (2009)	0.75	2	0.375	3a	9.95	9.95 / 0.375 = 27	**YES**
				3b	0.59	0.59 / 0.375 = 1.6	**YES**

[a]Where freshwater scenarios are: 3a - a generic freshwater, flowing environment, e.g., a bridge, walkway, or dock over a small waterway, and 3b - represents sheet piling in a small waterway.

Therefore, despite determining more sensitive endpoints, since the reported LC_{50} values of both Tofan et al. (2023) and Ochoa-Acunã et al. (2009) do not result in a change to the overall risk assessment outcomes, including mitigation measures, these two articles do not present uncertainty in the assessment.

Qi et al. (2015) (PMRA#3689052) and (2018) (PMRA#3689053) presented both acute and chronic ecotoxicology test results for *Daphnia magna* exposed to different enantiomers of tebuconazole. Both articles presented a range of EC_{50} values, and Qi et al. (2015) also presented a NOEC level. However, Health Canada selected endpoints that were more sensitive than or the same as the ones presented in either of these articles (acute EC_{50} values of 2.79 mg a.i./L (*D. magna*) and 1.9 mg a.i./L (*D. magna*, first instars), and chronic NOEC of 0.01 mg a.i./L; Table 12 in Proposed Re-evaluation Decision PRVD2021-08). Therefore, since the reported endpoints of both Qi et al. (2015) and (2018) do not result in a change to the overall risk assessment outcomes, these two articles do not present uncertainty in the assessment.

Consequently, argument 9d) does not present uncertainty because either: (1) individual data points were presented without the supporting citation (raw data were not available for assessment/verification of endpoints), (2) additional data/endpoints that were provided would not have changed the outcome of the assessment (Health Canada's assessment endpoints were more conservative or yielded the same risk assessment outcome and risk mitigation measures as those provided by the objector).

Consideration of Argument 9e)

In the Proposed Re-evaluation Decision PRVD2021-08, Tables 15 and 16 outline the values used in the screening-level and refined risk assessment for pollinators exposed to foliar applications of tebuconazole. In Table 15, the screening-level risk assessment indicated acceptable acute and chronic risks to honey bees from the foliar use of tebuconazole on soybean, field corn, asparagus, and SRIC poplar/willow. Potential risks were identified for bees exposed to foliar applications on turf. Further risk characterization considering off-field exposure to spray drift from application on turf indicated negligible off-field risks to honey bees (Table 16). Risks to bees as a result of turf uses were also further characterized considering factors such as the attractiveness of turf to bees, weed management on golf courses and sod farms, and considering the results of the screening-level risk assessment for bumblebees (non-Apis bees), which showed negligible risks to adults or larval bees at the application rate for turf. Based on the available information, risks to pollinators (Apis and non-Apis bees) were acceptable and no mitigation was required. However, during the consultation process for the proposed decision, additional information was submitted on risks to human health associated with the turf use, which resulted in this use being cancelled (Re-evaluation Decision RVD2024-09). Therefore, from an environmental standpoint:

- Risks to pollinators (Apis and non-Apis bees) from all uses of tebuconazole are acceptable and no mitigation measures are required.

Chauzat et al. (2009) (PMRA#3688949), David et al. (2016) (PMRA#3688965), and Roszko et al. (2016) (PMRA#3689057) are all monitoring studies conducted in European countries that detected tebuconazole in honey bee colony matrices. No direct effects on pollinators were evident in any of these studies after exposure to tebuconazole was confirmed. Therefore, these monitoring studies did not present uncertainty in the risk assessment for pollinators.

Consideration of Argument 9f)

In the Proposed Re-evaluation Decision PRVD2021-08, Tables 17 and 18 outline the values used in the screening-level and refined risk assessment for beneficial arthropods (which, for Health Canada, consist of predatory and parasitic arthropods) exposed to tebuconazole.

In Table 17, the screening-level risk assessment indicated an exceedance of the level of concern for off-field exposure of beneficial arthropods, as a result of tebuconazole use on turf. Further characterization of risks by applying a vegetation distribution factor (to adjust exposure estimates) indicated no exceedances of the level of concern for off-field exposure (Table 18). However, during the consultation process for the proposed decision, additional information was submitted on risks to human health associated with the turf use, which resulted in this use being cancelled (Re-evaluation Decision RVD2024-09). Tables 17 and 18 in PRVD2021-08 include information prior to the use of turf being removed. The refined risk assessment shows current uses of tebuconazole on crops (i.e., excluding the cancelled use on turf) do not cause harm to beneficial arthropods from in-field or off-field exposure. As a result, risks are considered acceptable and precautionary label statements to protect -beneficial arthropods are not required (Re-evaluation Decision RVD2024-09).

Many of the studies in USEPA (2021a) (PMRA# 3688995) draft ecological risk assessment for tebuconazole were available for the risk assessment of tebuconazole by Health Canada. The reports were not referenced directly in Health Canada's assessment as they did not provide new or different data compared to what was used in the decision. A comparison of the beneficial

arthropod endpoints selected and used in the Health Canada and USEPA risk assessments are captured in the table below.

Table 9. Comparison of the beneficial arthropods endpoints selected for use in risk assessments conducted by Health Canada and USEPA

Risk Assessment Organism Group	**Exposure**	**Health Canada Endpoint Value and Description**	**USEPA Endpoint Value and Description**	**References and Note**
Beneficial arthropods	Foliar-dwelling	LR_{50} = 58 g a.i./ha	Not applicable	PMRA# 2758983 NOTE: The USEPA does not conduct a beneficial arthropod risk assessment. They use the pollinator risk assessment results on file.
Beneficial arthropods	Ground-dwelling	LC_{50} = 79.8 mg a.i./kg soil	Not applicable	PMRA# 2758977 NOTE: The USEPA does not conduct a beneficial arthropod risk assessment. They use the pollinator risk assessment results on file.

The process/standard practice for ecotoxicity endpoint selection may differ between regulatory agencies in the US and Canada based on respective governmental policies and approaches. However, despite potential differences, USEPA (2021a) (PMRA# 3688995) did not present uncertainty because the conclusions/risk characterisations of tebuconazole were similar to that of Health Canada. Consequently, argument 9f) does not present uncertainty because the supporting information was already considered in the Health Canada risk assessment.

Objection 9/Criterion 1 – Overall Conclusion:
In summary, Objection 9 is linked to the evaluation of tebuconazole. However, fourteen (14) of the studies/reports provided with the NoO did not meet the criteria for scientific acceptability for use in the evaluation of a pest control product because they did not provide scientific evidence that would be applicable to the environmental risk assessment, they did not meet criteria for scientific acceptability as only endpoints were reported and no other information that may be useful or informative for the risk assessment was provided, or they provided endpoints that would not change the outcome of the risk assessment because they were not as conservative as those used in the Health Canada tebuconazole decision.
Two potential new acute toxicity endpoints were presented by Tofan et al. (2023) (PMRA#3689070) and Ochoa-Acunã et al. (2009) (PMRA#3689047) that met the criteria for scientific acceptability for use in the evaluation of a pest control product. However, the endpoint in Tofan et al. (2023) was not relevant to the objection since it was conducted on a fish that is not a species of sturgeon and is not listed as threatened or endangered according to the *Species at Risk Act* (SARA), and the reported LC_{50} endpoint would not result in a change in the fish risk assessment outcome. The endpoint in Ochoa-Acunã et al. (2009) was relevant but the resulting change in risk quotient calculation would not have changed the risk outcome already presented in the Proposed Re-evaluation Decision PRVD2021-08. Therefore, these two articles do not present uncertainty in the assessment.

Bernabo et al. (2016) (PMRA#3688940) and Wrubleswski et al. (2018) (PMRA#3689077) were both considered acceptable by Health Canada for use in the re-evaluation assessment of tebuconazole and appear in the list of references in the Proposed Re-evaluation Decision PRVD2021-08. Therefore, these two articles do not present uncertainty in the assessment. The other report (USEPA 2021a) (PMRA# 3688995) included potentially new ecotoxicity endpoints; however, they were either similar to values used by Health Canada or less conservative estimates than were already used to support the tebuconazole re-evaluation decision. Therefore, neither the objection nor the supporting information have raised scientific doubt regarding the scientific rigour of the risk assessment of tebuconazole.

Criterion 2: Would the advice of expert scientists assist in addressing the subject matter of the objection? To assess this question Health Canada will consider the following:

a) Is there a lack of agreement among federal regulatory scientists with respect to the evidence presented in the objection, and could it affect the outcome of the evaluation?

No, there is no lack of agreement among federal government regulatory scientists regarding the consideration of mitigation measures.

b) Is the area of science relatively new and the regulatory approach still under development globally and, in this context, does Health Canada believe that the advice of the panel will aid in the regulatory decision-making process?

No, Health Canada applies standard approaches in determining study acceptability and relevancy that are consistent with other regulatory authorities for pest control products. As such, Objection 9 does not raise scientifically founded doubt as to the validity of Health Canada's evaluation and the advice of expert scientists would not assist in addressing the subject matter of this objection.

c) Is there a lack of uniformity in global regulatory evaluations related to the health or environmental risks, or value, of the pest control product that is the subject matter of the objection?

i. Does the lack of uniformity concern an aspect of the evaluation that is relevant to the Canadian use pattern?

ii. Does the lack of uniformity relate to the scientific risk assessment or a legislative requirement in the foreign jurisdiction that is not applicable to the Canadian context?

No, the arguments and evidence provided do not reflect a lack of agreement among regulatory scientists in the consideration of mitigation measures to protect terrestrial plants from overspray uses; chronic risks to amphibians from aerial spraying uses; soybean uses; treated wood uses; risks to bees from foliar uses; and, off-field thresholds for beneficial arthropods.

<u>Objection 9/Criterion 2 - Overall Conclusion</u>:

Health Canada applies standard approaches in determining study acceptability and relevancy that are consistent with other regulatory authorities for pest control products. The arguments and acceptable evidence provided do not reflect a lack of agreement among regulatory scientists in the case of effects of tebuconazole on beneficial arthropods.

Objection 9 overall conclusion:
Six arguments were raised in this objection, none of which raised scientifically founded doubt on the approach Health Canada has taken. Health Canada applied standard approaches in determining study acceptability and relevancy, consistent with what is done internationally, and applied the same acceptability and relevancy criteria across the wide range of available data sources. As such, Objection 9 (arguments a) through f)) does not raise scientifically founded doubt as to the validity of the Health Canada evaluation and the advice of expert scientists would not assist in addressing the subject matter of this objection.

Impact on Fungus:

Objection 10: "There were no toxicological tests on environmental fungi, including beneficial fungi in agriculture which are essential to terrestrial plant immune functions including for crops. Aquatic fungi are also entirely neglected in the risk assessment even though they play an essential ecological role. The absence of any evaluation of the ecological effects of widespread agricultural use of fungicides on fungi and their beneficial relationships with terrestrial plants creates very considerable uncertainty about whether environmental harm will result from the use of tebuconazole. All registrations of tebuconazole and other triazoles should be cancelled until a fungal risk assessment is completed."

Health Canada Response:

Criterion 1: Does the information in the notice of objection raise a scientifically founded doubt as to the validity of the evaluations, on which the decision was based, of the health and environmental risks and value of the pest control product? To assess whether there is scientifically founded doubt, Health Canada will consider:

a) **Is the scientific basis for the objection directly linked to the evaluation of the pest control product?**

Yes, Objection 10 is directly linked to the evaluation of the pest control product, tebuconazole.

b) **Was the evidence supporting the objection considered in the evaluation?**
   i. **Was the information available prior to publishing the decision? If the information was available, was it considered in the assessment?**

Yes, the cited references for Objection 10 were available prior to publishing the final re-evaluation decision of tebuconazole. However, although available, Health Canada determined that the cited references were either not a scientific source, or there was no mention of tebuconazole, or the scope was not applicable to the Canadian context, therefore, scientific acceptability was not determined for these references.

   ii. **If the evidence was not considered, does the information meet the criteria for scientific acceptability for use in the evaluation of a pest control product?**

Health Canada applies modern, rigorous risk-assessment methods and policies that are protective against possible uncertainties related to the impact of pesticides. For this objection, as beneficial fungi are not among the array of representative non-target organisms used in Health Canada's environmental risk assessment, the citations were considered to not be relevant. Having said that,

Health Canada does recognize the role of fungal symbioses and other ecologically dependent relationships on overall plant health and that some relevant organisms may be impacted by tebuconazole in the immediate area of use. However, the value and efficacy information assessed at the time of initial registration of tebuconazole uses supported the net benefits of direct and targeted treatments against pathogenic fungi in protecting cultivated crops and their yield.

c) Does the scientific basis of the objection and the evidence provided in support of the objection, when considered with all scientifically reliable information available and considered by Health Canada at the time of decision, present uncertainty in an aspect of the evaluation?

The scientific basis of Objection 10 does not raise uncertainty in the approach that Health Canada has taken when considered with all scientifically reliable information provided in support of the objection and all scientifically reliable information considered by Health Canada at the time of the decision.

Toxicity to terrestrial and aquatic beneficial fungi is not part of Health Canada's risk assessment framework. Health Canada conducts environmental risk assessments according to the Guidance Document, A Framework for Risk Assessment and Risk Management of Pest Control Products (12 April 2024) and *Health Canada's Approach to Environmental Risk Assessment for Pest Control Products* (20 September 2023).

Objection 10/Criterion 1 – Overall Conclusion:
Health Canada applies modern, rigorous risk-assessment methods and policies that are protective against possible uncertainties related to the impact of pesticides. While Health Canada does not specifically consider the effects of pesticides applications on beneficial fungi, this objection does not raise scientific doubt regarding the scientific rigour of the risk assessment for tebuconazole.

Criterion 2: Would the advice of expert scientists assist in addressing the subject matter of the objection? To assess this question Health Canada will consider the following:

a) Is there a lack of agreement among federal regulatory scientists with respect to the evidence presented in the objection, and could it affect the outcome of the evaluation?

No, there is no lack of agreement among federal government regulatory scientists regarding the consideration of beneficial fungi in regulatory pesticide risk assessments.

b) Is the area of science relatively new and the regulatory approach still under development globally and, in this context, does Health Canada believe that the advice of the panel will aid in the regulatory decision-making process?

There are no standard internationally recognized risk assessment methods to assess impacts of fungicides on beneficial fungi. The area of science is not new. Research has been published on the effects of fungicides to soil and aquatic communities (including microbial communities, biofilms, fungi, and other microorganisms). However, toxicity to terrestrial and aquatic beneficial fungi is not part of Health Canada's or any other regulatory program worldwide. Therefore, a panel will not aid in the regulatory decision-making process for tebuconazole.

c) Is there a lack of uniformity in global regulatory evaluations related to the health or environmental risks, or value, of the pest control product that is the subject matter of the objection?

Regulatory frameworks for the European Union and the US are similar to Canada, whereby an environmental risk assessment of the effects of pesticides to beneficial terrestrial and aquatic fungi are not conducted. Therefore, there is no lack of uniformity in global regulatory evaluations related to the environmental risks of tebuconazole to terrestrial and aquatic beneficial fungi.

i. Does the lack of uniformity concern an aspect of the evaluation that is relevant to the Canadian use pattern?

Not applicable.

ii. Does the lack of uniformity relate to the scientific risk assessment or a legislative requirement in the foreign jurisdiction that is not applicable to the Canadian context?

Not applicable.

Objection 10/Criterion 2 - Overall Conclusion:

There are no standard internationally recognized risk assessment methods to assess impacts of fungicides on beneficial fungi. There is no lack of uniformity in global regulatory evaluations related to the environmental risks of tebuconazole to terrestrial and aquatic beneficial fungi. Therefore, the advice from expert scientists is not required to address the subject matter of this objection.

Objection 10 overall conclusion:

Objection 10 does not raise scientifically founded doubt as to the validity of Health Canada's evaluation and the advice of expert scientists would not assist in addressing the subject matter of this objection.

Health Canada's Overall Conclusion for the Notice of Objection:

Following careful examination of each of the objections raised in the NoO by Ecojustice, related to PRVD2021-08 and RVD2024-09, Health Canada has considered the factors set out in section 3 of the *Review Panel Regulations* and has concluded: (a) that the information provided in this NoO does not raise scientifically founded doubt as to the validity of the evaluations on which the decision (RVD2024-09) was based, regarding the health and environmental risk assessments for tebuconazole; and (b) that the advice of expert scientists would not assist in addressing the subject matter of the objections. As such, it is not necessary to establish a review panel to consider any of the objections raised in this NoO. As a consequence, this NoO is now closed.

Health Canada uses a well-defined, internationally-recognized risk assessment and risk management framework in its decision making. Health Canada routinely works collaboratively with other member countries in the OECD, including the USEPA, on the regulation of pesticides. As part of the re-evaluation of an active ingredient, Health Canada takes into consideration recent developments and new information on the status of a pesticide in other jurisdictions.

As part of the proposed continuous oversight policy, Health Canada will regularly monitor published scientific literature and the publications of other international regulatory authorities on pesticides registered in Canada. A special review would be initiated if monitoring reveals new information that presents reasonable grounds to believe that the health or environmental risks of the product are, or its value is, unacceptable.

Thank you for bringing these issues to the attention of the Health Canada. We appreciate your time and effort in raising this matter, as constructive input is essential to upholding the scientific integrity of our work and the rigour of our decision-making processes. Your engagement helps us identify areas where further clarification or consideration may be needed to ensure that our assessments remain robust and grounded in sound science. We value your contribution to supporting accountability and continuous improvement in our scientific approaches.

Should you have any questions regarding this letter, please submit them to the Notice of Objection e-mail account (Pesticides.noo-ado@hc-sc.gc.ca) and we will respond as soon as possible. Please quote Reference Number 2025-0231 in any correspondence regarding the Notice of Objection to the re-evaluation of tebuconazole.

Sincerely,

Digitally signed by
Flint, Jason
Date: 2026.08.10
15:30:06 -04'00'

Jason Flint
Chief Registrar
Pesticides Regulatory Directorate
Health Canada

APPENDIX I

Table 1. References provided by Laura Bowman as listed in the objection letter (PMRA# 3676648, Sub. No. 2025-0231) with associated PMRA Nos.

PMRA#	Reference	Objection #	Scientific Study acceptability[1]/ relevance
3688934	Al-Eryani, Identification of Environmental Chemicals Associated with development of toxicant-associated fatty liver disease in rats	1 and 2	Not relevant; acceptability not determined
3688935	Altekruse - Hepatocellular carcinoma incidence mortality and survival trends in the United States from 1975 to 2005	1 and 2	Not relevant; acceptability not determined
3688936	Amrhein - Retire statistical significance	1 and 2	Not relevant; acceptability not determined
3688937	Angrish - Tipping the Balance Hepatotoxicity and the 4 Apical Key Events of Hepatic Steatosis	1 and 2	Not relevant; acceptability not determined
3688944	Cedergreen - Quantifying Synergy - A Systematic Review of Mixture Toxicity Studies	1 and 2	Not relevant; acceptability not determined
3688959	Cui - Cumulative risk assessment of dietary exposure to triazole fungicides from 13 daily-consumed foods in China	1 and 2	Not relevant; acceptability not determined
3688966	De Rop - Cumulative probabilistic risk assessment of triazo pesticides in Belgium from 2011-2014.pdf	1 and 2	Not relevant; acceptability not determined
3688974	EFSA - Establishment of cumulative assessment groups of pesticides for their effects on the thyroid	1 and 2	Not relevant; acceptability not determined
3688976	EFSA-Scientific Opinion on Risk Assessment for a Selected Group of Pesticides from the Triazole Group to Test Possible Methodologies to Assess Cumulative Effects from Exposure through Food from these Pesticides on Human Health	1 and 2	Not relevant; acceptability not determined
3688978	Enoch - Sub-structure-based category formation for the prioritisation of genotoxicity hazard assessment for pesticide residues (part 2) - Triazoles	1 and 2	Not relevant; acceptability not determined
3688985	EPA - EDSP Weight of Evidence Analysis of Potential Interaction with Estrogen	1 and 2	Relevant, acceptable. Used to support PRVD2021-08
3688986	EPA - Guidance for Identifying Pesticide Chemicals and Other Substances That Have a Common Mechanism of Toxicity	1 and 2	Not relevant; acceptability not determined
3688987	EPA - Guidance on Cumulative Risk Assessment of Pesticide Chemicals That Have a Common Mechanism of Toxicity	1 and 2	Not relevant; acceptability not determined

PMRA#	Reference	Objection #	Scientific Study acceptability[1]/ relevance
3688988	EPA - Health Effects Test Guidelines. OPPTS 870.7600 - Dermal Penetration	4d)	Not relevant; acceptability not determined
3688990	EPA - Integrated approaches to testing and assessment strategy - use of new computational and molecular tools	1 and 2	Not relevant; acceptability not determined
3688991	EPA - Oxyfluorfen_ Proposed Interim Registration Review Decision, Case Number 2490	1 and 2	Not relevant; acceptability not determined
3688992	EPA - Pesticide Cumulative Risk Assessment - Framework for Screening Analysis Purpose	1 and 2	Not relevant; acceptability not determined
3688994	EPA - Propiconazole - Revised human health draft risk assessment of conventional uses to support registration review	1 and 2	Not relevant; acceptability not determined
3689001	EPA - Tetraconazole - Draft Human Health Risk Assessment for Registration Review	1, 2, 3	Not relevant; acceptability not determined
3689009	Fustinoni - Biological monitoring of exposure to tebuconazole in winegrowers	1 and 2	Not relevant; acceptability not determined
3689011	Hass - Evaluation of tebuconazole, triclosan, methylparaben and ethylparaben according to the Danish proposal for criteria for endocrine disrupters	1 and 2	Not relevant; acceptability not determined
3689013	Heise - Hepatotoxic combination effects of three azole fungicides in a broad dose range	1 and 2	Not relevant; acceptability not determined
3689014	Heise - Hepatotoxic effects of tri azole fungicides in a broad dose range	1 and 2	Not relevant; acceptability not determined
3689015	Hershman - Foliar Fungicide Use in Corn and Soybeans	1 and 2	Not relevant; acceptability not determined
3689025	Knebel - Pregnane X receptor mediates steatotic effects of propiconazole and tebuconazole in human liver cell lines	1 and 2	Relevant, acceptable. Used to support PRVD2021-08
3689026	Knebel - Unexpected effects of propiconazole, tebuconazole, and their mixture on the receptors CAR and PXR in human liver cells	3	Relevant, acceptable. Used to support RVD2024-09
3689027	Ku - Tebuconazole mediates cognitive impairment via the microbe-gut-brain axis (MGBA) in mice	1 and 2	Not relevant; acceptability not determined
3689028	Kwon - Effects of Flutriafol Fungicide on the Lipid Accumulation in Human Liver Cells and Rat Liver	1 and 2	Not relevant; acceptability not determined

PMRA#	Reference	Objection #	Scientific Study acceptability[1]/ relevance
3689029	Lasch - More than additive effects on liver triglyceride accumulation by combinations of steatotic and non-steatotic pesticides in HepaRG cells	1 and 2	Not relevant; acceptability not determined
3689036	Lozowicka - Health risk for children and adults consuming apples with pesticide residue	1 and 2	Not relevant; acceptability not determined
3689038	Ma - Low Dose of Carbendazim and Tebuconazole_ Accumulation in Tissues and Effects on Hepatic Oxidative Stress in Mice	1 and 2	Not relevant; acceptability not determined
3689058	Sanchez - Neurotoxicity assessment of triazole fungicides on mitochondrial oxidative respiration and lipids in differentiated human SH-SY5Y neuroblastoma cells	1 and 2	Relevant, acceptable. Used to support RVD2024-09
3689071	Torovic - Pesticide residues in fruit juice in Serbia_ Occurrence and health risk estimates	1 and 2	Not relevant; acceptability not determined
3689083	Zhou - Assessing Cytotoxicity of Metabolites of Typical Triazole Pesticides in Plants	1 and 2	Not relevant; acceptability not determined
3688977	Elcombe CR et al. (2014). Mode of action and human relevance analysis for nuclear receptor mediated liver toxicity: A case study with phenobarbital as a model constitutive androstane receptor (CAR) activator. Crit. Rev. Toxicol. 44(1): 64-82.	3	Not relevant; acceptability not determined
3688981	EPA (7/27/94). Carcinogenicity Peer Review of Difenoconazole. EPA, July 27, 1994.	3	Not relevant; acceptability not determined
3688999	EPA (5/16/18). Tebuconazole: Pesticide Tolerances. 83 Fed. Reg. 22595-601 at 22600 (May 16, 2018).	1,2 and 3	Not relevant; acceptability not determined
3689002	EPA (1/11/00). Tetraconazole – Report of the Cancer Assessment Review Committee. EPA, January 11, 2000. https://archive.epa.gov/pesticides/chemicalsearch/chemical/foia/web/pdf/120603/120603- 002.pdf.	3	Not relevant; acceptability not determined
3689018	Ilyushina NA, Egorova O v., Masaltsev G v., Averianova NS, Revazova YA, Rakitskii VN, et al. Genotoxicity of mixture of imidacloprid, imazalil and tebuconazole. Toxicology Reports. 2020;7.	3	Relevant, and scientifically unacceptable
3689020	Jeong JY et al. (2022). Residual Level, Histology, and Blood Biochemistry of Tebuconazole: A Repeated Dose 28-Day Oral Toxicity Study in Pigs. Food Sci. Anim Resou 42(4): 712-722.	3 and 4 a) and b)	Not relevant; acceptability not determined
3689037	Ma F, Li Y, Yu Y, Li Z, Lin L, Chen Q, et al. Gestational exposure to tebuconazole affects the development of rat fetal Leydig cells. Chemosphere. 2021;262.	4 a) and b);	Relevant and acceptable. Used to support RVD2024-09

PMRA#	Reference	Objection #	Scientific Study acceptability[1]/ relevance
3689044	Nesnow et al. (2009). Discrimination of Tumorigenic Triazole Conazoles from Phenobarbital by Transcriptional Analyses of Mouse Liver Gene Expression. Toxicological Sciences 110(1): 68- 83.	3	Not relevant; acceptability not determined
3688941	Cumulative dietary exposure to a selected group of pesticides of triazole group in different European countries according to the EFSA guidance on proba,	5	Not relevant; acceptability not determined
3688942	Environmental fungicides and triazole resistance in Aspergillus	5	Relevant, and acceptable.
3688943	Azole-resistant Aspergillus fumigatus in the environment	5	Relevant, and acceptable.
3688960	Pathogenesis of Aspergillus fumigatus in Invasive Aspergillosis	5	Not relevant; acceptability not determined
3688975	Impact of the use of azole fungicides other than as human medicines on the development of azole-resistant Aspergillus	5	Relevant, acceptability to be determined in AMR assessment
3688979	1,2,4-Triazole, Triazole Alanine, Triazole Acetic Acid - Human Health Aggregate	5	Not relevant; acceptability not determined
3688982	Difenoconazole - Response to comments on the proposed interim decision	5	Not relevant; acceptability not determined
3688996	Tebuconazole - Human Health Draft Risk Assessment of the Conventional Uses to Support Registration Review	5	Not relevant; acceptability not determined
3688997	Tebuconazole - Proposed Interim Registration Review Decision, Case No. 7004	5	Not relevant; acceptability not determined
3689003	Tetraconazole Fact Sheet. EPA, April 2005	1,2 and 5	Not relevant; acceptability not determined
3689004	Tetraconazole use on sugar beets. Evaluation of residue data and analytical methods	1, 2 and 5	Not relevant; acceptability not determined
3689005	Comments to EPA - Draft human health risk assessment for tebuconazole	1	Relevant, will be considered under the CRA
3689006	Threats posed by the fungal kingdom to humans, wildlife, and agriculture	5	Relevant, and acceptable.
3689007	Worldwide emergence of resistance to antifungal drugs challenges human health and food security	5	Relevant, and acceptable.
3689008	FRAC Code List 2021_Fungal control agents sorted by cross resistance pattern and mode of action	5	Not relevant; acceptability not determined

PMRA#	Reference	Objection #	Scientific Study acceptability[1]/ relevance
3689017	Isolation of azole-resistant Aspergillus fumigatus from the environment in the south-eastern USA.	5	Relevant, and acceptable.
3689021	Physicologically Based Toxicokinetic Models of Tebuconazole and Application in Human Risk Assessment	5	Not relevant; acceptability not determined
3689023	Evidence for the agricultural origin of antimicrobial resistance in a fungal pathogen of humans	5	Relevant, acceptability to be determined in AMR assessment
3689030	Enantioselective effect of the chiral fungicide tebuconazole on the microbiota community and antibiotic resistance genes in the soil and earthworm gut	5	Not relevant; acceptability not determined
3689035	A factory farm fungus among us	5	Relevant, and acceptable.
3689040	Biomonitoring and risk assessment of human exposure to triazole fungicides	5	Not relevant; acceptability not determined
3689041	The Connection of Azole Fungicides with Xeno-Sensing Nuclear Receptors, Drug Metabolism and Hepatotoxicity	5	Not relevant; acceptability not determined
3689042	Dispersal of Aspergillus fumigatus from sewage sludge compost piles subjected to mechanical agitation in open air	5	Not relevant; acceptability not determined
3689043	Occurrence of Aspergillus fumigatus during composting of sewage sludge	5	Not relevant; acceptability not determined
3689045	Identification of Cumulative Assessment Groups of Pesticides, External Scientific Report Submitted to EFSA	5	Not relevant; acceptability not determined
3689046	A mysterious infection, spanning the Globe in a Climate of Secrecy	5	Not relevant; acceptability not determined
3689056	Effects of Triazole Fungicides on Soil Microbiota and on the Activities of Enzymes Found in Soil - A Review	5	Not relevant; acceptability not determined
3689061	Environmental Hotspots for Azole Resistance Selection of Aspergillus fumigatus, the Netherlands	5	Relevant, and acceptable.
3689065	Triazole Fungicides Can Induce Cross-Resistance to Medical Triazoles in Aspergillus fumigatus	5	Relevant, and acceptable.
3689067	Pesticide exposure among Czech adults and children from the CELSPAC-SPECIMEn cohort_ Urinary biomarker levels and associated health risks	5	Not relevant; acceptability not determined
3689069	Trends in Agricultural Triazole Fungicide Use in the United States	5	Not relevant; acceptability not determined

PMRA#	Reference	Objection #	Scientific Study acceptability[1]/ relevance
3689072	Cumulative Exposure Assessment of Triazole Pesticides	5	Not relevant; acceptability not determined
3689073	Combined Toxicity of Insecticides and Fungicides Applied to California Almond Orchards to Honey Bee Larvae and Adults	5	Not relevant; acceptability not determined
3689074	Toxicant-Associated Steatohepatitis	5	Not relevant; acceptability not determined
3689075	Comparative examination on synergistic toxicities of chlorpyrifos acephate or tetraconazole mixed with pyrethroid insecticides to honey bees	5	Not relevant; acceptability not determined
3689076	Are Fungicides No Longer Just For Fungi - An Analysis of Foliar Fungicide Use in Corn	5	Not relevant; acceptability not determined
3689079	Fungicide Contamination Reduces Beneficial Fungi	5	Not relevant; acceptability not determined
3689081	Dynamics of Aspergillus fumigatus in Azole Fungicide-Containing Plant Waste in the Netherlands	5	Relevant, and acceptable.
3689082	Evolution of cross-resistance to medical triazoles in Aspergillus fumigatus through selection pressue of environmental fungicides	5	Relevant, acceptable.
3688938	Bound residues: environmental solution or future problem	6	Relevant, unacceptable
3688939	Effects of long-term exposure to two fungicides, pyrimethanil and tebuconazole, on survival and life history traits of Italian tree frog (*Hyla intermedia*)	9	Relevant, acceptable. Used to support PRVD2021-08
3688940	Tissues injury and pathological changes in *Hyla intermedia* juveniles after chronic larval exposure to tebuconazole	9	Relevant, unacceptable
3688948	Enantioselective behavior and bioactivity of chiral tebuconazole in apples	6 to 10	Not relevant, acceptability not determined
3688949	Influence of Pesticide Residues on Honey Bee	7 and 9	Relevant, and acceptable
3688950	Developmental exposures to an azole fungicide triadimenol at environmentally relevant concentrations cause reproductive dysfunction in females of medaka	6 to 10	Not relevant; acceptability not determined
3688958	Chiral triazole fungicide tebuconazole	6 to 10	Not relevant, acceptability not determined
3688965	Widespread contamination of wildflower and bee-collected pollen with complex mixtures of neonicotinoids and fungicides commonly applied to crops	7 and 9	Relevant, unacceptable

PMRA#	Reference	Objection #	Scientific Study acceptability[1]/ relevance
3688967	Attenuation of toxicity and occurrence of degradation products of the fungicide tebuconazole after combined vacuum UV and UVC treatment of drinking water	6 to 10	Not relevant, acceptability not determined
3688971	A comprehensive review on toxicological mechanisms and transformation products of tebuconazole_ Insights on pesticide management	6, 7, 8, and 9	Relevant, unacceptable
3688983	Ecological Effects Test Guidelines OCSPP 850.1400 - Fish Early Life Stage Toxicity Test	6 to 10	Not relevant; acceptability not determined
3688984	Ecological Effects Test Guidelines. OPPTS 850.1500. Fish life cycle toxicity	6 to 10	Not relevant; acceptability not determined
3688993	Propiconazole - Amendment to the Draft Ecological Risk Assessment for Registration Review	6 to 10	Not relevant; acceptability not determined
3688995	Tebuconazole - Draft Ecological Risk Assessment for Registration Review.	6, 8, and 9	Relevant, acceptable
3688998	Tebuconazole drinking water assessment for registration review	6	Relevant, acceptable (used in RVD2024-09)
3689000	Tetraconazole - Draft Ecological Risk Assessment for Registration Review	6 to 10	Not relevant; acceptability not determined
3689010	Harmful Effects of Fungicides- Current status	6 to 10	Not relevant; acceptability not determined
3689012	Pesticide Mixtures, Endocrine Disruption, and Amphibian Declines - Are we underestimating the impact	6 to 10	Not relevant; acceptability not determined
3689016	A comprehensive review of 1,2,4-triazole fungicide toxicity in zebrafish (Danio rerio) A mitochondrial and metabolic perspective	4d, 6, 7, and 9	Relevant, unacceptable
3689019	Aquatic Fungi - A disregarded trophic level in ecological risk assessment of organic fungicides	6 to 10	Not relevant; acceptability not determined
3689024	Effects of fungicides on arbuscular mycorrhizal fungi: Differential responses in alkaline phosphatase activity	6 to 10	Not relevant; acceptability not determined
3689031	Endocrine disrupting effects of tebuconazole on different life stages of zebrafish danio rerio	7 and 9	Relevant, unacceptable
3689032	Parental exposure to tebuconazole causes thyroid endocrine disruption in zebrafish and developmental toxicity in offspring	7 and 9	Relevant, unacceptable
3689033	Potential neurotoxicity, immunotoxicity, and carcinogenicity induced by metribuzin and tebuconazole exposure in earthworms	6 to 10	Not relevant; acceptability not determined

PMRA#	Reference	Objection #	Scientific Study acceptability[1]/ relevance
3689034	Tebuconazole induced oxidative stress related hepatotoxicity in adult and larval zebrafish	7 and 9	Relevant, unacceptable
3689039	Effect of short-term exposure to low concentration of tebuconazole morphological histometric and functional modifications in Danio rerio liver	7 and 9	Relevant, unacceptable
3689047	Toxicity of soybean rust fungicides to freshwater algae and Daphnia magna	9	Relevant, acceptable
3689048	Atrazine reduces reproduction in Japanese medaka (Oryzias latipes)	6 to 10	Not relevant; acceptability not determined
3689050	Synergism between EBI fungicides and a pyrethroid insecticide in the honeybee apis mellifera	6 to 10	Not relevant; acceptability not determined
3689051	Current trends and mismatches on fungicide use and assessment of the ecological effects in freshwater ecosystems	6 to 10	Not relevant; acceptability not determined
3689052	Comparative toxicity of rac- and S-tebuconazole to Daphnia magna	9	Relevant, acceptable
3689053	Racemic R and S tebuconazole altered chitinase and chitobiase activity of Daphnia magna	9	Relevant, acceptable
3689054	Synergistic interactions between a variety of insecticides and an ergosterol biosynthesis inhibitor fungicide in dietary exposures of bumble bees	6 to 10	Not relevant; acceptability not determined
3689055	Before applying fungicides to corn - Stop Look Consider	6 to 10	Not relevant; acceptability not determined
3689057	Levels of Selected Persistent Organic Pollutants (PCB, PBDE) and Pesticides in Honey Bee Pollen	7 and 9	Relevant, acceptable
3689059	A Set of Scientific Issues Being Considered by the EPA Regarding Pollinator Risk Assessment Framework	6 to 10	Not relevant; acceptability not determined
3689060	Common pesticides disrupt critical ecological interactions	6 to 10	Not relevant; acceptability not determined
3689063	Propiconazole Inhibits Steroidogenesis and Reproduction in the Fathead Minnow (Pimephales promelas)	6 to 10	Not relevant; acceptability not determined
3689064	Accumulation of pesticides in pacific chorus frogs	9	Relevant, acceptable with limitations
3689066	Effects of pesticides on soil bacterial fungal and protist communities soil functions and grape quality in vineyards	6 to 10	Not relevant; acceptability not determined t
3689068	Life cycle exposure to propiconazole reduces fecundity by disrupting the steroidogenic pathway	6 to 10	Not relevant; acceptability not determined

PMRA#	Reference	Objection #	Scientific Study acceptability[1]/ relevance
3689070	Multiple Assays on Non-Target Organisms to Determine the Risk of Acute Environmental Toxicity in Tebuconazole-Based Fungicides Widely Used in the Black Sea Costal Area	7 and 9	Relevant, acceptable
3689077	Acute and chronic toxicity of pesticides on tadpoles of Physalaemus cuvieri	9	Relevant, acceptable. Used to support PRVD2021-08
3689078	Combined toxic impacts of thiamethoxam and four pesticides on the rare minnow Gobiocypris rarus	6 to 10	Not relevant; acceptability not determined
3689084	Synergistic toxicity and physiological impact of imidacloprid alone and binary mixtures with seven representative pesticides on honey bees	6 to 10	Not relevant; acceptability not determined
3689085	Fungicides - an overlooked pesticide class	5, 7 and 9	Relevant, not acceptable

[1] As per Information Note – Determining Study Acceptability for use in Pesticide Risk Assessments, the PMRA uses studies that are acceptable (that is, acceptable and acceptable with limitations) in its risk assessments, when they are found to be relevant. PMRA takes into account any study limitations or deficiencies and the consistency of the information.

- An **Acceptable** study is defined as one that is compliant with accepted guidelines and good laboratory practices (for guideline studies), scientifically sound, and that includes raw data. Such studies provides valid endpoints that may be used in a quantitative risk assessment or endpoints or other information that may be used in a qualitative weight-of-evidence risk assessment.
- A study that is **Acceptable with limitations** is defined as one that is scientifically sound but with potential limitations. For guideline studies, they may not fully comply with accepted guidelines and may deviate from good laboratory practices. Raw data may or may not be available. Study provides valid endpoints that may be used in a quantitative risk assessment or endpoints or other information that may be used in a qualitative weight-of-evidence risk assessment, taking into account the limitations of the study.
- An **unacceptable** study is defined as one that does not comply with accepted guidelines (for guideline studies), has major design flaws and that does not provide valid endpoints nor information that may be useful or informative for the risk assessment.

APPENDIX II

Additional References cited in Health Canada's Response to the NoO

PMRA#	Reference
1155896	1992. Assessment of the Potential Ecological and Biological Effects of NTN 33893 on Aquatic Ecosystems as Measured in Fiberglass Pond Systems. 791 pp.
2744281	Roessink, I., Hartgers, E., Rico, A. (2015), Amendment - Outdoor microcosm study to the effects of IMIDACLOPRID SL 200 on the summer generation of the mayfly *Cloeon dipterum*.
2142779	CCME (2007b). Canadian Water Quality Guidelines for the Protection of Aquatic Life: Imidacloprid. Canadian Council of the Ministers of the Environment, 8 pp.
3133554	De Snoo, G.R. and Luttik, R. (2004), Availability of pesticide-treated seed on arable fields. Pest Management Science Volume 60: Pages 501 to 506
3872911	Pest Management Centre- Agriculture and Agri-Food Canada. (2006). Crop Profile for Field Corn in Canada. *http://publications.gc.ca/collections/collection_2009/agr/A118-10-13-2006E.pdf* (accessed on Feb 10, 2026)

APPENDIX III

Additional References:

There were 4 references (see Table 1 below), which were indicated by the objector to have been provided in support of all objections, however upon further consideration by Health Canada, the references were found to not be relevant to any specific objection. Due to the content of the provided information (ie: not a scientific source, no mention of tebuconazole, or the scope was not applicable to the Canadian context), scientific acceptability was not determined for these references.

Table 1. References not relevant to any objections

PMRA#	Reference	Relevancy
3688945	Comments on proposed interim registration decision for tebuconazole, DACO: 11.1	Not a scientific source; not relevant to the Canadian context
3688973	Conclusion regarding the peer review of the pesticide risk assessment of the active substance - Tetraconazole, DACO: 11.1	Not relevant to tebuconazole; not relevant to the Canadian context
3689049	Registration Review docket for Cyproconazole, Fenbuconazole, Ipconazole, Metconazole, Propiconazole, Prothioconazole, Tebuconazole, DACO: 11.1	Not a scientific source; not relevant to the Canadian context

PMRA#	Reference	Relevancy
3689080	Zhang - Characteristics of Pesticide Residues and Dietary Exposure Risk Assessment on Commercial Grapes of Hubei Province in 2022	Not relevant to the Canadian context

Under Table 2, the following 14 references were determined to be out of scope of how Health Canada conducts science-based risk assessments. Studies and reports are evaluated for relevancy by Health Canada according to the scope and processes outlined in Health Canada's Approach to Environmental Risk Assessment for Pest Control Products guidance document. For additional information on the environmental risk assessment data requirements, please review the Revised Environmental Data Requirements (PRO2016-01).

Table 2. References not relevant to Objections 6, 7, 8, 9, or 10 due to being out of scope

PMRA#	Reference	Rationale for non-relevancy to any objections
3688948	Enantioselective behavior and bioactivity of chiral tebuconazole in apples	Not relevant to the scope of Health Canada's risk assessment. This study investigated the dissipation kinetics of tebuconazole enantiomers in various apple fruit varieties under field conditions. This study provided insights into the stereoselective behaviour and bioactivity of tebuconazole in apples. Dissipation trends between apple varieties were noted. The environmental risk assessment would not typically use this information for risk assessment or exposure assessment.
3688958	Chiral triazole fungicide tebuconazole: enantioselective bioaccumulation, bioactivity, acute toxicity, and dissipation in soils	This study reported an assessment/ comparison of the environmental toxicity and behaviour of enantiomers of tebuconazole. Fungicidal activity of tebuconazole to phytopathogens is outside the scope of Health Canada's environmental risk assessment. The acute toxicity to earthworm (*Eisenia fetida*), and enantioselective bioaccumulation of rac-tebuconazole in *E. fetida* were not aspects of concern in the objections. Soil incubations of R- and S-tebuconazole indicated that differences in dissipation times were governed by soil type. Dissipation times (DT_{50}) were reported for enantiomer/soil treatments and were shorter than the dissipation half-lives that were used in Health Canada's environmental risk assessment. Full study details were not provided, including number of replicates (if any) that were used; therefore these data can not be used quantitatively for a risk assessment or for inputs to water modelling. Lower DT_{50} values do not support Objection 6, which indicates a concern for accumulation of tebuconazole in the environment. Thus, this citation does not address the aspects of concern in the objections and does not raise doubt regarding the scientific integrity of the Health Canada risk assessment.
3688967	Attenuation of toxicity and occurrence of degradation products of the fungicide tebuconazole after combined vacuum UV and UVC treatment of drinking water	This citation investigated the degradation kinetics, occurrence of transformation products, and ecotoxicity changes of tebuconazole and 1,2,4-triazole after treatment with combined Vacuum UV/UVC irradiation in drinking water (organisms tested were bacteria, microalgae, fungus, *Daphnia magna*). This citation looks at ways of treating water to remove tebuconazole and its metabolites. This study does not address environmental exposure of tebuconazole in natural waters to aquatic organisms. Health Canada does not conduct an environmental risk assessment for the effects of water treatment on drinking water. This is out of the scope of the environmental risk assessment.

PMRA#	Reference	Rationale for non-relevancy to any objections
3688972	Screening Assessment - Triazines and Triazole Group	This document from Environment and Climate Change Canada reports a screening assessment of three substances, amitrole (a herbicide that is no longer registered in Canada), sodium dichloroisocyanurate and hexa(methoxymethyl)melamine (latter two are not pesticides). Tebuconazole is not mentioned in this report. Therefore, this document is not relevant to any arguments presented and is outside the scope of the objections.
3689006	Threats posed by the fungal kingdom to humans, wildlife, and agriculture	This is a general review article, citing examples of emerging fungal threats in each of three areas: human health (e.g., fungal infections, fungal allergies, increasing resistance of fungal pathogens to antifungals, mycotoxins causing cancer), wildlife biodiversity (e.g., effects on plant biodiversity, widespread disease spread in crops and into trees), and food security (diseases devastating crops relied upon by millions of people). The article discusses fungicide-resistant strains and cross-resistance to fungicides and antifungals. This is not within the scope of environmental risk assessment of pesticides and tebuconazole is not mentioned in the article.
3689008	FRAC Code List 2024: Fungal control agents sorted by cross resistance pattern and mode of action (including coding for FRAC Groups on product labels)	This document is a table that lists fungicides, mainly for use in plant protection, according to their mode of action and resistance risk. Grouping considers the biochemical mode of action, but a main driver is to identify cross-resistance patterns between chemistries. This article is not related to ecotoxicological testing on fungi (beneficial or otherwise) or environmental affects of fungicides on other non-target organisms. This document classifies all fungicides (which includes tebuconazole) that are used to control fungal pests. This information in this list is provided to CropLife International and the RAC. It is stated in a Disclaimer that users of this document do so at their own "risk". This document is not relevant for environmental risk assessment or assessment of toxicity of fungicides and their impacts on beneficial terrestrial and aquatic fungi.
3689019	Aquatic Fungi: A disregarded trophic level in ecological risk assessment of organic fungicides	Not relevant to the scope of Health Canada's risk assessment. Ittner et al. (2018) is a literature review on research regarding the effects of organic fungicides on aquatic fungi. The article describes the taxonomic classification, biodiversity, and importance/role of fungi in freshwater ecosystems. The exposure and effects of fungicides (including tebuconazole) on freshwater is summarized. The article concludes that aquatic fungi play a crucial role in aquatic ecosystems and that current risk assessments for fungicides (based on a review of EU regulation) are not explicitly protective of fungal communities. This article makes recommendations of relevant taxonomic groups for future bioassay development or improvement, and that fungicide risk assessment for aquatic organisms should be extended to fungal species. This article is not relevant as it is a review paper (details of individual studies not provided) and the subject area is outside the scope of Health Canada's environmental risk assessment of pesticides.
3689033	Potential neurotoxicity, immunotoxicity, and carcinogenicity induced by metribuzin and tebuconazole exposure in earthworms (*Eisenia fetida*) revealed by transcriptome analysis	This article states that, apart from endocrine disruption, little is known about the toxicological effects of metribuzin and tebuconazole on organisms without thyroid organs, at the transcriptional level. To explore this toxicity, RNA-seq technology was used to analyze and compare the gene expression profiles of earthworms exposed to these two chemicals. No objections or arguments on earthworms were submitted. Additionally, this article is outside the scope/framework of Health Canada's environmental risk assessment of pesticides as

PMRA#	Reference	Rationale for non-relevancy to any objections
		endpoints concerning neurotoxicity, immunotoxicity, and carcinogenicity are not used in the assessment.
3689030	Enantioselective effect of the chiral fungicide tebuconazole on the microbiota community and antibiotic resistance genes in the soil and earthworm gut	Antibiotic resistance genes (ARGs) are considered as emerging environmental contaminants, and they can be transferred vertically and horizontally between microbiota community in the soil. The research presented in this article looked at the enantioselective effect of tebuconazole on the microbiota community and ARGs in the soil and earthworm gut. Tebuconazole enantiomers showed different bioconcentration behaviours in earthworms. This article is not relevant as no objections or arguments on earthworms were submitted. Also, effects on microbial communities and antibiotic resistant genes are outside the scope/framework of Health Canada's environmental risk assessment for pesticides.
3689051	Current trends and mismatches on fungicide use and assessment of the ecological effects in freshwater ecosystems.pdf	This is a literature review and did not provide specific information on tebuconazole. The citation was looking at worldwide trends in sales, literature and research related to fungicides. The literature review stated there was a mismatch between the most sold and most studied fungicides. There was a focus on European information. As there was no focus on environmental effects or other information specific to tebuconazole, the subject of this article is outside the scope and not relevant to tebuconazole and the objections.
3689056	Effects of triazole fungicides on soil microbiota and on the activities of enzymes found in soil: A review	Not relevant to the scope of Health Canada's risk assessment. A literature review on the effects of triazole fungicides (including tebuconazole) on soil microbiota and activity of soil enzymes, as well as effects on fungal communities. The report summarizes specific research for various fungicides, including tebuconazole. For tebuconazole, it was mentioned that for one study, tebuconazole inhibited the increase of fungi populations in soil; the fungi population decreased from 2.12% (dose 0.125 mg/kg) to 36.81% (dose 2.499 mg/kg) when compared to controls. A second study reported a reduction in the population of fungi in soil, especially for the highest doses of tebuconazole that were tested. This citation is a literature review (details of individual studies not provided) and the subject area is outside the scope of Health Canada's environmental risk assessment of pesticides.
3689061	Environmental Hotspots for Azole Resistance Selection of *Aspergillus fumigatus*, the Netherlands	Azole resistance is a major concern for treatment of infections of humans with *Aspergillus fumigatus*. Exposure of immunosuppressed humans to *A. fumigatus* spores can result in aspergilloisis, which is a life-threatening disease. This study looked at identifying and sampling hot spots in environment that can lead to azole fungicide resistance in *A. fumigatus*. A panel of experts applied criteria to select potential hotspots and recommendations made on how to prevent conditions for growth of this pathogen. Pathogen resistance/resistance management is not an aspect of concern for the environmental risk assessment of pesticides. Tebuconazole was mentioned as one of the fungicides detected in these hotspots (e.g., sources of plant waste from flower production, household, food production, manure, and silage). The subject area is outside the scope of Health Canada's environmental risk assessment of pesticides.
3688983	Ecological Effects Test Guidelines OCSPP 850.1400 - Fish Early Life Stage Toxicity Test	This is one of a series of test guidelines established by the USEPA's Office of Chemical Safety and Pollution Prevention (OCSPP) for use in testing pesticides to develop data for submission to regulatory authorities. These guidelines are similar to those developed by the OECD. Both test guideline series are accepted scientific protocols and

PMRA#	Reference	Rationale for non-relevancy to any objections
		methodologies considered to be acceptable by Health Canada for providing scientific data for pesticide active ingredients. This citation does not provide any information about specific chemicals, including tebuconazole, and therefore does not support any of the objections or arguments.
3688984	Ecological Effects Test Guidelines. OPPTS 850.1500. Fish life cycle toxicity	This is one of a series of test guidelines established by the USEPA's Office of Chemical Safety and Pollution Prevention (OCSPP) for use in testing pesticides to develop data for submission to regulatory authorities. These guidelines are similar to those developed by the OECD. Both test guideline series are accepted scientific protocols and methodologies considered to be acceptable by Health Canada for providing scientific data for pesticide active ingredients. This citation does not provide any information about specific chemicals, including tebuconazole, and therefore does not support any of the objections or arguments.

Under Table 3, the following 21 references were determined to not support **any** of the environmental objections because they were **not conducted on the active ingredient of concern**, tebuconazole. Studies and reports are evaluated for relevancy by Health Canada according to Health Canada's Approach to Environmental Risk Assessment for Pest Control Products guidance document. In section 3.0 of this document, it outlines that for both pre-market and post-market assessments, Health Canada requires information on the environmental fate, behaviour and ecotoxicity of the pesticide active ingredient be submitted. For additional information on Health Canada's environmental risk assessment data requirements, please review the Revised Environmental Data Requirements (PRO2016-01).

Table 3. References submitted that do not support any environmental objections because they were not conducted on Tebuconazole

PMRA#	Reference	Rationale for Non-Relevancy to any Objections
3688950	Developmental exposures to an azole fungicide triadimenol at environmentally relevant concentrations cause reproductive dysfunction in females of medaka fish	Not relevant to the active ingredient of concern. The study is on the effects of triadimenol, a metabolite of another triazole fungicide (triadimenol is a metabolite of triadimenfon) on medaka fish (reproductive dysfunction in females). Some sublethal endpoints are presented. Triadimenfon is not a registered pesticide in Canada.
3689010	Harmful Effects of Fungicides- Current status.	Not relevant to the active ingredient of concern. This general review articles discusses fungicide resistance status in India. Fungicides play a major role in the management of plant diseases. But, excessive and irrational use of fungicides causes environment deterioration and has non-target effects on plants and animals. The review discusses that there can be harmful effects on soil microorganisms, and other plants and animals from the use of fungicides. For example, negative effects on soil microbes, saprophyte populations of microorganisms, as well as potential for fungicide resistance. However, there is no mention of tebuconazole in the article. This discussion is not relevant for the environmental risk assessment of pesticides and the objections that were provided.
3689012	Pesticide Mixtures, Endocrine Disruption, and Amphibian Declines - Are	Not relevant to the active ingredient of concern. The article reported on experiments that were conducted with four herbicides, three insecticides and two fungicides (metalaxyl and propiconazole) to investigate the

PMRA#	Reference	Rationale for Non-Relevancy to any Objections
	we underestimating the impact?	effects of exposure of *Rana pipiens* and *Xenopus laevis* on amphibian mortality, metamorphosis, gonadal development, and flavobacterial responses. Tebuconazole was not included in these studies.
3689024	Effects of fungicides on arbuscular mycorrhizal fungi: differential responses in alkaline phosphatase activity of external and internal hyphae	Not relevant to the active ingredient of concern. The research paper investigates the effects of fenpropimorph and propiconazole on beneficial fungi. Test substances were applied at 1 and 1000 times the recommended field application to plant-fungal test units. The effect of four fungicides on alkaline phosphatase (ALP) activity in internal and external hyphae of an arbuscular mycorrhizal (AM) fungus was examined. Study looked at non-target plant growth effects (fungicides can affect the fungi that are involved in increasing plant nutrition acquisition). This study did not include tebuconazole. Also, effects on beneficial fungi are outside of the current scope of Health Canada's risk assessment framework for pesticides.
3689048	Atrazine reduces reproduction in Japanese medaka (*Oryzias latipes*)	Not relevant to the active ingredient of concern. This study investigated a population endpoint (egg production) in conjunction with histological (reproductive stage, gonad pathology) and biochemical (aromatase activity, sex hormone production) phenotypes associated with atrazine exposure in Japanese medaka. Tebuconazole was not included in this study.
3689050	Synergism between EBI fungicides and a pyrethroid insecticide in the honeybee, *Apis mellifera* L (thesis, University of Southampton)	Not relevant to the active ingredient of concern. This scientific thesis focused on synergistic effects for ergosterol biosynthesis inhibiting (EBI) fungicides + pyrethroids in honeybee (i.e., lambda cyhalothrin plus triazole and imidazole fungicides). Tebuconazole was not one of the chemicals used in the research for this thesis.
3689054	Synergistic interactions between a variety of insecticides and an ergosterol biosynthesis inhibitor fungicide in dietary exposures of bumble bees	Not relevant to the active ingredient of concern. This study investigated the synergistic effects of various insecticides with the fungicide imazalil on the dietary exposures of bumblebees. Tebuconazole was not one of the test substances for this investigation.
3689055	Before applying fungicides to corn: Stop! Look! Consider! (This article appears on Iowa State University Extension and Outreach website)	Not relevant to the active ingredient of concern. This citation is a publication for extension and outreach by Iowa State University Integrated Pest Management. It discusses the importance of scouting fields and identifying disease pressures before applying any fungicides to corn. The article discusses profitability of fungicide applications on corn. There is no discussion of any environmental effects/impacts of applying fungicides, to pollinators or other organisms, or effects on persistence. Tebuconazole is not mentioned. It was also published after the date of publication of the final re-evaluation decision for tebuconazole.
3689060	Common pesticides disrupt critical ecological interactions	Not relevant to the active ingredient of concern. This is an opinion article promoting the use of integrated pest management (IPM) practices in general over prophylactic pesticide applications in order to support ecosystem health. The article mentions that above- and below-ground ecological relationships (such as plant relationships to arbuscular mycorrhizal fungi and endophytic fungi) could be harmed by use of fungicides in agroecosystems, having effects on crop yields and profits. Tebuconazole is not mentioned specifically.
3689063	Propiconazole Inhibits Steroidogenesis and Reproduction in the	Not relevant to the active ingredient of concern. This 21-day study evaluated apical reproductive endpoints (fecundity, fertility, hatch) and

PMRA#	Reference	Rationale for Non-Relevancy to any Objections
	Fathead Minnow (*Pimephales promelas*)	markers for endocrine disrupting chemicals in male and female fish exposed to propiconazole.
3689066	Effects of pesticides on soil bacterial, fungal and protist communities, soil functions, and grape quality in vineyards	Not relevant to the active ingredient of concern. The study investigated over three consecutive years how different soil microbial groups (bacteria, fungi, protists), their associated soil functions (soil respiration, litter decomposition), and agroecosystem services (grape quality) are affected by long-term herbicide application (glyphosate) and soil copper content in 29 vineyards in Switzerland. Endpoints are not relevant to HC-PMRA environmental risk assessment framework, and tebuconazole was not part of the study.
3689068	Life cycle exposure to propiconazole reduces fecundity by disrupting the steroidogenic pathway and altering DNA methylation in zebrafish (*Danio rerio*)	Not relevant to the active ingredient of concern. In this study, zebrafish (*Danio rerio*) were exposed to environmentally-relevant levels of propiconazole throughout the life cycle, from embryo to sexually mature adults, and the effects on growth, reproduction, and offspring viability were investigated. Tebuconazole was not included in this study.
3689059	Meeting Minutes of the FIFRA Scientific Advisory Panel Meeting held September 11-14, 2012 on "Pollinator Risk Assessment Framework"	Not relevant to the active ingredient of concern. The meeting minutes captured the discussion of "A Set of Scientific Issues Being Considered by the EPA Regarding Pollinator Risk Assessment Framework." Meeting minutes do not represent information that has been approved or disseminated by the USEPA, nor does it represent the views and policies of the USEPA or other Agencies that were involved. The purpose of the SAP meeting was to advise on the proposed process for quantifying potential risks of pesticides to honey bees. This Pollinator Risk Assessment Framework would apply to all pesticide active ingredients, and was a framework being worked on with the collaboration of Health Canada.
3689000	Draft Ecological Risk Assessment for Registration Review of Tetraconazole	Not relevant to the active ingredient of concern. This is an environmental risk assessment of a different active ingredient, tetraconazole.
3688993	Propiconazole - Amendment to the Draft Ecological Risk Assessment for Registration Review	Not relevant to the active ingredient of concern. This is an amendment to the propiconazole draft risk assessment (DRA) but is not the comprehensive ecological DRA, a different active ingredient.
3689073	Combined Toxicity of Insecticides and Fungicides Applied to California Almond Orchards to Honey Bee Larvae and Adults	Not relevant to the active ingredient of concern. The objective of this study was to test commonly used insecticides and fungicides (commonly used during almond bloom) on honey bee larval development (in vitro larval rearing assays) and adults (feeding studies) using laboratory bioassay procedures. The fungicides used were propiconazole, iprodione and a boscalid-pyraclostrobin mixture. Tebuconazole was not one of the test substances used for this investigation.
3689075	Comparative examination on synergistic toxicities of chlorpyrifos, acephate or tetraconazole mixed with pyrethroid insecticides to honey bees (*Apis mellifer* L.)	Not relevant to the active ingredient of concern. The toxicities of individual and mixtures of chlorpyrifos (CHL), acephate (ACE), or tetraconazole (TET) with nine pyrethroid insecticides to honey bees (*Apis mellifera* L.) were evaluated to reveal any aggregated interaction between pesticides. Tebuconazole was not one of the test substances used in this study.
3689076	Are Fungicides No Longer Just For Fungi - An Analysis of Foliar Fungicide Use in Corn	Not relevant to the active ingredient of concern. This is a general article about use of fungicides on corn over time, impact of fungicides on corn growth and yields, fungal resistance to fungicides and strategies for resistance management, and negative effects on beneficial fungi and

PMRA#	Reference	Rationale for Non-Relevancy to any Objections
		other organisms. No data or toxicity values are reported in the article, but statements are included to indicate that fungicides are toxic to frogs, mussels, algae, and water fleas. This is a very general information article, not original research. There is no mention of tebuconazole.
3689078	Combined toxic impacts of thiamethoxam and four pesticides on the rare minnow (*Gobiocypris rarus*)	Not relevant to the active ingredient of concern. To examine pesticide mixture toxicity to aqueous organisms, this study assessed the single and combined toxicities of thiamethoxam and four other pesticides (chlorpyrifos, beta-cypermethrin, tetraconazole, and azoxystrobin) to the rare minnow (*Gobiocypris rarus*). Tebuconazole was not included in this study.
3689079	Fungicide Contamination Reduces Beneficial Fungi	Not relevant to the active ingredient of concern. The study looked at correlation between fungicide use (tebuconazole was not mentioned specifically) and reduction of beneficial fungi in bee bread (field study). Author states that evidence supports that concentrations of fungicides that are being applied in the field are sufficiently high to get into bee colonies by way of pollen (and subsequently bee bread). This reduced the amount of beneficial bee bread fungi; however, bees appear capable of managing the effect of fungicide contamination at the level of the concentrations that are applied in the field for these studies. Negative effects were not noted and were not related to mortality, growth, or reproduction of bees.
3689084	Synergistic toxicity and physiological impact of imidacloprid alone and binary mixtures with seven representative pesticides on honey bees	Not relevant to the active ingredient of concern. This study looked at synergistic effects of various pesticide mixtures which included imidacloprid with seven other pesticides. Tebuconazole was not used in this study (tetraconazole was the azole used to represent this group of fungicides). Three replicates of 25 bees per treatment "cage" (polypropylene jars) were sprayed (through a hole in the jar lid) with one of the mixtures and mortality recorded.

Under Table 4, two references were submitted as background information and it was specified by the objector that they did not support any specific objection. These two documents were deemed not relevant since they were not used to support any specific objections, nor were they related to the re-evaluation of tebuconazole.

Table 4. References submitted for background information only

PMRA#	Reference
3688989	Implementing the Pesticide Registration Improvement Act Fiscal Year 2018, DACO: 11.1
3689062	Management of Verticillium wilt in strawberry using vegetable crop rotation, DACO: 11.1