Proposed Re-evaluation Decision PRVD2021-04

Cymoxanil and Its Associated End-use Products

Consultation Document

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Proposed re-evaluation decision for cymoxanil and associated end-use products

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

Cymoxanil is a fungicide registered for use on potatoes, field tomatoes and caneberries. Currently registered products containing cymoxanil can be found in the Pesticide Label Search and in Appendix I.

This document presents the proposed re-evaluation decision for the re-evaluation of cymoxanil, including the proposed amendments (risk mitigation measures) to protect human health and the environment, as well as the science evaluation on which the proposed decision is based. All products containing cymoxanil that are registered in Canada are subject to this proposed re-evaluation decision. This document is subject to a 90-day public consultation period,[1] during which the public including the pesticide manufacturers and stakeholders may submit written comments and additional information to PMRA Publications. The final re-evaluation decision will be published after taking into consideration the comments and information received during the consultation period.

Proposed re-evaluation decision for cymoxanil

Under the authority of the *Pest Control Products Act* and based on an evaluation of available scientific information, Health Canada is proposing continued registration of cymoxanil and all associated end-use products registered for sale and use in Canada.

With respect to human health, occupational and postapplication risks were shown to be acceptable when cymoxanil is used according to proposed conditions of registration, which include new mitigation measures. Dietary risks were shown to be acceptable when used according to current conditions of registration.

Based on available scientific information, the risks to the environment were shown to be acceptable when cymoxanil is used according to proposed conditions of registration, which includes new mitigation measures.

Cymoxanil has value in disease control for potato, field tomato and caneberry growers, due to its protective, curative and broad spectrum disease control properties. It is the only Group 27 fungicide registered in Canada, which makes it important as a resistance management tool.

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

Risk mitigation measures

Registered pesticide product labels include specific directions for use. Directions include risk mitigation measures to protect human health and the environment and must be followed by law. The proposed label amendments including any revised/updated label statements and/or mitigation measures, as a result of the re-evaluation of cymoxanil, are summarized below. Refer to Appendix X for details.

Human health

Label improvements to meet current standards:

- The spray volume for all aerial application is 50 L/ha (for consistency between product labels).

Risk mitigation:
To protect the mixers/loaders/applicators, the following risk-reduction measures are proposed:

- Groundboom application for potatoes:
    - Chemical-resistant coveralls over long-sleeved shirt and long pants, chemical-resistant gloves for mixers/loaders and applicators, plus a respirator for mixers/loaders.
    - Limit of 35 kg a.i./day cymoxanil products handled.
- Airblast application for caneberries:
    - Chemical-resistant coveralls over long-sleeved shirt and long pants, chemical-resistant gloves for mixers/loaders and applicators (no gloves if enclosed cab).
    - Chemical resistant headgear for applicators using open cab airblast equipment.
- Handheld application (spot applications):
    - Chemical-resistant coveralls over a single layer of clothing, chemical-resistant gloves for mixers/loaders and applicators, plus a respirator for mixers/loaders.
- Aerial application:
    - For potatoes:
        - Chemical-resistant coveralls over long-sleeved shirt and long pants, chemical resistant gloves for mixing/loading, plus a respirator for workers mixing/loading of cymoxanil products.
        - Limit of 52.5 kg a.i./day cymoxanil products handled.

To protect workers entering treated sites, the following risk-reduction measures are proposed:

- Revised Restricted-entry intervals (REIs):
    - 18 days for hand-set irritation for potatoes.
    - 6 days for roguing potatoes.
    - 8 days for hand-set irrigation for field tomatoes.
    - 11 days for hand-set irrigation for caneberries.

To protect bystanders from spray drift:

- A statement to promote best management practices to minimize human exposure from spray drift or spray residues resulting from drift.

Environment

Label improvements to meet current standards:

- Update label statements related to disposal of the product containers and product storage.

Risk mitigation:
To protect the environment, the following risk-reduction measures are proposed:

- Environmental hazard statements are required on end-use product labels for aquatic organisms.
- Spray buffer zones are required on the co-formulated product of cymoxanil and famoxadone to protect aquatic habitats.
- Precautionary label statements for sites with characteristics that may be conducive to runoff and when heavy rain is forecast are required.

International context

As of 15 July 2020, cymoxanil is currently acceptable for use in other Organisation for Economic Co-operation and Development (OECD) member countries, including the United States and the European Union. No decision by an OECD member country to prohibit all uses of cymoxanil for health or environmental reasons has been identified.

Next steps

Upon publication of this proposed re-evaluation decision, the public, including the registrants and stakeholders are encouraged to submit additional information that could be used to refine risk assessments during the 90-day public consultation period.

All comments received during the 90-day public consultation period will be taken into consideration in preparation of the re-evaluation decision document,[2] which could result in revised risk mitigation measures. The re-evaluation decision document will include the final re-evaluation decision, the reasons for it and a summary of comments received on the proposed re-evaluation decision with Health Canada's responses.
Refer to Appendix I for details on specific products impacted by this proposed decision.

Additional scientific information

No additional scientific data are required at this time.

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

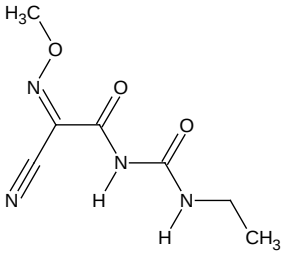
Science Evaluation

1.0 Introduction

Cymoxanil is a fungicide registered for use on potatoes, field tomatoes and caneberries. It can be applied with ground and aerial application equipment. Cymoxanil is applied 3–4 times per year as a foliar application (ground and aerial). Appendix I lists all cymoxanil products that are registered under the authority of the *Pest Control Products Act*. Appendix II lists all the uses for which cymoxanil is presently registered.

2.0 Technical grade active ingredient

2.1 Identity

Common name		Cymoxanil
Chemical Family		cyanoacetamide oxime
Chemical name		
1	**International Union of Pure and Applied Chemistry (IUPAC)**	PIN: (2*Ξ*)-2-cyano-*N*-(ethylcarbamoyl)-2-(methoxyimino)acetamide IUPAC: 1-[(*EZ*)-2-cyano-2-methoxyiminoacetyl]-3-ethylurea
2	**Chemical Abstracts Service (CAS)**	2-cyano-*N*-[(ethylamino)carbonyl]-2-(methoxyimino)acetamide
CAS Registry Number		57966-95-7
Molecular Formula		$C_7H_{10}N_4O_3$
Structural Formula		
Molecular weight		198.18

Registration Number	Purity of the Technical Grade Active Ingredient
26285	98.7 %
32385	98.8 %

2.2 Physical and chemical properties

Property	Result
Vapour pressure at 20°C	0.15 mPa
Ultraviolet (UV) / visible spectrum	The absorbance maximum was 244 nm, tailing off by 320 nm.
Solubility in water at 20–25 °C	0.89 g/kg at pH 5
n-Octanol/water partition coefficient	pH log K_{ow} 5 0.59 7 0.67
Dissociation constant at 20–25°C	pKa = 9.7 (decomposition)

3.0 Human health assessment

3.1 Toxicology summary

Cymoxanil is a cyanoacetamide fungicide with local systemic activity and an unknown mode of action. A detailed review of the toxicology database for cymoxanil, and its metabolites was conducted. The database is complete, consisting of the full array of toxicity studies currently required for hazard assessment purposes. The studies were carried out in accordance with currently accepted international testing protocols and Good Laboratory Practices. The human health risk assessment also considered information found in the published scientific literature. The scientific quality of the data is acceptable and the database is considered adequate to characterize the potential health hazards associated with cymoxanil and its metabolites.

Radiolabelled cymoxanil was rapidly absorbed in rats following either a single low- or high-exposure, or a repeated low exposure. The peak plasma concentration was reached within 3–5 hours. Tissue retention was minimal after 96 hours, with the liver and kidneys showing the highest tissue concentration of radiolabel in rats. The urinary route was the predominant route of excretion, accounting for up to 64% of the administered dose (AD), followed by the facal route (24%). Oral administration of a single low-dose resulted in similar elimination via the bile in both sexes (7%). The half-life of elimination was similar between all dose groups and in both sexes. The low dose used is representative of the critical studies used for the human health risk assessment.

The main urinary metabolites of cymoxanil were free/conjugated amino acids, 2-cyano-2-methyoxyiminoacetic acid (IN-W3595), and other unidentified metabolites. The parent compound was not detected in the urine. There were no major differences between males and females. Selected metabolites are identified in Appendix III, Table 1.

Cymoxanil was of moderate to high acute oral toxicity in rats, with clinical signs including ataxia, lethargy, ocular discharge, laboured breathing and hair loss. Cymoxanil was of low acute dermal and inhalation toxicity in rats. In rabbits, cymoxanil was minimally irritating to the eye and skin. In guinea pigs and mice, cymoxanil was not a skin sensitizer when assessed by the Maximization and local lymph node assay test methods, respectively.

Repeat-dose dietary studies conducted in mice, rats, and dogs revealed the testes, liver, and potentially thyroid as target sites of toxicity. Decreased bodyweight and bodyweight gain were also common effects. Increased duration of dosing resulted in increased severity of treatment-related toxicity in all species tested. Dogs were the species most sensitive to the toxicological effects induced by cymoxanil, particularly to the prostate and testes. Testicular effects included degeneration of the testes, epididymis, and spermatids together with decreased testes weight. There was no effect on fertility in the rat 2-generation reproductive toxicity study; however more sensitive measures, such as sperm parameters (motility and morphology) were not examined. Hepatic effects were largely limited to rodents, and included hepatic lesions in mice, and liver inflammation in rats. In dogs, there was an increased incidence of swollen eye fibres, and a change in several clinical chemistry parameters, such as reduced levels of circulating lymphocytes, red blood cells, and haemoglobin. With respect to thymic effects, mice and dogs had decreased thymus weights, and dogs also displayed thymic lymphoid atrophy and involution in one of two 1-year dietary studies. There is a low level of concern for these thymic effects in dogs due to the high incidence of thymic lymphoid atrophy and involution in control animals, and the lack of a dose-response or corroborating effects in the other dog toxicity studies. This low level of concern is supported by the 28-day immunotoxicity studies in mice and rats, which revealed no evidence of immunosuppression.

The immunotoxic potential of cymoxanil was examined in short-term dietary immunotoxicity studies in mice and rats in which animals were immunized with sheep red blood cells. In both female mice and rats, decreased bodyweight, bodyweight gain, and food consumption occurred, with female mice also having decreased thymus weights. There were no treatment-related immunological effects in mice and rats up to the highest dose tested.

A repeat-dose dermal toxicity study in rats showed no local irritation, changes to the dermis, or systemic toxicity up to the highest dose tested. A repeat-dose inhalation toxicity study was not available.

In rat and mouse dietary chronic toxicity and/or oncogenicity studies, there was no evidence of treatment-related oncogenicity at any dose level. Cymoxanil was not genotoxic in two in vitro assays (bacterial gene mutation assay, mammalian gene mutation assay in Chinese hamster ovary cells). However, cymoxanil showed positive genotoxicity in two other in vitro assays (unscheduled DNA synthesis assay in primary rat hepatocytes, chromosomal aberration assay in human peripheral lymphocytes). Cymoxanil was not genotoxic in an ex vivo unscheduled DNA synthesis assay in primary rat hepatocytes and spermatocytes, and was not genotoxic in an in vivo mouse cytogenetics assay in mice. Overall, the weight of evidence suggests that cymoxanil is not likely to be genotoxic.

In a dietary 2-generation reproductive toxicity study in rats, decreased bodyweight, bodyweight gain, and food consumption were noted in the parental and offspring generations starting at the mid- and high-dose levels, respectively. The F_1 offspring also had decreased viability on postnatal day (PND) 1–4, reduced litter survival, and males had decreased survival on PND 4-21 at the highest dose level tested. Clinical signs included gasping, subcutaneous hemorrhage, and weakness at the highest dose tested. There were no reproductive effects noted in this study. However, due to the age of the 2-generation reproductive toxicity study, more sensitive endpoints such as ovarian follicle counts, estrous cycle length and periodicity, or sperm parameters (motility, morphology), were not assessed.

In a gavage rat developmental toxicity study, cymoxanil exposure resulted in a higher incidence of malformations, particularly cleft palate, vertebrae and ribs, with ossification delays in the vertebrae and ribs. These malformations occurred in the presence of maternal toxicity consisting of decreased body weight gains and food consumption. There was also a decreased sex ratio starting at the mid-dose level, and more resorptions and fewer live fetuses at the high-dose level. The exposure did not cover the period of sexual differentiation, therefore effects such as genital malformations, and changes to the weight and morphology (gross and microscopic) for male sex and accessory sex organs have not been fully characterized. Overall, these studies showed evidence of treatment-related malformations in the presence of maternal toxicity in rats.

Three gavage rabbit developmental toxicity studies were available. Two of these studies were considered supplemental due to the dose within each study being from different sources. One of these supplemental studies showed an increased incidence of skeletal malformations of the cervical and thoracic vertebrate (scoliosis, hemivertebra, fused or absent vertebrae, fused/absent/branched ribs) in the absence of maternal toxicity. Maternal toxicity was observed at the next highest dose level and consisted of decreased bodyweight and bodyweight gain. No treatment-related fetal effects were observed in the second supplemental study. The one acceptable study showed the same pattern of malformations at the same dose level as those observed in the one supplemental study, however maternal toxicity was not observed at any dose level. In all of the rabbit studies, there were no identified endocrine effects. However, exposure did not cover the period of sexual differentiation therefore effects such as genital malformations, and changes to the weight and morphology (gross and microscopic) for male sex and accessory sex organs have not been fully characterized. Overall, these studies showed evidence of treatment-related malformations and sensitivity of the young in rabbits.

In a rat dietary short-term neurotoxicity study there were no effects on functional observational battery parameters or neuropathology. In a rat developmental neurotoxicity (DNT) study, there were no significant treatment related differences in motor activity, auditory startle habituation, passive avoidance, or water maze parameters. Furthermore, there were no changes in brain morphometrics or neuropathology in offspring following treatment with cymoxanil. The DNT study was considered supplemental because a full functional observational battery was not performed and positive control data were incomplete.

IN-KP533 is a major transformation product in water, a minor product in soil, but is not a rat metabolite. IN-KP533 was of low acute oral toxicity in mice and was not genotoxic in either a bacterial gene mutation assay or a chromosomal aberration assay in human peripheral

lymphocytes. There are currently no short- or long-term toxicity studies for IN-KP533. A quantitative structure activity relationship (QSAR) analysis by the registrant did not identify potential toxicity alerts. A second QSAR analysis was completed by Health Canada that considered IN-KP533 along with the major rat metabolite IN-W3535. Overall, the models showed no new alerts of toxicological concern for either metabolite, however the reliability of these predictions was not high. Overall, there remains uncertainty with respect to the potential toxicity of IN-KP533.

The identity of select cymoxanil rat metabolites is presented in Appendix III, Table 1. Results of the toxicology studies conducted on laboratory animals with cymoxanil are summarized in Appendix III, Table 2. The toxicological reference values for use in the human health risk assessment are summarized in Table 3 of Appendix III.

3.1.1 Pest Control Products Act Hazard Characterization

For assessing risks from potential residues in food or from products used in or around homes or schools, the *Pest Control Products Act* requires the application of an additional 10-fold factor to take into account completeness of the data with respect to the exposure of, and toxicity to infants and children, and potential prenatal and postnatal toxicity. A different factor may be determined to be appropriate on the basis of reliable scientific data.

With respect to the completeness of the toxicity database as it pertains to the toxicity to infants and children, the database contains the full complement of required studies including oral developmental toxicity studies in rats and rabbits and a dietary 2-generation reproductive toxicity study in rats. However, the developmental toxicity studies did not dose during the period of male sexual differentiation. In addition, in light of reported effects on reproductive tissues (testes, epididymis) within the database the potentially relevant adverse effects have not been fully characterized. Although there were some limitations in the DNT study, it still provides sufficient information for regulatory purposes.

With respect to potential prenatal and postnatal toxicity, in the rat 2-generation reproductive toxicity study, there was decreased pup viability, reduced F_1 litter survival, fewer viable F_1 males, decreased pup body weights and increased clinical signs in the presence of maternal toxicity.

In the rat developmental toxicity study, increased incidences of fetal malformations such as cleft palate and vertebrae and rib malformations, were observed in the presence of maternal toxicity. In the rabbit developmental toxicity study, skeletal malformations including scoliosis, hemivertebra and fused/extra/forked, enlarged or malpositioned ribs were observed at doses that did not result in maternal toxicity. In the DNT study, decreased pup viability and reduced pup body weights were noted at maternally toxic doses.

The fetal malformations were considered serious endpoints, particularly in the rabbit gavage developmental toxicity study where malformations were observed in the absence of maternal toxicity. Accordingly, the 10-fold PCPA factor was retained for scenarios in which this endpoint was used for risk assessment. For all other scenarios, the PCPA factor was reduced to onefold.

3.2 Dietary exposure and risk assessment

In a dietary exposure assessment, Health Canada determines how much of a pesticide residue, including residues in milk and meat, may be ingested with the daily diet. Exposure to cymoxanil from potentially treated imported foods is also included in the assessment. These dietary assessments are age specific and incorporate the different eating habits of the population at various stages of life (infants, children, adolescents, adults and seniors). For example, the assessments take into account differences in children's eating patterns, such as food preferences and the greater consumption of food relative to their body weight when compared to adults. Dietary risk is then determined by the combination of the exposure and the toxicity assessments. High toxicity may not indicate high risk if the exposure is low. Similarly, there may be risk from a pesticide with low toxicity if the exposure is high.

Health Canada considers limiting use of a pesticide when exposure exceeds 100% of the reference dose. Health Canada's Science Policy Note SPN2003-03, *Assessing Exposure from Pesticides, A User's Guide*, presents detailed acute and chronic assessment procedures.

The residue definition for enforcement in Canada is the following:

- Cymoxanil (2-cyano-N-[(ethylamino)carbonyl]-2-(methoxyimino)acetamide) for all plant and animal commodities.

The residue definitions for risk assessment in Canada are the following:

- The current residue definition for risk assessment is cymoxanil only for all commodities, except leafy vegetables and hops. No change to the residue definition for plant commodities or animal commodities is proposed.
- The residue definition for risk assessment in leafy vegetables and hops is cymoxanil and the metabolite IN-KQ960. No change to this residue definition is proposed.

Residue estimates used in the dietary risk assessment may be based conservatively (using upper bound estimates) on the maximum residue limits (MRLs) or the field trial data representing the residues that may remain on food after treatment at the maximum label rate. Surveillance data representative of the national food supply may also be used to derive a more accurate estimate of residues that may remain on food when it is purchased. These include the Canadian Food Inspection Agency (CFIA) National Chemical Residue Monitoring Program and the United States Department of Agriculture's Pesticide Data Program (USDA's PDP). Theoretical and experimental processing factors as well as specific information regarding the percent of crops treated may also be incorporated to the greatest extent possible.

Sufficient information was available to adequately assess the dietary exposure and risk to cymoxanil. Acute and chronic dietary (food and drinking water) exposure and risk assessments for cymoxanil were conducted using the Dietary Exposure Evaluation Model - Food Commodity Intake Database™ (DEEM-FCID™; Version 4.02, , 05-10-c) program which incorporates food consumption data from the National Health and Nutrition Examination Survey/What We Eat in America (NHANES/WWEIA) dietary survey for the years 2005-2010 available through the

Centers for Disease Control and Prevention's National Center for Health Statistics. For more information on dietary risk estimates or residue chemistry information used in the dietary assessment, see Appendices IV and V.

The acute and chronic exposure estimates are considered to be refined (more precise) as food monitoring data, and experimental processing factors were used to the extent possible. However, the assessments retained a certain level of conservatism due to the use of MRLs/tolerances or anticipated residues (from crop field trials).

3.2.1 Determination of acute reference dose

Acute reference dose (females 13–49 years of age)

To estimate acute dietary risk in females 13–49 years of age, the rabbit gavage developmental toxicity study with a NOAEL of 4 mg/kg bw/day was selected for risk assessment. At the LOAEL of 8 mg/kg bw/day, an increased incidence of skeletal malformations of the cervical and thoracic vertebrae and ribs were observed in the absence of maternal toxicity. These effects may have been the result of a single exposure and are therefore relevant to an acute risk assessment. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied. As discussed in the *Pest Control Products Act* Hazard Characterization section, the PCPA factor was retained at 10-fold. **The composite assessment factor (CAF) is thus 1000.**

The ARfD (females 13–49 years of age) is calculated according to the following formula.

$$\text{ARfD} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{4 \text{ mg/kg bw}}{1000} = 0.004 \text{ mg/kg bw of cymoxanil}$$

Acute reference dose (general population – excluding females 13–49 years of age)

To estimate acute dietary risk for the general population, the rat gavage developmental toxicity study with a NOAEL of 10 mg/kg bw/day was selected for the risk assessment. At the LOAEL of 25 mg/kg bw/day, maternal bodyweight gains were reduced during the first two days, which could be attributed to a single dose of cymoxanil. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied. As discussed in the *Pest Control Products Act* Hazard Characterization section, the PCPA factor was reduced to onefold. **The CAF is thus 100.**

The ARfD (general population) is calculated according to the following formula.

$$\text{ARfD} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{10 \text{ mg/kg bw}}{100} = 0.1 \text{ mg/kg bw of cymoxanil}$$

3.2.2 Acute dietary exposure and risk assessment

The acute dietary risk from food and drinking water was calculated considering the highest ingestion of cymoxanil that would be likely on any one day, and using food and water consumption, and food and water residue values. The expected intake of residues is compared to the ARfD, which is the dose at which an individual could be exposed on any given day and expect no adverse health effects. When the estimated exposure is less than the ARfD, the acute dietary exposure is not of concern.

The acute assessment was conducted for all subpopulations using anticipated residues (from crop field trials), MRLs/tolerances were used for commodities for which no anticipated residues were available. Additionally, monitoring data from the USDA's PDP were used to refine residue estimates for commodities that were significant risk contributors. Experimental processing factors were used when available and theoretical (default) processing factors were used when experimental processing factors were not available. Drinking water contribution to the exposure was accounted for by direct incorporation of the estimated environmental concentrations (EECs) distribution, obtained from water modelling (see Section 3.3) into the dietary exposure evaluation model (DEEM). The assessment was conducted using a deterministic method and percent crop treated information was not incorporated.

The acute dietary exposure estimates at the 95th percentile for all subpopulations range from 1.62% to 53.9% of the ARfD, and are shown to be acceptable. The most sensitive subpopulation was females 13–49 years of age.

3.2.3 Determination of acceptable daily intake

Acceptable daily intake (females 13–49 years of age)

To estimate dietary risk from repeated dietary exposure in females 13–49 years of age, the rabbit gavage developmental toxicity study with a NOAEL of 4 mg/kg bw/day was selected for the risk assessment. At the LOAEL of 8 mg/kg bw/day, an increased incidence of skeletal malformations of the cervical and thoracic vertebrae, and ribs were observed in the absence of maternal toxicity. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied. As discussed in the *Pest Control Products Act* Hazard Characterization section, the PCPA factor was retained at 10-fold. **The CAF is thus 1000.**

The ADI (females 13–49 years of age) is calculated according to the following formula.

$$\text{ADI} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{4 \text{ mg/kg bw/day}}{1000} = 0.004 \text{ mg/kg bw/day of cymoxanil}$$

Acceptable daily intake (general population – excluding females 13–49 years of age)

To estimate dietary risk from repeated dietary exposure in the general population, the dog 12-month dietary toxicity study with a NOAEL of 1.3 mg/kg bw/day was selected. At the LOAEL of 2.8 mg/kg bw/day, there was decreased bodyweight, bodyweight gain and food consumption, as well as increased incidences of swollen lens fibers in the eye, testicular atrophy

and lymphoid inflammation in the prostate. This study provides the lowest NOAEL in the database. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied. As discussed in the *Pest Control Products Act* Hazard Characterization section, the PCPA factor was reduced to onefold. **The CAF is thus 100.**

The ADI (general population) is calculated according to the following formula.

$$\text{ADI} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{1.3 \text{ mg/kg bw/day}}{100} = 0.013 \text{ mg/kg bw/day of cymoxanil}$$

While there is reasonable concern that the potential for certain endocrine and reproductive effects were not evaluated in the 2-generation reproductive study and/or developmental toxicity studies due to the age of the studies, an additional database deficiency factor is not warranted based on the margins afforded by the ADI and ARfD for females (aged 13–49). The ADI and ARfD for females (aged 13–49), and short- and intermediate- term dermal and inhalation scenarios uses the rabbit developmental study to derive its reference value. The current CAF is 1000 due to the sensitivity of the young (developmental effects) and the retention of the 10-fold PCPA factor. It currently provides adequate margins of approximately:

1800 to the NOAEL of the 2-generation reproductive study in the rat (decreased maternal bodyweight, bodyweight gain, and food consumption).

2500 to the NOAEL of the developmental study in the rat (fetal malformations and decreased maternal bodyweight gain).

325 to the NOAEL of the 1-year oral toxicity study in the dog (decreased bodyweight, bodyweight gain and food consumption, as well as increased incidences of swollen lens fibers in the eye, testicular atrophy and lymphoid inflammation in the prostate).

3.2.4 Cancer assessment

There was no evidence of carcinogenicity and therefore, a cancer risk assessment was not necessary.

3.2.5 Chronic dietary exposure and risk assessment

The chronic dietary risk from food and drinking water was calculated using the average consumption of different foods and water, and the average residue values on those foods and water. This estimated exposure to cymoxanil was then compared to the ADI. When the estimated exposure is less than the ADI, the chronic dietary exposure is not of concern.

The chronic assessment was conducted using anticipated residues (from crop field trials), and MRLs/tolerances for commodities for which no anticipated residues were available. Experimental processing factors were used when available and theoretical processing factors were used when experimental processing factors were not available. Drinking water contribution to the exposure was accounted for by direct incorporation of the chronic EEC value obtained from modelling (see Section 3.3) into DEEM. Percent crop treated information was not used.

The chronic dietary exposure estimates for the general population and all subpopulations range from 2.5% to 11.7% of the ADI, and are shown to be acceptable. The most sensitive subpopulation was females 13–49 years of age.

3.3 Exposure from drinking water

Residues of cymoxanil and its metabolites IN-U3204, IN-R3273, IN-KP533, IN-4226, IN-KQ960 and IN-JX915 in potential drinking water sources were estimated from water modelling.

3.3.1 Concentrations in drinking water

Estimated environmental concentrations (EECs) in potential drinking water (surface and groundwater) were modelled using the Pesticide Water Calculator (PWC, version 1.52) for the combined residue of cymoxanil and transformation products IN-U3204, IN-R3273, IN-KP533, IN-T4226, IN-KQ960 and IN-JX915. The Level 1 EECs were calculated using conservative inputs with respect to application rate, application timing, and geographic scenario.

EECs for surface water were modelled using a single conservative use pattern (3 applications of 210 g a.i./ha with intervals of 5 and 20 days). Modelling for surface water used a standard Level 1 scenario, a small reservoir adjacent to an agricultural field and thus the EECs cover all crops in all regions of Canada. EECs in groundwater were calculated for several scenarios representing different regions of Canada but only the highest EECs across these scenarios were reported. All scenarios were run for 50 years. Modelling used initial application dates between 1 May and 5 September. The highest daily EEC (30 µg/L) was used in the acute assessment and the highest yearly EEC (13 µg/L) was used for the chronic assessment.

Major fate input parameters used in the modelling are presented in Appendix VIII, Table 1 and modelling results are presented in Appendix VIII, Tables 2–4. For more information on water modelling refer to Appendix IX.

3.3.2 Drinking water exposure and risk assessment

Drinking water exposure estimates were combined with food exposure estimates, with EEC values incorporated directly in the dietary (food and drinking water) assessments. Please refer to Section 3.2 for details and conclusions.

3.4 Occupational and non-occupational exposure and risk assessment

Occupational risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies to calculate a margin of exposure (MOE). This is compared to a target MOE incorporating uncertainty factors protective of the most sensitive subpopulation. If the calculated MOE is less than the target MOE, it does not necessarily mean that exposure will result in adverse effects, but mitigation measures to reduce risk would be required.

3.4.1 Toxicology endpoint selection for residential and occupational exposure

3.4.1.1 Short-, intermediate-term dermal and inhalation routes

A route-specific 28-day dermal toxicity study in rats was not considered appropriate for risk assessment as it did not assess the relevant endpoints of concern (developmental effects). Furthermore, a short-term inhalation toxicity study was not available. Thus, for the short- and intermediate-term dermal and inhalation risk assessments, an oral point of departure was used to evaluate dermal and inhalation exposures. A NOAEL of 4 mg/kg bw/day from the rabbit gavage developmental toxicity study was selected. At the LOAEL of 8 mg/kg bw/day, developmental toxicity was observed as malformations in the cervical and thoracic vertebrate and ribs.

Cymoxanil is not registered for residential use. For occupational exposure scenarios, the target MOE is 1000, which includes an uncertainty factor of 10-fold for interspecies extrapolation, 10-fold for intraspecies variability, as well as a factor of 10-fold for the reasons outlined in the *Pest Control Products Act* Hazard Characterization section. The selection of this study and target MOE is considered protective of all worker populations, which could include women who may be pregnant or nursing.

3.4.1.2 Cancer assessment

There was no evidence of oncogenicity and therefore a cancer risk assessment was not required.

3.4.1.3 Dermal absorption

A dermal absorption value of approximately 10% was chosen, based on results from a rat dermal in vivo study on file.

3.4.2 Non-occupational exposure and risk assessment

There is potential for exposure to cymoxanil in occupational scenarios to workers handling cymoxanil during the mixing/loading/application process, and potential for postapplication exposure to workers entering areas previously treated with cymoxanil.

3.4.2.1 Mixer, loader, and applicator exposure and risk assessment

There are potential exposures to mixers, loaders, and applicators. The following scenarios were assessed:

- Mixing/loading of dry flowable, and application using groundboom (potatoes and field tomatoes).
- Mixing/loading of dry flowable, and application using airblast (caneberries).
- Mixing/loading of dry flowable for aerial application (potatoes and field tomatoes)
- Aerial application (potatoes and field tomatoes).

Based on the number of applications and the timing of application, workers applying cymoxanil would generally have a short-term (<30 days) or intermediate-term exposure (1–6 months) depending on the crop.

Exposure was estimated for personal protective equipment (PPE) that are currently included on the label: coveralls or chemical resistant coveralls over long pants, long-sleeved shirt and chemical-resistant gloves.

No appropriate chemical-specific handler exposure data were available for cymoxanil. Therefore, dermal and inhalation exposures were estimated using data from the Pesticide Handlers Exposure Database Version 1.1 (PHED) and the Agricultural Handlers Exposure Task Force (AHETF) studies. PHED is a compilation of generic mixer/loader applicator passive dosimetry data with associated software that facilitates the generation of scenario-specific exposure estimates based on formulation type, application equipment, mix/load systems and level of PPE. The AHETF was formed in 2001 with the objective of providing more up-to-date generic exposure studies compared to the PHED studies. When available, the more modern AHETF studies were used, which meet current standards of acceptability.

Route-specific MOEs for mixers/loaders and applicators for agricultural crops are outlined in Appendix VI

Groundboom application

The risk assessment for mixers/loaders and applicators using groundboom equipment is outlined in Appendix VI, Table 1:

Tomato: For the tomato use, calculated dermal, inhalation, and combined (dermal plus inhalation) MOEs for mixer/loaders and applicators exceeded target MOEs, and the occupational risk is considered acceptable under the current conditions of use.

Potato: For the potato use, under current use conditions, the calculated dermal MOE exceeded the target MOE. However, inhalation and combined (dermal plus inhalation) MOEs are below the target MOE.

Based on the above, the potential risk to mixers/loaders and applicators using groundboom is not considered to be acceptable under current conditions of use. To mitigate potential risks to mixers/loaders and applicators, and for consistency between end-use product labels, the following mitigation measures are proposed:

- PPE consisting of chemical-resistant coveralls over a single layer of clothing, chemical-resistant gloves for mixers/loaders and applicators, plus a respirator for mixers/loaders.
- A limit of active ingredient handled of 35 kg a.i./day.

With the proposed mitigation measures, potential risks to mixers/loaders and applicators using groundboom equipment was shown to be acceptable.

Airblast application

The risk assessment for mixers/loaders and applicators using airblast equipment on caneberries is outlined in Appendix VI, Table 2:

Caneberries: Calculated inhalation MOEs for mixers/loaders and applicators for cymoxanil exceeded the target MOE under current conditions of use. However, the calculated dermal and combined (dermal plus inhalation) MOEs for mixers/loaders and applicators for cymoxanil are below the target MOEs.

To mitigate potential risk, additional PPE, a chemical resistant hat, is proposed for applicators using open cab airblast equipment. With the proposed mitigation measure, potential risks to mixers/loaders and applicators using airblast equipment was shown to be acceptable.

Handheld application

The use of handheld equipment for cymoxanil applications is not specifically stated on current product labels. However, handheld equipment (for example, backpack sprayer) can be used for spot treatment for controlling small outbreaks of pest, or for treating parts of the field that cannot be treated during broadcast application. A spot treatment is considered likely on high value crops like tomatoes and caneberries. Therefore the risk for an applicator during occasional spot treatment was also considered according to current PMRA practice.

Exposure of MLA to cymoxanil while wearing PPE required on the label and using handheld equipment for spot applications is expected to be lower than the exposure of workers using groundboom or airblast equipment for applications to tomatoes and caneberries, respectively.

Aerial application

The risk assessment for mixers/loaders and applicators using aerial equipment on potatoes and tomatoes is outlined in Appendix VI, Table 3:

Tomatoes: Under the current conditions of use, the calculated dermal, inhalation, and combined (dermal plus inhalation) MOEs for mixers/loaders and applicators for cymoxanil exceeded target MOEs for tomatoes. Therefore, occupational risk is considered to be acceptable under the current conditions of use for tomatoes. Additional risk mitigation measures are not proposed. However, for consistency between the product labels, the spray volume is proposed to be indicated as 50 L of product/ha for aerial application.

Potatoes: Under the current conditions of use, the calculated inhalation and combined (dermal plus inhalation) MOE for mixers/loaders for the potato use is below the target MOE, and occupational risk (M/L) was not shown to be acceptable. The potential risk to applicators (pilots) is considered to be acceptable under current conditions of use, and additional risk mitigation measures are not proposed for applicators.

To mitigate the potential risks for mixer/loaders (M/L), and for consistency between products, the following mitigation measures are proposed:

- Additional PPE consisting of chemical-resistant coveralls over a single layer of clothing and a respirator for workers mixing/loading of cymoxanil products.
- A limit of active ingredient handled of 52.5 kg a.i./day.
- The spray volume for aerial application is 50 L/ha (for consistency between product labels).

With the proposed mitigation measures, the potential risk to workers mixing/loading cymoxanil products for aerial application on potatoes were shown to be acceptable.

3.4.2.2 Postapplication worker exposure and risk assessment

The postapplication occupational risk assessment considered exposures to workers who enter treated sites to conduct agronomic activities involving foliar contact (for example, hand harvesting). Based on the use pattern, there is potential for short- (<30 days) and intermediate-term (1–6 months) postapplication exposure to cymoxanil residues for postapplication workers.

Potential exposure to postapplication workers was estimated using updated activity-specific transfer coefficients (TCs), default dislodgeable foliar residue (DFR) values, and chemical-specific DFR data. The DFR refers to the amount of residue that can be dislodged or transferred from a surface, such as leaves of a plant. The TC is a measure of the relationship between exposure and DFRs for individuals engaged in a specific activity, and is calculated from data generated in field exposure studies. The TCs are specific to a given crop and activity combination, and reflect standard agricultural work clothing worn by adult workers. Activity-specific TCs from the Agricultural Re-entry Task Force (ARTF) were used. Postapplication exposure activities for agricultural crops include (but are not limited to): harvesting, weeding and scouting. For more information about estimating worker postapplication exposure, refer to PMRA's regulatory proposal PRO2014-02, *Updated Agricultural Transfer Coefficients for Assessing Occupational Post-Application Exposure to Pesticides.*

A chemical specific DFR study was considered in the postapplication risk assessment. DFRs for tomatoes and potatoes were calculated using a tomato DFR study. For caneberries, since no acceptable chemical-specific DFR studies were available for cymoxanil, default values were used (peak DFR of 25% of the application rate for all crops, with 10% dissipation per day). For further information on these default values, refer to PMRA's Science Policy Note SPN2014-02, *Estimating Dislodgeable Foliar Residues and Turf Transferable Residues in Occupational and Residential Post-application Exposure Assessments*.

For workers entering a treated site, restricted-entry intervals (REIs) are calculated to determine the minimum length of time required before people can safely enter after application. An REI is the duration of time that must elapse before residues decline to a level where performance of a specific activity results in exposures above the target MOE.

Postapplication exposure is short- to intermediate-term and would be primarily via the dermal route. Based on the vapour pressure, cymoxanil is relatively non-volatile, and inhalation exposure would be low provided that the required REIs are followed.

The risk assessment for workers conducting postapplication activities is summarized in Appendix VI, Table 4. The calculated short- to intermediate-term MOEs for postapplication workers are below the target MOE of 1000 for handset irrigation (all crops), and for roguing potatoes. On this basis, postapplication risks for workers entering treated outdoor sites are not considered to be acceptable under current conditions of use for certain postapplication activities. To mitigate potential risks to postapplication workers, the following revised REIs are proposed:

- 18 days for hand-set irritation for potatoes.
- 6 days for roguing potatoes.
- 8 days for hand-set irrigation for field tomatoes.
- 11 days for hand-set irrigation for caneberries.

Provided that the proposed REIs are followed, postapplication risks to workers performing activities such as hand-set irrigation (all crops), and roguing potatoes were shown to be acceptable. Updated REIs are proposed to be added to the labels.

3.4.3 Non-occupational exposure and risk assessment

Non-occupational (residential) risk assessment involves estimating risks to the general population, including youth and children, during or after pesticide application.

Since there are no domestic-class products containing cymoxanil registered, a residential handler assessment was not required. Furthermore, based on the registered use pattern, commercial application to residential areas is not expected.

There is potential for bystander exposure during agricultural applications. Potential exposure is expected to be significantly lower than exposure of applicators. To further minimize the potential for exposure, all current end-use product labels include a standard advisory spray drift label statement, which will be updated to be consistent with currently accepted advisory statements. Overall, the potential risks to bystanders is considered to be acceptable.

3.5 Aggregate exposure and risk assessment

Aggregate exposure is the total exposure to a single pesticide that may occur from dietary (food and drinking water), residential and other non-occupational sources, and from all known or plausible exposure routes (oral, dermal, and inhalation). For cymoxanil, the aggregate assessment consisted of combining food and water exposure only (see Section 3.2), since residential exposure was not expected. The aggregate risk for bystanders was considered to be acceptable as the contribution to the total aggregate exposure (dietary and drinking water) would be minimal. As presented in the dietary exposure section, above, risks from food and drinking water were shown to be acceptable.

3.6 Cumulative assessment

The *Pest Control Products Act* requires that the Agency consider the cumulative exposure to pest control products with a common mechanism of toxicity. Accordingly, an assessment of a potential common mechanism of toxicity with other pest control products was undertaken.

Cymoxanil belongs to the cyanoacetamide-oxime structural class of fungicides, for which it is the only member. The fungicidal mode of action for cymoxanil is unknown. Overall, there are no mechanism of action data to establish a common mammalian mechanism of toxicity between cymoxanil and other pest control products with respect to structure and function. Therefore, a cumulative risk assessment for cymoxanil is not required at this time.

Cymoxanil has metabolites, such as oxalic acid and oxamic acid, in common with other pest control products. Oxalic acid is a minor transformation product of cymoxanil and other pesticides, such as mancozeb. However, oxalic acid is also present in certain end-use products as an active ingredient, or as a formulant and is a naturally occurring compound that transforms rapidly under environmental conditions. As a result, oxalic acid is not likely to be a metabolite of toxicological concern at levels resulting from exposure to cymoxanil. Oxamic acid (IN-18474) is a photoproduct of the pesticides aminopyralid and triclopyr, and is a minor transformation product of cymoxanil found in soils and detected in the leachate of soil column leaching studies. Although, the toxicological significance of oxamic acid is unknown, it is not likely to be a metabolite of toxicological concern at levels resulting from exposure to cymoxanil, as it is predicted to degrade in water, sediment and soil to oxalic acid and carbon dioxide. Therefore, a cumulative risk assessment for oxalic acid is not required at this time.

3.7 Health incident reports

As of 21 August 2020, no human or domestic animal incident reports involving cymoxanil have been submitted to the PMRA.

4.0 Environmental assessment

4.1 Fate and behaviour in the environment

A summary of environmental fate data for cymoxanil is presented in Appendix VII, Tables 1–4.

Cymoxanil enters the terrestrial environment when it is used as a fungicide on a variety of crops and can enter aquatic environments through spray drift and run-off from the application site. Cymoxanil is very soluble in water (780 mg/L at pH 7) and is not expected to volatilize from moist soil or water surfaces (vapour pressures: 1.10E-06 mm Hg, Henry's law constant: 3.70E-10 atm × m^3/mol). Cymoxanil is unlikely to bioaccumulate (log K_{ow} = 0.67).

Cymoxanil is non-persistent in the environment. Abiotic transformation is a major route of cymoxanil transformation. Hydrolysis of cymoxanil is pH dependent (<1 day at pH 9, stable at pH 5). Photolysis in water is quick (half-life of 2.2–5 days) but is slower in soil (half-life of 37.4 days). Laboratory studies indicated cymoxanil is non-persistent in soil, with aerobic half-lives of 0.2–10 days and an anaerobic half-life of 0.7 days. In water, biotransformation half-lives ranged from 0.1–8.6 days under aerobic conditions and 0.1–1.3 day under anaerobic conditions.

The rapid degradation of cymoxanil produces a number of major transformation products (IN-U3204, IN-R3273, IN-T4226, IN-KQ960, IN-JX915, IN-W3595, and IN-KP533) along with significant amounts of CO_2 and unextracted residues (up to more than 50% of the applied). An available biotransformation study for IN-KQ960 indicated that it is non-persistent in soil (half-life of 2.2–4.35 days).

Cymoxanil is highly to very highly mobile in soil (K_{oc} of 13.4-76.3). Despite being highly mobile and very soluble, cymoxanil is expected to have a low potential to leach and reach groundwater as cymoxanil degrades rapidly (half-life: <10 days in soil, <1 day for hydrolysis), which is supported by the outcome of groundwater ubiquity score (GUS) analysis (Gustafson, 1989). Available terrestrial field studies support this conclusion, with cymoxanil being non-persistent (half-lives of <1 day to 8.0 days) and not susceptible to leaching. Cymoxanil has not been detected in available Canadian or United States water monitoring data (Appendix VIII).

Information on the leaching potential of major transformation products is limited. Major transformation products are expected to be highly mobile in soil based on their low K_{oc} (3.0 to 27.9 L/kg for IN-KQ960, IN-W3595, IN-T4226 and IN-KP533).

4.2 Environmental risk characterization

The environmental risk assessment integrates the environmental exposure and ecotoxicology information to estimate the potential for adverse effects on non-target species. This integration is achieved by comparing exposure concentrations with concentrations at which adverse effects occur. EECs are concentrations of pesticide in various environmental media, such as food, water, soil and air. The EECs are estimated using standard models that take into consideration the application rate(s), chemical properties and environmental fate properties, including the dissipation of the pesticide between applications. Ecotoxicology information includes acute and

chronic toxicity data for various organisms or groups of organisms from both terrestrial and aquatic habitats including invertebrates, vertebrates, and plants. To characterize acute risks, acute toxicity endpoints (such as LC_{50}, LD_{50}, or EC_{50}) are used, and the NOEC or NOEL values are used to characterize chronic risks. Toxicity endpoints used in risk assessments are adjusted to account for potential differences in species sensitivity as well as varying protection goals (in other words, protection at the community, population, or individual level).

The risk assessment is conducted in a tiered approach. A screening level risk assessment is initially 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 (for example, direct application at a maximum cumulative application rate) and sensitive toxicity endpoints. Risks associated with the use of pesticides are quantified through calculation of risk quotients (RQ). The RQ is calculated by dividing the EECs estimated for different matrices by an appropriate toxicity endpoint (RQ = exposure estimate ÷ (toxicity endpoint ÷ uncertainty factors)), and the RQ is then compared to the level of concern. The LOC is 1 for majority of organisms with a few validated exceptions. The LOC is 2 for beneficial arthropods at the screening level assessment when the endpoints are derived from a glass plate test for two standard species (*Typhlodromus pyri,* and *Aphidius rhopalosiphi*). The LOC is 0.4 for honey bees at the screening level assessment for an acute oral and contact exposure. If the screening level risk quotient is below the LOC, the risk is considered negligible and no further risk characterization is necessary. If the screening level risk quotient is equal to or greater than the LOC, a refined risk assessment is performed to further characterize the risk. A refined assessment takes into consideration of 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.

A summary of ecotoxicity endpoints is presented in Appendix VII, Tables 5 and 6. The most sensitive endpoints for each taxa were chosen as surrogates for the screening level assessment. The calculated RQ values are presented in Appendix VII, Tables 7–10.

4.2.1 Risks to terrestrial organisms

Cymoxanil does not pose a risk to earthworms and terrestrial plants.

At the screening level, acute risks were identified for predators and parasitoids (RQ <2.5), and reproductive risks were identified for predatory mites (RQ = 5.4). A refined risk assessment using endpoints derived from extended laboratory tests indicated RQ values did not exceed the level of concern. In addition, available field and semi-field studies reported no treatment-related effects at test rates greater than the maximum Canadian label rates. These studies suggested that the risks to invertebrate predators and parasitoids in the field are unlikely.

The screening level risk assessment indicates no acute risks to bees. The adult chronic RQ (1.3) slightly exceeded the LOC at the screening level and chronic bee larval studies were not available. However, studies discussed previously that show no effects of cymoxanil to other beneficial insects at application rates much higher than Canadian label rates suggest risks to bees in the field are not expected. The slight exceedance of the LOC for chronic exposure for adults at the screening level is unlikely to result in unacceptable risks to bees at the colony/population level in the field.

The screening level assessment for birds and mammals conservatively assumes diets consist of 100% of a particular contaminated food item. At the worst case application scenario (3 × 210 g a.i./ha), although a potential on-field reproductive risk was identified for small-sized insectivorous birds (RQ = 1.1), the level of concern was only slightly exceeded. Risks to birds are not expected in the field. For mammals, screening level RQ values calculated for reproduction slightly exceeded the level of concern for some food guilds for on-field exposure (in other words, small-sized and medium-sized insectivores (RQ = 1.4), medium-sized herbivores (RQ = 1.2)) and off-field exposure (small-sized insectivores and medium herbivores (RQ = 1.0)). Given the conservative nature of the screening level risk assessment, the slight exceedances of the level of concern for reproduction are not expected to pose risks to wild mammals in the field.

4.2.2 Risks to aquatic organisms

Available toxicity data indicated that the cymoxanil transformation product IN-KQ960 and the co-formulated product of cymoxanil and famoxadone, are more toxic to aquatic organisms than cymoxanil alone. As a result, in addition to cymoxanil, risk assessments were further conducted for aquatics for IN-KQ960 and the co-formulated product using the available toxicity information. The results of the risk assessments for cymoxanil and IN-KQ960 are presented in Appendix VII, Table 9. The results of the risk assessment for the co-formulated product of cymoxanil and famoxadone are presented in Appendix VII, Table 10.

At the screening level, cymoxanil and IN-KQ960 were shown not to pose a risk to aquatic organisms with the exception of a potential chronic risk to amphibians (RQ > 4.8). The amphibian endpoint was conservatively derived using fish endpoints. Cymoxanil and IN-K960 are not expected to pose risks to aquatic organisms.

For the co-formulated end use product, potential risks were identified at the screening level (RQ = 4 to 208.4). The risk to aquatic organisms from drift was characterized by taking into consideration the concentration of the co-formulated product that could be deposited in off-field aquatic habitats that are downwind and directly adjacent to the treated field. The maximum application rate (3 × 210 g a.i./ha) and different application methods were examined. Potential risks due to drift were identified for all application methods (airblast RQ = 3 to 154, aerial RQ = 1 to 54.2 and boom spray RQ = 0.2 to 12.5). These risks can be mitigated with spray buffer zones. As cymoxanil did not show a risk to aquatic organisms at the screening level, a refined risk assessment for run-off is not required at this time.

4.2.3 Environmental incident reports

As of 21 August 2020, no incidents relevant to the environment involving cymoxanil had been reported to the PMRA. The USEPA Ecological Incident Information System reports one incident related to use on celery (browning of leaves) which they classified as "possible". The single incident does not suggest that any further mitigation action is needed.

4.3 Toxic substances management policy considerations

The Toxic Substances Management Policy (TSMP) is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances, (in other words, those that meet all four criteria outlined in the policy: persistent in air, soil, water and/or sediment), bio-accumulative, primarily a result of human activity and toxic as defined by the *Canadian Environmental Protection Act*. The *Pest Control Products Act* requires that the TSMP be given effect in evaluating the risks of a product.

During the review process, cymoxanil and its transformation products were assessed in accordance with the PMRA Regulatory Directive DIR99-03[3] and evaluated against the Track 1 criteria. The PMRA has reached the conclusion that cymoxanil and its transformation products do not meet all of the TSMP Track 1 criteria.

Please refer to Appendix VII, Table 11 for further information on the TSMP assessment.

4.3.1 Formulants and contaminants of health or environmental concern

During the review process, contaminants in the active ingredient as well as formulants and contaminants in the end-use products are compared against Parts 1 and 3 of the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern.*[4] The list is used as described in the PMRA Science Policy Note SPN2020-01[5] and is based on existing policies and regulations, including the Toxic Substances Management Policy[3] and Formulants Policy,[6] and taking into consideration the Ozone-depleting Substances and Halocarbon Alternatives Regulations under the Canadian Environmental Protection Act, 1999 (substances designated under the Montreal Protocol).

The PMRA has reached the conclusion that cymoxanil and its end-use product do not contain any formulants or contaminants identified in the List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern.

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3 DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*

4 SI/2005-114, last amended on June 24, 2020. See Justice Laws website, Consolidated Regulations, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*.

5 PMRA's Science Policy Note SPN2020-01, *Policy on the List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern under paragraph 43(5)(b) of the Pest Control Products Act*

The use of formulants in registered pest control products is assessed on an ongoing basis through PMRA formulant initiatives and Regulatory Directive DIR2006-02.[6]

5.0 Value assessment

Cymoxanil is a preventive, curative and locally systemic, broad-spectrum agricultural fungicide registered for control of early and late blights on potatoes and tomatoes, and a number of diseases on caneberries (raspberry, blackberry and loganberry). Due to its systemic and curative properties, a postinfection application of cymoxanil can delay the development of these diseases. It is highly valued for potato and field tomato growers as it is used in a season-long disease management program, and in rotation with other fungicides to manage early and late blight diseases, which can have a significant economic impact on producers.

Cymoxanil is a valuable resistance management tool for vegetable and berry growers since it is the only Group 27 fungicide registered in Canada, and can be rotated with other fungicides in a disease management program. A number of alternative active ingredients to cymoxanil are registered for all site-pest combinations; however, cymoxanil is the only active ingredient registered to manage spur blight on blackberries, a disease which can reduce marketable yields.

6 DIR2006-02, *Formulants Policy and Implementation Guidance Document*.

List of abbreviations

↑	increased
↓	decreased
µg	micrograms
µg/L	microgram(s) per litre
♀	females
♂	males
a.i.	active ingredient
abs	absolute
AD	administered dose
ADI	acceptable daily intake
AHETF	Agricultural Handlers Exposure Task Force
ARfD	acute reference dose
ARTF	Agricultural Re-entry Task Force
ATPD	area treated per day
BAF	Bioaccumulation Factor
BCF	Bioconcentration Factor
bw	body weight
bwg	bodyweight gain
CAESAR	Computer Assisted Evaluation of Industrial Chemical Substances According to Regulations
CAF	composite assessment factor
CAS	chemical abstracts service
cm	centimeters
cm^2	centimeters squared
cm^2/hr	centimeters squared per hour
CR	chemical resistant
CYO	cymoxanil
DA	dermal absorption
DACO	data code
DEEM	Dietary Exposure Evaluation Model
DFR	dislodgeable foliar residue
DFOP	Double First Order in Parallel kinetics
DNT	developmental neurotoxicity
DT_{50}	dissipation time 50% (the time required to observe a 50% decline in concentration)
EDE	estimated daily exposure
EEC	estimated environmental exposure concentration
EFSA	European Food Safety Authority
ER_{50}	effective rate on 50% of the population
F_1	1st generation offspring
F_2	2nd generation offspring
fc	food consumption
FCID™	Food Commodity Intake Database™
fe	food efficiency

g	gram(s)
GC	gas chromatography
ha	hectare(s)
Hb	haemoglobin
Hct	haematocrit
HPLC	high performance liquid chromatography
hr(s)	hour(s)
IORE	Indeterminate Order Rate Equation Kinetics
IUPAC	International Union of Pure and Applied Chemistry
iv	intravenous
kg	kilogram(s)
K_d	soil-water partition coefficient
K_F	Freundlich adsorption coefficient
K_{oc}	organic-carbon partition coefficient
K_{ow}	octanol-water partition coefficient
L	litre(s)
LC_{50}	lethal concentration required to kill 50% of the test group
LD	lactation day
LD_{50}	lethal dose required to kill 50% of the test group
LDH	lactic acid dehydrogenase
LOAEL	lowest observed adverse effect level
LOD	limit of detection
LOC	level of concern
LOQ	limit of quantitation
LR_{50}	lethal rate 50%
m	meters
M/L/A	Mixer/Loader/Applicator
MAS	mean average score
MCHC	mean corpuscular hemoglobin concentration
MCV	mean corpuscular volume
MIS	maximum irritation score
mg	milligram(s)
mL	millilitre(s)
MOE	margin of exposure
MRL	Maximum Residue Limit
MS	mass spectrometry
NA	not applicable
NAFTA	North American Free Trade Agreement
NHANES	National Health and Nutrition Examination Survey
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEDD	no observed effect dietary dose
NOEL	no observed effect level
NPD	Nitrogen Selective Detection
NR	not required
nss	not statistically significant

OC	organic carbon content
OM	organic matter content
PCPA	*Pest Control Product Act*
PHED	Pesticide Handlers Exposure Database
p*K*a	dissociation constant
PMRA	Pest Management Regulatory Agency
PND	postnatal day
PPE	personal protective equipment
ppm	parts per million
QSAR	quantitative structure activity relationship
RBC	red blood cells
REI	restricted-entry interval
rel	relative
RQ	Risk quotient
SFO	Single first order kinetics
SRBC	sheep red blood cell
TC	transfer coefficient
TLC	thin layer chromatography
TSMP	Toxic Substances Management Policy
UE	Unit exposure
USEPA	United States Environmental Protection Agency
UV	ultraviolet
VEGA	Virtual models for property Evaluation of chemicals within a Global Architecture
WWEIA	What We Eat In America

Appendix I Registered products containing cymoxanil in Canada[1]

Table 1 Products containing cymoxanil subject to proposed label amendments

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Active ingredient (%)
26285	Technical	Production Agriscience Canada Company	Cymoxanil Technical Fungicide	Solid	Cymoxanil 98.7%
32385	Technical	SIPCAM Agro USA, Inc.	Cymoxanil Technical	Solid	Cymoxanil 98.8%
26284	Commercial	Production Agriscience Canada Company	Curzate Fungicide	Dry Flowable	Cymoxanil 60%
27435	Commercial	Production Agriscience Canada Company	Tanos Fungicide	Dry Flowable	Famoxadone 25%; Cymoxanil 25%

[1]as of 6 November 2020, excluding discontinued products or products with a submission for discontinuation

Appendix II Registered uses of cymoxanil in Canada[1]

Site(s)	Pest(s)	Formulation Type	Application Method	Application Rate (g a.i./ha)		Maximum Number of Application per year	Minimum Interval Between Applications (days)
				Maximum Single	Maximum Cumulative		
Potatoes	Early blight,	Dry flowable	Ground and aerial	210	630	3	12
	Late blight			135	540	4	5
Tomatoes (field)	Early blight, late blight			140	420	3	12
Caneberries	Spur blight, cane botrytis, caneberry anthracnose, preharvest fruit rot		Ground	210	630	3	12

[1]as of 6 November 2020, excluding discontinued products or products with a submission for discontinuation

Appendix III Toxicology risk assessment

Table 1 Identification of select metabolites of cymoxanil

Common Name (Other names)	Chemical Name (IUPAC)
Cymoxanil	1-(2-Cyano-2-methoxyiminoacetyl)-3-ethylurea
	Rat metabolites
IN-W3595	2-cyano-2-methyoxyiminoacetic acid
IN-T4226 (IN-4226)	1-Ethylimidazolidine-2,4,5-trione
	Environmental metabolites
IN-U3204	6-Imino-1-methyl-5-methylenedihydropyrimidine-2,4(1H,3H)-dione
IN-R3273	1-Methyl-5-methyleneimidazolidine-2,4-dione
IN-KP533	[[(Ethylamino)carbonyl]amino](oxo)acetic acid
IN-T4226 (IN-4226)	1-Ethylimidazolidine-2,4,5-trione
IN-KQ960	3,4-Dimethyl-2,5-dioxoimidazolidine-4-carboxamide
IN-JX915	3,4-Dimethyl-2,5-dioxoimidazolidine-4-carbonitrile

Table 2 Toxicity profile of technical cymoxanil

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

Study Type/Animal/ PMRA#	Study Results
TOXICOKINETIC STUDIES – CYMOXANIL	
Absorption, Distribution, Metabolism and Excretion (ADME) Sprague-Dawley rats PMRA# 1163789	**Dosing:** Non-cannulated rats received either a single- or repeat- low dose (2.5 mg/kg bw), or a single high-dose (120 mg/kg bw) of [^{14}C]cymoxanil. **Absorption** Cymoxanil was readily and extensively absorbed. The peak plasma concentration was reached within 3 to 5 hr. **Distribution** Less than 1% in tissues after 96 hr. The highest tissue levels occurred in liver, kidney and skin. **Excretion** Cymoxanil was rapidly and almost completely eliminated within 96 h. Excretion occurred mostly through urine (64–75%), but also in feces (16–24%), and expired air (5%). Only trace amounts (< 1%) were excreted unchanged in feces. **Metabolism** Metabolized completely to 2-cyano-2-methoxyiminoacetic acid and glycine, which was either reincorporated in peptides or conjugated and eliminated as hippuric acid and phenylaceturic acid. Cymoxanil had limited bioaccumulation and there were no sex or dose differences in tissue distribution, metabolism or bioelimination.

Study Type/Animal/ PMRA#	Study Results
Absorption, Distribution, Metabolism and Excretion (ADME) Sprague-Dawley rats PMRA# 1169706	**A continuation of the previous study using an additional treatment group with bile-cannulated rats.** **Dosing:** Bile-cannulated rats received a single low-dose (2.5 mg/kg bw) of [^{14}C]cymoxanil. There were no significant differences between cannulated and non-cannulated rats. Biliary excretion was similar between sexes, and accounted for 7% of the AD.
ACUTE TOXICITY STUDIES	
Acute Oral Toxicity (gavage) Sprague-Dawley rats PMRA# 1163781	LD_{50} = 760 mg/kg bw (♂) LD_{50} = 1200 mg/kg bw (♀) Clinical observations included lethargic behaviour, hunched posture, and red ocular or nasal discharges. **Moderate acute toxicity**
Acute Oral Toxicity (gavage) Sprague-Dawley rats PMRA# 1738683	LD_{50} < 250 mg/kg bw (♂/♀) Clinical observations included ataxia, lethargy, low posture, abnormal gait, hyper-reactivity, prostrate posture, ocular discharge, moribundity, cold to touch, splayed limbs, dehydration, hair loss, decreased muscle tone, laboured breathing and head shake **High acute toxicity**
Acute Oral Toxicity (gavage) Sprague-Dawley rats (♂) PMRA# 1738682	LD_{50} = 310.2 mg/kg bw (♂) Clinical signs included ataxia, slow breathing, abnormal gait, ocular or nasal discharge, hyperactivity, tremors, high carriage, moribundity, and stained fur and hair loss. **High acute toxicity**
Acute Dermal Toxicity New Zealand White rabbits PMRA# 1163766	LD_{50} > 2000 mg/kg bw (♂/♀) No mortality. Slight erythema noted in one male. **Low acute toxicity**
Acute Dermal Toxicity Sprague-Dawley rats PMRA# 1738684	LD_{50} > 5000 mg/kg bw (♂/♀) No dermal irritation or clinical signs of toxicity were observed. A wound on the neck and hair loss were observed in one female rat during week 2 which persisted until end of the study. **Low acute toxicity**

Study Type/Animal/ PMRA#	Study Results
Acute Inhalation Toxicity (nose-only) Sprague-Dawley rats PMRA# 1163767	LC_{50} > 5.06 mg/L (♂/♀) One male died. Clinical signs included ocular, nasal and oral discharge, low carriage, hunched posture, vocalization, lethargy and abnormal mobility. **Low acute toxicity**
Acute Inhalation Toxicity (nose-only) Sprague-Dawley rats PMRA# 1738688	LC_{50} > 4.1 mg/L (♂/♀) Clinical signs included decreased defecation and urination in one male and one female. Two females exhibited hypoactivity, which resolved within 24 h. One cyst was noted on the right kidney of one female. **Low acute toxicity**
Skin Irritation New Zealand White rabbits PMRA# 1163769	MIS = 1.0 at 1 hr MAS (at 24, 48, 72 hr) = 0.056 **Minimally irritating**
Skin Irritation New Zealand White rabbits PMRA# 1738685	MIS = 1.0 at 1 hr MAS (at 24, 48, 72 hr) = 0.11 **Minimally irritating**
Eye Irritation ♂ New Zealand White rabbits PMRA# 1163768	MIS = 2.33 at 1 hr MAS (at 24, 48, 72 hr) = 0.33 **Minimally irritating**
Eye Irritation ♂ New Zealand White rabbits PMRA# 1738686	MIS = 10.0/110 at 1 hr MAS (at 24, 48, 72 hr) = 1.3/110 **Minimally irritating**
Skin Sensitization (Maximization Test) Hartley guinea pigs PMRA# 1163770	**Negative skin sensitizer**

Study Type/Animal/ PMRA#	Study Results
Skin Sensitization (local lymph node assay) ♀ CBA mice PMRA# 1738687	**Negative skin sensitizer**
SHORT-TERM TOXICITY STUDIES	
90-day Oral Toxicity (diet) CD-1 mice PMRA# 1163771	NOAEL = 8.25/121 mg/kg bw/day (♂/♀) **≥ 82.4/433 mg/kg bw/day:** ↓ bwg (♂/♀) **≥ 566/846 mg/kg bw/day:** ↑ liver weight, ↑ spleen weight (♀) **1306/1130 mg/kg bw/day:** ↑ pancreatic necrosis (♂/♀), ↑ cerebral hemorrhage (♀) All surviving males and females were sacrificed in extremis on day 15 and 10, respectively.
90-day Oral Toxicity (diet) Beagle dogs PMRA# 1163772, 1169267	NOAEL = not established LOAEL = 3 mg/kg bw/day **≥ 3 mg/kg bw/day:** ↓ RBC, ↓ Hb, ↓ Hct (♂); ↓ bw, ↓ bwg, ↓ fc, ↓ fe (nss) (♀) **≥ 5 mg/kg bw/day:** ↓ fc, ↓ fe (♂); ↓ RBC, ↓ Hb, ↓ Hct (nss) (♀) **≥ 11 mg/kg bw/day:** ↑ Howell-Jolly bodies, ↑ hypochromasis, ↑ diarrhea, ↑ dermal atonia, ↑ APTT, ↓ calcium, ↓ phosphorus, ↓ Albumin/Globulin ratio (nss) (♂/♀); ↓ bw, ↓ bwg, ↓ PT, ↓ chloride, ↓ abs/rel testes weight (nss), ↓ abs/rel epididymis weight (nss), ↓ aspermatogenesis (♂)**;** ↑ segmented neutrophils(wk 6), ↓ lymphocytes, ↓ total protein, ↓ liver weight, ↓ kidney weight, ↓ thyroid weights (♀) **The 5 mg/kg bw/day group were increased to 11 mg/kg bw/day at week 2. One female in the group was sacrificed in extremis at week 10.**
12-month dietary Beagle dogs PMRA# 1163784	NOAEL = 3.0/3.1 mg/kg bw/day (♂/♀) **5.7 mg/kg bw/day:** ↓ RBC, ↓ Hb, ↓ Hc, ↓ MCHC, ↑ MCV (♂) The pre-test values in 4/5 dogs were decreased compared to controls. The effects were still considered adverse based on the RBC effects observed in the other studies in the database.
12-month dietary Beagle dogs PMRA# 1685840	NOAEL = 1.3/2.9 mg/kg bw/day (♂/♀) **≥ 2.8 mg/kg bw/day:** ↑ erythema, ↓ bw, ↓ terminal bw, ↓ bwg, ↓ fc, ↑ swollen eye lens fibers, ↑ testicular atrophy, ↑ prostate lymphoid inflammation (♂) **≥ 5.6 mg/kg bw/day:** ↑ emaciation, ↑ bilateral lenticular degeneration, ↑ seminiferous cell debris, ↑ epididymal atrophy in one male (♂)

Study Type/Animal/ PMRA#	Study Results
28-day Dermal Toxicity Sprague-Dawley rats PMRA# 1171155	NOAEL (systemic) ≥ 1000 mg/kg bw/day (♂/♀) There were no irritation or treatment-related systemic findings in either sex.
CHRONIC TOXICITY AND ONCOGENICITY STUDIES	
18-Month Chronic Toxicity/Oncogenicity (diet) CD-1 mice PMRA# 1163797, 1163798, 1163820, 1163831	NOAEL = 4.19/5.83 mg/kg bw/day (♂/♀) **≥ 42.0/58.1 mg/kg bw/day:** ↑ hepatic lesions (♂/♀); ↓ testes weight, ↑ degeneration of testes and epididymis (♂); ↑ gastroenteropathies (♀) **≥ 216/298 mg/kg bw/day:** ↓ bw, ↓ bwg (♂/♀) **446/582 mg/kg bw/day:** ↑ pallor, ↑ weakness, ↑ hunched posture, ↑ bone marrow congestion (♂/♀); ↓ erythrocyte mass (♂); ↑ mortality, ↑ pancreatic necrosis (♀) **No evidence of oncogenicity**
2-year Chronic Toxicity/Oncogenicity (diet) Sprague-Dawley rats PMRA# 1163785, 1163786	NOAEL = 4.08/5.36 mg/kg bw/day (♂/♀) **≥ 30.3/38.4 mg/kg bw/day:** ↑ retinal atrophy (♂/♀); ↓ bw, ↓ bwg, ↓ fe, ↑ hyperactivity, ↑ elongate spermatid degeneration (♂); ↑ liver inflammation / necrosis / fibrosis/ haemorrhage, ↑ sciatic nerve atrophy (♀) **90.1/126 mg/kg bw/day:** ↑ aggressiveness, ↑ lung granulomas (♂); ↑ lung discolouration / histiocytosis / granulomas, ↑ inflammation and polyarteritis of the pancreas and intestines, ↑ intestinal thickening, ↓ fe (♀) **No evidence of oncogenicity**
REPRODUCTIVE / DEVELOPMENTAL TOXICITY STUDIES	
2-Generation Reproductive Toxicity (dietary/gavage) Sprague-Dawley rats PMRA# 1163787	**Parental Toxicity** NOAEL = 6.95/7.4 mg/kg bw/day (♂/♀) **≥ 34.75/38.1 mg/kg bw/day:** ↓ bwg (P_1) (♂/♀); ↓ bw (P_1), ↓ premating fc (P_1, F_1) (♂); ↓ gestation fc (F_1), ↓ bw (F_1) (♀) **111.95/119.6 mg/kg bw/day**: ↓ bw (F_1), ↓ bwg (F_1), ↓ fe (P_1), ↑ missing tails (F_1), ↑ tails with necrotic tips (F_1), ↑ sores (F_1) (♂/♀),↓ fc (P_1, F_1), ↓ absolute testes weight (♂); ↓ bw (P_1), ↓ gestation bw (P_1, F_1), lactation bw (P_1 [day 0], F_1), ↓ bwg (P_1), ↓ gestation bwg (P_1, F_1), ↓ lactation bwg (F_1a), ↓ fc (F_1), ↓ gestation fc (P_1, F_1), ↓ fe (F_1), ↓ gestation fe (P_1, F_1), ↑ stained fur (F_1, F_2), ↑ mastitis (F_1 dams), ↑ death (F_1 dams) (♀) **Offspring Toxicity** NOAEL = 38.1 mg/kg bw/day **119.6 mg/kg bw/day:** ↓ pup bw (F_1, F_2), ↓ litter survival (F_1), ↓ viability PND 1–4 (F_1), ↑ gasping (F_1), ↑ weakness (F_1), ↓ milk spots (F_1), ↑ stained perineum (F_2), ↑ subcutaneous hemorrhage (F_1, F_2) (♂/♀); ↑ death PND 4-21 (F_1) (♂)

Study Type/Animal/ PMRA#	Study Results
	Reproductive Toxicity NOAEL = 111.95/119.6 mg/kg bw/day (♂/♀) No reproductive effects were observed; however, sperm parameters (motility and morphology), estrous cycle length and periodicity, and ovarian follicle were not examined **No evidence of sensitivity of the young**
Developmental Toxicity (gavage) Sprague-Dawley rats PMRA# 1163790	**Maternal toxicity** NOAEL = 10 mg/kg bw/day **≥ 25 mg/kg bw/day:** ↓ bwg, ↓ fc, ↑ alopecia **≥ 75 mg/kg bw/day:** ↓ bw **Developmental toxicity** NOAEL = 10 mg/kg bw/day **≥ 25 mg/kg bw/day:** ↑ incidence of overall malformations (particularly cleft palate and vertebrae and rib malformations), ↑ incidence of ossification delays (vertebrae and ribs), ↑ incidence of wavy ribs **≥ 75 mg/kg bw/day:** ↓ number of male pups per litter **150 mg/kg bw/day:** ↓ live fetuses per litter, ↑ mean resorptions per litter, ↓ fetal bw **Evidence of treatment-related malformations**
Developmental Toxicity (gavage) New Zealand White rabbits PMRA# 1169313	**Supplemental study** **Maternal Toxicity** No treatment-related effects **Developmental Toxicity** No treatment-related effects **No evidence of treatment-related malformations or sensitivity of the young**

Study Type/Animal/ PMRA#	Study Results
Developmental Toxicity (gavage) New Zealand White rabbits PMRA# 1169314	**Supplemental study** **Maternal toxicity** **≥ 16 mg/kg bw/day:** ↓ gestational bw (nss); ↓ bwg, ↑ cold ears, ↑ anorexia, ↓ faecal output **Fetal toxicity** **≥ 8 mg/kg bw/day:** ↑ incidence of skeletal malformations of the cervical and thoracic vertebrae and ribs (scoliosis, hemivertebra, fused or absent vertebra, fused/absent/branched ribs).
Developmental Toxicity (gavage) New Zealand White rabbits PMRA# 1163788	**Maternal Toxicity** NOAEL = 32 mg/kg bw/day No treatment-related effects **Developmental Toxicity** NOAEL = 4 mg/kg bw/day **≥ 8 mg/kg bw/day:** ↑ incidence of skeletal malformations of cervical and thoracic vertebrae and ribs (hemivertebra, fused vertebra, extra, fused, forked, enlarged or malpositioned ribs) **32 mg/kg bw/day:** ↑ cleft palate **Evidence of treatment-related malformations**
GENOTOXICITY STUDIES	
Bacterial Reverse Mutation Assay *S. typhimurium* (TA98, TA100, TA1535, TA1537); *E. coli* (WP2uvrA) PMRA# 1163791	**Negative** Cytotoxicity at ≥ 750 µg/mL (–S9) Cytotoxicity at ≥ 1000 µg/mL (+S9)
In vitro mammalian gene mutation at HGPRT locus Chinese hamster ovary cells PMRA# 1163792	**Negative**

Study Type/Animal/ PMRA#	Study Results
Unscheduled DNA synthesis Primary rat hepatocytes PMRA# 1163795	**Positive at 5 to 500 µg/mL** Cytotoxicity ≥ 750 µg/mL
In vitro mammalian cytogenetics (chromosomal aberration) Human peripheral lymphocytes PMRA# 1163794	**Positive ≥ 0.85 mg/mL ± S9 activation**
Unscheduled DNA synthesis ex vivo DNA damage and repair Primary rat hepatocytes and spermatocytes PMRA# 1163796	**Negative**
Micronucleus assay (in vivo) CD1-mice PMRA# 1163793	**Negative**
NEUROTOXICITY STUDIES	
90-day dietary toxicity/neurotoxicity Sprague-Dawley rats PMRA# 1163773, 1163783	NOAEL = 47.6/59.9 mg/kg bw/day (♂/♀) **≥ 102/137 mg/kg bw/day:** ↓ lymphocytes, ↓ monocytes, ↑ testicular and epididymal effects; ↓ food efficiency (♀) **224/333 mg/kg bw/day:** ↓ bw, ↓ bwg (♂/♀) No effects on functional observational battery or neuropathology **No evidence of selective neurotoxicity**
Developmental Neurotoxicity Sprague-Dawley rats	**Supplemental** **Maternal toxicity** NOAEL = 50 mg/kg bw/day

Study Type/Animal/ PMRA#	Study Results
PMRA# 1072319	**100 mg/kg bw/day:** ↓ bw, ↓ bwg, ↓ fc **Offspring toxicity** NOAEL = 50 mg/kg bw/day **100 mg/kg bw/day:** ↓ viability index, ↓ litter size, ↑ number of deaths during pre-weaning, ↓ pup bw (LD 5, LD 8-12, LD 30) **Developmental Toxicity** NOAEL = 100 mg/kg bw/day No-treatment related effects No effects on functional observation battery, behavioural tests, or brain weights. Small changes in brain morphometrics were not considered adverse. **No evidence of selective neurotoxicity**
IMMUNOTOXICITY STUDIES	
28-day oral immunotoxicity (SRBC immunization/plaque count) CD-1 mice PMRA# 1028030	**Systemic Toxicity** NOAEL = 218/269 mg/kg bw/day **552 mg/kg bw/day:** ↓ bw, ↓ bwg, ↓ fc, ↓ fe, ↓ abs/rel thymus weight (♀) **Immunotoxicity** NOAEL = 218/552 mg/kg bw/day No treatment-related effects were observed
28-day oral immunotoxicity (SRBC immunization/plaque count) Sprague-Dawley rats PMRA# 1028031	**Systemic Toxicity** NOAEL = 54/31 mg/kg bw/day **≥ 59 mg/kg bw/day:** ↓ bw, ↓ bwg, ↓ fc, ↓ fe (♀) **108 mg/kg bw/day:** ↓ bw, ↓ bwg, ↓ fc, ↓ fe (♂) **Immunotoxicity** NOAEL = 108/117 mg/kg bw/day No treatment-related effects were observed
METABOLITE STUDIES	
Acute Oral Toxicity (gavage) CD-1 mice **IN-KP533** PMRA# 2897312	LD_{50} > 2000 mg/kg bw (♀) **Low acute toxicity**

Study Type/Animal/ PMRA#	Study Results
Bacterial Reverse Mutation Assay *S. typhimurium* (TA98, TA100, TA1535, TA1537); *E.coli* (WP2uvrA) **IN-KP533** PMRA# 2897313	**Negative** Tested up to a limit concentration
In vitro mammalian cytogenetics (chromosomal aberration) Human peripheral lymphocytes **IN-KP533** PMRA# 2897311	**Negative** Tested up to a limit concentration
Comparative QSAR Analysis **IN-KP533** PMRA# 2896700	Toxicity was predicted for the cymoxanil transformation product IN-KP533 using DEREK. The alerts generated for IN-KP533 states that there is nothing to report and makes no prediction regarding toxicity.
Comparative QSAR Analysis **IN-KP533, IN-W3595** PMRA# 2938792	Toxicity was predicted for two cymoxanil transformation products: IN-W3595 and IN-KP533 using Derek Nexus, VEGA-CAESAR, and OECD QSAR Toolbox. The models predicted that IN-KP533 was not mutagenic, carcinogenic, or a developmental or reproductive toxicant. Similarly, the models predicted that IN-W3595 was not mutagenic, or a developmental or reproductive toxicant, however gave mixed predictions for carcinogenicity. Overall, the reliability of these predictions were not high. Both compounds were flagged as a High Toxic Hazard by Cramer Class II rules.

Table 3 Toxicology reference values for use in the cymoxanil health risk assessment

Exposure Scenario	Study	Point of Departure and Endpoint	CAF or Target MOE[1]
Acute dietary (females 13–49 years of age)	Developmental toxicity in rabbits (gavage)	NOAEL = 4 mg/kg bw Fetal malformations of cervical and thoracic vertebrae and ribs (hemivertebra, fused vertebra, extra, fused, forked, enlarged or malpositioned ribs)	1000
ARfD = 0.004 mg/kg bw			
Acute dietary (general population, excluding females 13–49 years of age)	Developmental toxicity in rats (gavage)	NOAEL = 10 mg/kg bw Decreased maternal body weight gains during the first two days of dosing	100
ARfD = 0.1 mg/kg bw			
Chronic dietary (females 13–49 years of age)	Developmental toxicity in rabbits (gavage)	NOAEL = 4 mg/kg bw/day Fetal malformations of cervical and thoracic vertebrae and ribs (hemivertebra, fused vertebra, extra, fused, forked, enlarged or malpositioned ribs)	1000
ADI = 0.004 mg/kg bw/day			
Chronic dietary (general population, excluding females 13–49 years of age)	12-month toxicity in dog (dietary)	NOAEL = 1.3 mg/kg bw/day Decreased body weights, body weight gains and food consumption; increased incidences of swollen lens fibers in the eye, testicular atrophy and lymphoid inflammation in prostate of males	100
ADI = 0.013 mg/kg bw/day			
Short- and intermediate-term dermal[2] and inhalation[3]	Rabbit developmental toxicity	NOAEL = 4 mg/kg bw/day Fetal malformations of cervical and thoracic vertebrae and ribs (hemivertebra, fused vertebra, extra, fused, forked, enlarged or malpositioned ribs)	1000
Cancer	No evidence of carcinogenicity in mice or rats. A cancer risk assessment is not required.		

[1] CAF (Composite assessment factor) refers to the total uncertainty and PCPA factors for dietary and residential risk assessment; MOE refers to the target margin of exposure for occupational assessment.
[2] Since an oral NOAEL was selected, a dermal absorption factor of 10% was used for route-to-route extrapolation.
[3] Since an oral NOAEL was selected, an inhalation absorption factor of 100% (default value) was used for route-to-route extrapolation.

Appendix IV Dietary exposure and risk assessment

Table 1 Summary of acute dietary exposure and risk from cymoxanil

Population Subgroup	Acute Dietary (95th percentile)[1]			
	Food only		Food + Water	
	Exposure (mg/kg bw)	%ARfD	Exposure (mg/kg bw)	%ARfD
General Population[2]	Not applicable		Not applicable	
All Infants (<1 year old)	0.000246	0.25	0.005500	5.50
Children 1–2 years old	0.000754	0.75	0.002720	2.72
Children 3–5 years old	0.000898	0.90	0.002276	2.28
Children 6–12 years old	0.000751	0.75	0.001763	1.76
Males 13–19 years old	0.000701	0.70	0.001616	1.62
Males 20–49 years old	0.001123	1.12	0.002156	2.16
Adults 50+ years old	0.000942	0.94	0.001900	1.90
Females 13–49 years old	0.001006	25.2	0.002155	53.9

[1]Acute Reference Dose (ARfD) of 0.1 mg/kg bw for the general population (excluding females aged 13–49). ARfD of 0.004 mg/kg bw for females 13–49 years old.
[2] The risk estimate was not determined for the general population, as separate ARfDs were selected for females aged 13–49 years, and for the other population groups.

Table 2 Summary of chronic dietary exposure and risk from cymoxanil

Population Subgroup	Chronic Dietary[1]			
	Food only		Food + Water	
	Exposure (mg/kg bw/day)	%ADI	Exposure (mg/kg bw/day)	%ADI
General Population[2]	Not applicable		Not applicable	
All Infants (<1 year old)	0.000247	1.9	0.001228	9.4
Children 1–2 years old	0.000714	5.5	0.001075	8.3
Children 3–5 years old	0.000518	4.0	0.000812	6.2
Children 6–12 years old	0.000260	2.0	0.000479	3.7
Males 13–19 years old	0.000155	1.2	0.000323	2.5
Males 20+ years old	0.000222	1.7	0.000466	3.6
Adults 50+ years old	0.000232	1.8	0.000486	3.7
Females 13–49 years old	0.000210	5.2	0.000466	11.7

[1]Acceptable Daily Intake (ADI) of 0.013 mg/kg bw/day for all subpopulations (excluding females aged 13–49). ADI of 0.004 for females 13–49 years old.
[2] The risk estimate was not determined for the general population, as separate ADIs were selected for females aged 13–49 years, and for the other population groups.

Appendix V Food residue chemistry summary

Metabolism in livestock and plants

The nature of the residue in plant commodities is adequately understood. In potato, tomato and lettuce, cymoxanil was rapidly metabolized to glycine and other natural components such as glucose. The metabolite IN-KQ960 was also observed in the lettuce metabolism study. Cymoxanil was metabolized to natural products in goats including fatty acids, glycerol, glycine and other amino acids, lactose, and acid hydrolyzable formyl and acetyl groups. A cymoxanil poultry metabolism study is not on file, and is not required to support continuing registration as this active is not registered for use on animal feed items.

Residue definition

The residue definition in all crops for enforcement purposes is the parent, cymoxanil (2-cyano-N-[(ethylamino)carbonyl]-2-(methoxyimino)acetamide), only. For risk assessment, the residue definition in leafy vegetables is cymoxanil + the metabolite IN-KQ960 (3-ethyl-4-(methoxyamino)-2,5-dioxo-4-imidazolidinecarboxamide), and for all other commodities it is cymoxanil only. There are no changes in residue definition proposed for these commodities. If the use of cymoxanil expands to include poultry feed items, a poultry metabolism study may be required and the residue definition in animal commodities may require revision. The residue definition for risk assessment in drinking water is revised from the parent only to cymoxanil and its six transformation products IN-U3204, IN-R3273, IN-KP533, IN-4226, IN-KQ960 and IN-JX915 with this re-evaluation.

Maximum residue limits

Canadian maximum residue limits (MRLs) for cymoxanil are currently specified for several commodities. Residues of cymoxanil in/on the registered commodities tomatoes and tomato processed commodities are currently regulated under subsection B.15.002(1) of the **Food and Drugs Regulations** applies. This requires that residues not exceed the general MRL of 0.1 ppm. There are no proposed changes to the established MRLs.

Analytical methodology

Several analytical methods for cymoxanil have been deemed acceptable for data collection, enforcement and multi-residue analysis. Quantitation of the residues of cymoxanil is performed by high performance liquid chromatography with UV detection (HPLC/UV), gas chromatography with nitrogen selective detection (GC/NPD), and HPLC with confirmatory tandem mass spectrometry (HPLC/MS/MS). The HPLC/MS/MS method that has been reviewed was also determined to be adequate for the determination of IN-KQ960 residues in leafy vegetables.

Magnitude of the residue

Sufficient information was available to assess the dietary exposure and risk from exposure to cymoxanil and the metabolite IN-KQ960. Residue field trial data for the registered uses of cymoxanil were determined to be adequate to support the current use patterns.

Crop rotation studies

Adequate data were available for confined crop rotation. Since cymoxanil residues were <LOD in all samples harvested from the confined rotational study, field crop rotation data and plant back interval restrictions are not required.

Processing studies

Processing studies were available for potatoes and tomatoes and deemed adequate. Experimental processing factors from these studies were applied in the risk assessment for dried potatoes, tomato paste, and tomato puree.

Livestock, poultry, egg and milk residue data

Cymoxanil is not registered for use on livestock feed commodities. Thus, livestock feeding data are not required.

Adequacy of the food residue database

Overall, sufficient information were available to adequately assess the dietary risk and exposure from cymoxanil and its metabolites.

Appendix VI Occupational mixer/loader/applicator and postapplication risk assessment

Table 1 Short/intermediate-term risks to mixers/loaders/applicators using groundboom equipment

Crop	M/L and application type	ML UEs (µg/kg a.i.)		Applicator UEs (µg kg a.i.)		AR[a] (kg a.i./ha)	ATPD (ha) [b]	dermal exposure (mg/kg bw/day) [c]	dermal MOE[e]	inhalation exposure (mg bw/day)[d]	inhalation MOE[e]	combined MOE[f]
		dermal	inhalation	dermal	inhalation							
Potato	**Open mix/load of dry flowable (AHETF) and application using groundboom (AHETF)**											
	M/L/A CR coveralls + CR gloves (no gloves if enclosed cab); ML with (*) or without respirator											
	open M/L + open cab	39.13	21.8	11.77	1.680	0.21	100	0.0013	2994	0.0062	649	533
	open M/L + open cab	39.13	2.18*	11.77	1.680		**165**	0.0022	1814	0.0017	2393	1032
	open M/L + closed cab	39.13	21.8	3.09	0.060		100	0.0011	3609	0.0057	697	584
	M/L/A coveralls + CR gloves (no gloves if enclosed cab); ML with (*) or without respirator											
	open M/L + open cab	46.59	21.8	14.19	1.680	0.135	170	0.0017	2294	0.0067	594	472
	open M/L + open cab	46.59	2.18*	14.19	1.680		**231**	0.0024	1688	0.0015	2658	1033
	open M/L + closed cab	46.59	21.8	4.42	0.060		170	0.0015	2733	0.0063	638	517
	M/L/A CR coveralls + CR gloves (no gloves if enclosed cab); ML with (*) or without respirator											
	open M/L + open cab	39.13	21.8	11.77	1.680	0.135	170	0.0015	2739	0.0067	594	488
	open M/L + open cab	39.13	2.18*	11.77	1.680		**257**	0.0022	1812	0.0017	2389	1031
	open M/L + closed cab	39.13	21.8	3.09	0.060		170	0.0012	3303	0.0063	638	535
Tomato	**M/L/A CR coveralls + CR gloves**											
	open M/L + open cab	39.13	21.8	11.77	1.680	0.14	26	0.0002	17272	0.0011	3744	3077

Shaded cells indicate risks that are not considered to be acceptable (MOEs that are less than the target MOE of 1000).

ML = Mixer/Loader; UE = Unit Exposure; MOE = margin of exposure; AHETF = Agricultural Handlers Exposure Database; CR = chemical resistant CF = conversion factor

[a] Maximum AR (kg a.i./ha) = Maximum Application Rate - as per current product labels.

[b] ATPD (ha) = Area Treated Per Day - as per current product labels for potatoes, and on the PMRA Area Treated Per Day Memo for tomatoes (value for fruits and vegetables). Text in **bold** shows the proposed ATPD.

[c] Dermal exposure (mg/kg bw/day) = Dermal unit exposure (µg/kg a.i.) x CF (1 mg/1000µg) × ATPD (ha) × Maximum AR (kg a.i./ha) × 10% dermal absorption/ average worker body weight (80 kg)

[d] Inhalation exposure (mg/kg bw/day) = Inhalation unit exposure (µg/kg a.i.) × CF (1 mg/1000µg) × ATPD (ha) × Maximum AR (kg a.i./ha)/average worker body weight (80 kg)

[e] Based on a dermal and inhalation NOAEL of 4 mg/kg/bw; target MOE of 1000 (Appendix III).

[f] Combined MOE = NOAEL / (Exp_{dermal} + $Exp_{inhalation}$); target MOE = 1000

Table 2 Short/intermediate-term risks to mixers/loaders/applicators using airblast equipment

Crop	M/L and application type	ML UEs (µg/kg a.i.)		Applicator UEs (µg kg a.i.)		AR[a] (kg a.i./ha)	ATPD (ha) [b]	dermal exposure (mg/kg bw/day) [c]	dermal MOE[e]	inhalation exposure (mg bw/day)[d]	inhalation MOE[e]	combined MOE[f]
		dermal	inhalation	dermal	inhalation							
Cane-berries	**Open mix/load of dry flowable (AHETF) and application using airblast (AHETF)**											
	M/L/A CR coveralls + CR gloves (no gloves if enclosed cab); with (*) or without respirator; with ($^{\Delta}$) or without CR headgear											
	open M/L + open cab	39.13	21.8	3323.5	9.080	0.21	20	0.0177	227	0.0016	2467	208
	open M/L + open cab	39.13	2.18*	3323.5	0.91*		20	0.0177	227	0.0002	24657	225
	open M/L + closed cab	39.13	21.8	13.03	0.32		20	0.0003	14607	0.0012	3444	2787
	open M/L + open cab	39.13	21.8	106.77$^{\Delta}$	9.08		20	0.0008	5222	0.0016	2467	1676

Shaded cells indicate risks that are not considered to be acceptable (MOEs that are less than the target MOE of 1000).

ML = Mixer/Loader; UE = Unit Exposure; MOE = margin of exposure; AHETF = Agricultural Handlers Exposure Database; CR = chemical resistant CF = conversion factor

[a] Maximum AR (kg a.i./ha) = Maximum Application Rate - as per current product labels

[b] ATPD (ha) = Area Treated Per Day - based on the PMRA Area Treated Per Day Memo for airblast.

[c] Dermal exposure (mg/kg bw/day) = Dermal unit exposure (µg/kg a.i.) × CF (1 mg/1000µg) × ATPD (ha) × Maximum AR (kg a.i./ha) × 10% dermal absorption/ average worker body weight (80 kg)

[d] Inhalation exposure (mg/kg bw/day) = Inhalation unit exposure (µg/kg a.i.) × CF (1 mg/1000µg) × ATPD (ha) × Maximum AR (kg a.i./ha)/average worker body weight (80 kg)

[e] Based on a dermal and inhalation NOAEL of 4 mg/kg/bw; target MOE of 1000 (Appendix III).

[f] Combined MOE = NOAEL / (Exp_{dermal} + $Exp_{inhalation}$); target MOE = 1000

Table 3 Short/intermediate-term risks to mixers/loaders/applicators using aerial equipment

Crop	M/L and application type	ML UEs (µg/kg a.i.)		Applicator UEs (µg kg a.i.)		AR[a] (kg a.i./ha)	ATPD (ha) [b]	dermal exposure (mg/kg bw/day) [c]	dermal MOE[e]	inhalation exposure (mg bw/day)[d]	inhalation MOE[e]	combined MOE[f]
		dermal	inhalation	dermal	inhalation							
Potato	**Open mix/load of dry flowable (AHETF)**											
	M/L CR coveralls + CR gloves; with (*) or without respirator											
	Open M/L	39.13	21.8	-	-	0.21	100	0.0010	3894	0.0057	699	593
	Open M/L	39.13	2.18*	-	-		**250**	0.0026	1558	0.0014	2796	1000
	M/L CR coveralls + CR gloves; with (*) or without respirator											
	Open M/L	39.13	21.8	-	-	0.135	220	0.0015	2753	0.0081	494	419
	Open M/L	39.13	2.18*	-	-		**389**	0.0026	1557	0.0014	2795	1000
Tomato	**M/L CR coveralls + CR gloves**											
	Open M/L	39.13	21.8	-	-	0.140	26	0.0002	22467	0.00099	4033	3419
Potato and Tomato	**Application using aerial equipment (AHETF)**											
	Single layer + no gloves inside											
	Pilot	-	-	2.67	0.00969	0.21	400	0.0003	14268	0.00001	>100,00	13,768

Shaded cells indicate risks that are not considered to be acceptable (MOEs that are less than the target MOE of 1000).

ML = Mixer/Loader; UE = Unit Exposure; MOE = margin of exposure; AHETF = Agricultural Handlers Exposure Database; CR = chemical resistant CF = conversion factor

[a] Maximum AR (kg a.i./ha) = Maximum Application Rate - as per current product labels.

[b] ATPD (ha) = Area Treated Per Day – as per current label restrictions for potatoes, and on the PMRA Area Treated Per Day Memo for tomatoes (value for fruits and vegetables). Text in **bold** shows the proposed ATPD.

[c] Dermal exposure (mg/kg bw/day) = Dermal unit exposure (µg/kg a.i.) × CF (1 mg/1000 µg) × ATPD (ha) × Maximum AR (kg a.i./ha) × 10% dermal absorption / average worker body weight (80 kg)

[d] Inhalation exposure (mg/kg bw/day) = Inhalation unit exposure (µg/kg a.i.) × CF (1 mg/1000 µg) × ATPD (ha) × Maximum AR (kg a.i./ha)/average worker body weight (80 kg)

[e] Based on a dermal and inhalation NOAEL of 4 mg/kg/bw; target MOE of 1000 (Appendix III).

f Combined MOE = NOAEL / (Exp_{dermal} + $Exp_{inhalation}$); target MOE = 1000

Table 4 Occupational postapplication exposure and risk assessment

Crop	Use directions[a]			Peak DFR (µg/cm²)	Activity	TC (cm²/hr)	Dermal exposure (mg/kg bw/day)	Dermal MOE (day 0)	REI
	Maximum AR (kg a.i./ha	No. of applications	RTI (days)						
Field Tomatoes	0.14	3	12 (1st-2nd application) 24 (2nd-3rd application)	0.305	Hand-set irrigation	1750	0.0053	**749**	8 days
					Tying/training, hand harvesting	1100	0.0034	1191	12 hours
					Scouting	210	0.00064	6240	12 hours
					Hand weeding/ pruning	70	0.00021	18,721	12 hours
Potatoes [Tanos Fungicide]	0.21	3	12 (1st-2nd application) 24 (2nd-3rd application)	0.458	Hand-set irrigation	1750	0.0080	**499**	18 days
					Roguing	1100	0.0050	**794**	6 days
					Scouting	210	0.0010	4160	12 hours
Potatoes [Curzate Fungicide]	0.135	4	5 (1st-2nd application 3rd-4th application) 20 (2nd -3rd application)	0.453	Hand-set irrigation	1750	0.0079	**505**	17 days
					Roguing	1100	0.0050	**803**	6 days
					Scouting	210	0.0009	4207	12 hours
Caneberries	0.21	3	12	0.2771	Hand-set irrigation	1750	0.0125	**320**	11 days
					Hand harvesting, tying/training	1400	0.0100	**400**	9 days
					Scouting, hand pruning/weeding	640	0.0046	**874**	1 day
					Transplanting	230	0.0016	2432	12 hours

Shaded cells indicate risks that are not considered to be acceptable (MOEs that are less than the target MOE of 1000).

AR = application rate; RTI = re-treatment interval; DFR = dislodgeable foliar residue; TC = transferable residues; MOE = margin of exposure

[a] Use directions as per current product labels

[b] Peak DFR (µg/cm²) –For field tomatoes and potatoes, DFR levels are based on the chemical-specific tomato DFR study. For caneberries, a default DFR value was estimated assuming 25% of the application rate and a dissipation rate of 10% per day.

[c] TC (cm²/hr) - highest TC value for a given crop (ARETF, 2015)

[d] Dermal exposure = Peak DFR (µg/cm²) × 1000 µg/mg × TC (cm²/hr) × 8 hours / average worker body weight of 80 kg

Dermal MOE based on a NOAEL of 4 mg/kg bw/day; target MOE = 1000 (Appendix III).

Appendix VII Environmental risk assessment

Table 1 Abiotic transformation of cymoxanil

Type of Study	Test Conditions	Test pH	DT_{50} (days)	Kinetics	Comments	PMRA#
Hydrolysis	10 ppm, 15°C	5	Stable	SFO		1163827
		7	6.1			
		9	<1.0			
	10 ppm, 60°C	7	<1.0			
	300 ppm, 15°C, short test period (<2 days)	6	141			
		7	5.7			
		8	0.7			
	300 ppm, 15°C, long test period (33 days)	5	249			
		7	7.1			
		9	<1.0			
	25 ppm, 25°C	5	167	SFO		1169714
		7	1.1			
		9	0.02			
	5.97 ppm, 20°C (results from HPLC, TLC1 and TLC2 analytical methods)	4	Stable	SFO	Note: Modelling input is 9.6 days (adjusted with the most conservative values at pH 7 to 20°C with Q10 of 2.	2807555
			362			
			714			
		7	2.1			
			2.1			
			2.4			
		9	0.04			
			0.05			
			0.05			

Phototransformation	Water at 25°C	5	1.7	SFO	Adjusted for dark control, equivalent to 4.6 day natural light	1163828
		5	2.9	SFO	Artificial light, equivalent to 5.0 days natural light	2807558
	Soil at 25°C	4.8–5	12.8	DFOP	Artificial light, equivalent to 37.4 days natural light	1169715

SFO = Single first order kinetics
DFOP = Double First Order in Parallel kinetics

Table 2 Biotransformation of cymoxanil and IN-KQ960

Test systems	Test conditions				DT_{50} (day)						PMRA#
	pH	OM (%)	Temp. (°C)	Duration (days)	CYO		Drinking water TRC		ETRC (CYO+IN-KQ960)		
					Values	Kinetic model	Values	Kinetic model	Values	Kinetic model	
Aerobic Soil Biotransformation: cymoxanil											
Tama (silty clay loam)	5.7	1.9	20	12	0.7	SFO	0.8	SFO	NA	NA	2811698
Porterville (sandy loam)	7.7	0.8	20	12	0.5	IORE	2.2	IORE	NA	NA	2811698
Arrow (sandy loam soil)	6.0	2.1	20	90	0.2	IORE	0.8	IORE	NA	NA	2807563
Propstei (sandy loam)	6.5	1.7	20	100	3.9	IORE	4.6	IORE	NA	NA	1163801 2963615
Sermoise (sandy loam)	7.8	2.9	20	100	1.0	SFO	0.9	SFO	1.14	SFO	1163801 2963615
Evensham (sandy clay loam)	5.7	1.7	20	100	10.0	IORE	9.6	IORE	NA	NA	1163801 2963615
Sassafras (sandy loam)	6.4	0.8	25	92	5.5	IORE	9.6	IORE	NA	NA	1072321 1169716
Cranfield soil 230 (sandy loam)	5.1	1.4	20	16	4.6	SFO	11.3	IORE	NA	NA	2807560
Cranfield soil 164 (silt loam soil)	7.2	3.4	20	16	0.9	SFO	1.1	SFO	NA	NA	2807560
Cranfield soil 115(clay loam)	8.1	2.8	20	16	0.2	SFO	0.4	SFO	NA	NA	2807560
Cranfield soil 164 (silt loam soil)	7.1	5.2	10	7	1.4	SFO	1.7	SFO	NA	NA	2807562

Test systems	Test conditions				DT_{50} (day)						PMRA#
	pH	OM (%)	Temp. (°C)	Duration (days)	CYO		Drinking water TRC		ETRC (CYO+IN-KQ960)		
					Values	Kinetic model	Values	Kinetic model	Values	Kinetic model	
90th centile confidence on the mean of 10 values adjusted to 20°C using Q10 of 2, using the mean for the same soil if there are more than one value (averaging the two values for Cranfield soil 164)					4.5						
Anaerobic Soil Biotransformation: cymoxanil											
Speyer 2.3 soil (sandy loam)	6.3	2.1	20	30	0.7	IORE	2	IORE	NA	NA	2807561
Aerobic Aquatic Biotransformation (total system): cymoxanil											
Goose River	8.6	6.3	20	64	0.1	SFO	31.4	DFOP	0.3	IORE	2811699
Chula	7.4	1.3	20	64	0.5	SFO	43.9	DFOP	7.5	DFOP	2811699
Brandywine	6.6	NR	20	127	0.5	SFO	16.4	IORE	3.7	IORE	1072320
Lums Pond	6.6	NR	20	70	1.6	SFO	3.7	IORE	1.64	SFO	1072320
Schoonrewoerdsewiel	8.3	NR	20	100	0.2	SFO	14.6	IORE	0.16	IROE	2807564
Oostvaardersplassen	8.9	NR	20	100	0.1	SFO	25.9	IORE	6.3	IROE	2807564
Bickenbach	7.8	NR	20	102	4.2	IORE	18.4	IORE	NA		1163803
Unter Widdersheim	7.5	NR	20	102	8.6	SFO	27.4	IORE	NA		1163803
80th centile of 8 values adjusted to 20°C					3.1						
Anaerobic Aquatic Biotransformation (total system): cymoxanil											
Goose River	8.6	6.3	20	64	1.3	SFO	81	SFO	1.3	SFO	2811700
Chula	7.4	1.3	20	64	1.1	SFO	142	DFOP	1.1	SFO	2811700
Middlecreek	6.6	1.5	25	100	0.1	SFO	71.2	IORE	0.1	SFO	1169718
80th centile of 3 values adjusted to 20°C					1.2						

Aerobic Soil Biotransformation: IN-KQ690

Test systems	Test conditions				DT_{50} (day)		PMRA#
	pH	OM (%)	Temp. (°C)	Duration (days)	Values	Kinetic model	
Speyer 2.2	6	3.3	20	21	2.8	SFO	2807545
Tama	6.4	4.3	20	21	2.2	SFO	2807545

Test systems	Test conditions				DT_{50} (day)						PMRA#
	pH	OM (%)	Temp. (°C)	Duration (days)	CYO		Drinking water TRC		ETRC (CYO+IN-KQ960)		
					Values	Kinetic model	Values	Kinetic model	Values	Kinetic model	
Nambsheim	7.7	2.1	20	21	3.7	SFO					2807545
Lleida	7.4	2.8	20	21	4.4	SFO					2807545
Sassafras	4.9	1.3	20	21	2.2	SFO					2807545
80th centile of 5 values adjusted to 20˚C					3.8						

OM = Organic matter; Temp. = Temperature; CYO = Cymoxanil; TRC = total residue of concerns for drinking water (sum of cymoxanil, IN-U3204, IN-KQ960, IN-T4226, IN-JX915, IN-R3273, and IN-KP533, wherever relevant information is available; ETRC = total residue of concerns for ecoscenario (sum of cymoxanil and IN-KQ960, wherever relevant information is available; SFO = Single First Order kinetics; IORE = Indeterminate Order Rate Equation Kinetics; DFOP = Double First Order in Parallel kinetics; Q_{10}=rate of enzymatic reaction or physiological process due to an increase of temperature by 10°C, assume to be 2.

Table 3 Summary of field dissipation studies of cymoxanil

Test scenario	Results	PMRA#
Test site: Somerset, Nova Scotia (sandy loam) and Carberry, Manitoba (loam), Canada. **Application:** 21 kg/ha Curzate M-8 Fungicide (equivalent to 1.68 kg cymoxanil/ha). Note: This test rate is greater than the maximum cumulative label rate in Canada (630 g a.i./ha). **Soil sampling:** Nonsystematically to a depth of 90 cm (0–15, 15–30, 30–45, 45–90 cm segments). **Sampling days**: 0, 1, 3, 7, 14, 28, 00, and 90 days after application.	DT_{50}: 5.7–8.0 days. Cymoxanil dissipated quickly from the maximum concentrations in 0–15 cm soil from 0.22 mg a.i./kg soil and 0.39 mg a.i./kg soil at day 0, to <LOQ (0.05 ppm) by day 14 and by day 60, respectively, at two test locations. Not susceptible to leaching in the field. Cymoxanil was not detected (<LOQ) in all soil samples below 15 cm, with one exception sample collected at day 7 at the Somerset site, where cymoxanil was detected at 0.08 mg a.i./kg soil in 15-30 cm soil and 0.10 mg a.i./kg soil in 30–45 cm soil. Soil samples from the field study were not analysed for transformation products.	1173334
Test site: Elkton, MD, United States **Application:** Curzate M-8 (equivalent to 1.21 kg cymoxanil a.i/ha). Note: This test rate is greater that the maximum cumulative label rate in Canada (630 g a.i./ha).	DT_{50}: <1 day. Cymoxanil dissipated quickly from a concentration of 0.29 mg a.i./kg soil in 0–15 cm top soil at day 0 to <LOD (0.02 mg a.i./kg soil) at day 3. Not susceptible to leaching in the field. Cymoxanil was not detected in any soil below 15 cm during	1169696

Soil sampling: Nonsystematically to a depth of 90 cm (0–15, 15–30, 30–45, 45–90 cm segments). **Sampling days:** 0, 1, 3, 7, 10, 14, 30, 60, 90 and 120 days after application.	the study. The soil samples were not analysed for any transformation products.	

Table 4 Adsoprtion/desorption of cymoxanil and transformation products

Type of Study	Compound	Medium	Temperature (°C)	pH	OC (%)	Kd	*Koc*	Mobility*	PMRA#
Adsorption/Desorption	Cymoxanil	Speyer 2.1	20°C	6.9	0.59	0.08	13.40	Very high	2807566
		Midwest 1		5.7	1	0.76	76.32	high	
		Cranfield 115		8.1	1.6	0.35	21.98	Very high	
		Cranfield 164		7.2	2	0.68	33.84	Very high	
		20th centile					18.55	Very high	
	IN-KQ960	Gross-Umstadt	20°C	6.7	1.1	0.03	3.13	Very high	2807548
		Drummer		5.8	3.1	0.18	5.88	Very high	
		Lleida		7.7	1.2	0.11	8.98	Very high	
		Nambsheim		7.4	1.6	0.05	3.02	Very high	
		Sassafras		4.9	0.76	0.03	3.31	Very high	
		20th centile					3.11	Very high	
	IN-U3204	NA	NA	NA	NA	NA	27.9	Very high	2811662
	IN-KQ960	NA	NA	NA	NA	NA	21.6	Very high	
	IN-W3595	NA	NA	NA	NA	NA	13.8	Very high	
	IN-T4226	NA	NA	NA	NA	NA	17.7	Very high	
	IN-KP533	NA	NA	NA	NA	NA	12.9	Very high	

*: Classification determined based on McCall et al., 1981.

Table 5 Toxicity endpoints used in the risk assessment for terrestrial organisms

Organism	Type of study	Test item	Effect parameters/Test conditions	Endpoint	Endpoint values	PMRA No.
Earthworms						
Eisenia fetida	Chronic	Cymoxanil 50 WP (50.6% CYO)	Reproduction	56-d NOEC	= 9.6 mg a.i./kg dry soil)	2807584
Bees/pollinators						
Honey bee, *Apis mellifera*	Acute contact adult	Technical grade active ingredient	Mortality	48-h LD_{50}	>25 µg a.i./bee	1163814
	Acute oral adult	Technical grade active ingredient	Mortality	48-h LD_{50}	>85.59 µg a.i./bee	2807570
	Acute larva	Technical grade active ingredient	Mortality	72-h LD_{50}	> 99.3 µg a.i/bee	2811668
	Chronic adult	Technical grade active ingredient	Mortality	10-d NOEDD 10-d/NOEC	= 4.55 µg a.i./bee/day = 112.00 mg a.i./kg diet	2811670
Predator mites						
Typhlodromus pyri	Glass plate test	Cymoxanil (DPXT3217) 60%WG	Mortality	7-d LR_{50}	>120 g a.i./ha	2811672
			Reproduction	14-d ER_{50}	= 56 g a.i./ha	2811673
	Extended laboratory test	Cymoxanil 6 + Mancozeb 70WP	Mortality	7-d LR_{50}	>6.4 kg product/ha (equivalent to >(384.0 g cymoxanil + 4512 g mancozeb)/ha, the only tested rate, with and without aging on leaves	2807590
			Reproduction	14-d ER_{50}	<6.4 kg product/ha (equivalent to <(384.0 g cymoxanil + 4512 g mancozeb)/ha, the only tested rate, without aging on leaves >6.4 kg product/ha (equivalent to >(384.0 g cymoxanil + 4512 g mancozeb)/ha, the only tested rate, without aging on leaves	
	Field study	DPX-MS546 72.5WG (4.5% Cymoxanil + 68% Mancozeb)	Population	Population dynamics and recovery	6 × 2319 g prod/ha reduce the field population. Recovery within 329 days.	2811676

Organism	Type of study	Test item	Effect parameters/Test conditions	Endpoint	Endpoint values	PMRA No.
Parasitoids wasp						
Aphidius rhopalosiphi	Glass plate test	Cymoxanil (DPX-T3217) 60WG	Mortality	48-h LR_{50}	>120 g a.i./ha	2811682
			Reproduction	14-d ER_{50}	>120 g a.i./ha	
	Extended laboratory test	Cymoxanil 50 + Chlorothalonil 375 g/L	Mortality	48-h LR_{50}	>7.9 kg product/ha (> (324 g Cymoxanil + 243 g Chlorothalonil)/ha	2807598
			Reproduction	12-d ER_{50}	>7.9 kg product/ha (> (324 g Cymoxanil + 243 g Chlorothalonil)/ha	
Aphidius colemani	Semi-field	DPX-KP481 WG 50 (Cymoxanil 25%/ Famoxadone 25%)	Parasitization	10-day population	6-9 × 0.7 kg product/ha showed no adverse effects on the parasitic potential and populations of *A. colemani*	2969573
Wild birds						
Mallard Duck	Acute oral	Technical grade active ingredient	Mortality	14-d LD_{50}	>2000 mg/kg bw	2807576
	Acute dietary	Technical grade active ingredient	Mortality	8-d LD_{50}	= 947.9 mg/kg bw	2807578
	Chronic	Technical grade active ingredient	reproduction	21-week NOEL	= 14.9 mg a.i./kg bw/d	1169700 3052526
Mammals						
Rat	Acute Oral	Curzate® 60DF (60% CYO)	Mortality	14-d LD_{50}	≤251 mg a.i./kg bw/d	1185894
Mouse	Chronic	Technical grade active ingredient	Body weight	90-d NOEL	= 8.3 mg a.i./kg bw/d	1163771
Rat	Chronic	Technical grade active ingredient	Two-generation reproduction	NOEL	= 6.95 mg a.i./kg bw/d	3052524 3052526 1163787

Organism	Type of study	Test item	Effect parameters/Test conditions	Endpoint	Endpoint values	PMRA No.
Terrestrial vascular plants						
Three monocots and three dicots	Vegetative vigor	DPX-T3217 60WG (60% CYO)	Vegetative vigour	21-d ER_{50} 21-d NOER	> 720 g a.i./ha = 720 g a.i./ha	2969574
Four monocots and six dicots	Seedling emergence	Cymoxanil 60WG (60% CYO)	Seedling emergence	ER_{50} (28-d) NOER (28-d)	> 720 g a.i./ha = 720 g a.i./ha	2969575

Table 6 Toxicity endpoints used in the risk assessment for aquatic organisms

Test organism	Type of study	Test item	Test conditions and effect parameters	Type of Endpoint (Duration)	Endpoint value (mg a.i./L)	PMRA#
Freshwater species						
Freshwater invertebrates						
Daphnia magna	Acute	Cymoxanil technical grade active ingredient	Static, immobility	48-h EC_{50}	6.10	2807571
	Acute	IN-KQ960		48-h EC_{50}	0.80	2811689
	Acute	Tanos Fungicide: (25% CYO + 25% FAD)	Flow through or static, immobility	48-h EC_{50}	0.014	3052526
	Chronic	Cymoxanil technical grade active ingredient	Adult survival and offspring number	21-d NOEC	0.067	1163818
	Chronic	IN-KQ960	Adult survival	21-d NOEC	0.30	2811690
Freshwater fish						
Lepomis macrochirus	Acute	Cymoxanil technical grade active ingredient	Static, mortality	96-h LC_{50}	29.00	1163812
Oncorhynchus mykiss	Acute	Cymoxanil technical grade active ingredient		96-h LC_{50}	61.00	1163811
	Acute	IN-KQ960		96-h LC_{50}	>120.00	2811694
	Acute	Tanos Fungicide: (25% CYO + 25% FAD)	Static and flow through, immobility	96-h LC_{50}	0.0076	3052526
	Chronic	Cymoxanil technical grade active ingredient	Flow-through, length and wet weight	90-d NOEC	<0.03	1169710

Test organism	Type of study	Test item	Test conditions and effect parameters	Type of Endpoint (Duration)	Endpoint value (mg a.i./L)	PMRA#
Freshwater algae						
Navicula pelliculosa	Acute	Cymoxanil technical grade active ingredient	Static, cell counts	120-h EC_{50}	0.20	1169703
Anabaena flos-aquae	Acute	IN-KQ960	Static, growth inhibition	96-h EC_{50}	>108.30	2807553
Freshwater vascular plants						
Lemna gibba	Chronic	Cymoxanil technical grade active ingredient	Static, frond number and biomass	14-d EC_{50}	> 0.70	1169707
Estuarine/marine species						
Estuarine/marine invertebrate						
Crustacean (*Mysidopsis bahia)*	Acute	Cymoxanil technical grade active ingredient	Flow-through, mortality	96-h LC_{50}	>44.40	1169734
	Chronic	Cymoxanil technical grade active ingredient	Flow-through, number of young, length of males and females	28-d NOEC	1.70	1169745
Estuarine/marine fish						
Cyprinodon variegatus	Acute	Cymoxanil technical grade active ingredient	Flow-through, mortality	96-h LC_{50}	>47.50	1169709
	Chronic	Cymoxanil technical grade active ingredient	Flow-through, reduced survival	36-d NOEC	0.09	1169711, 1169723
Estuarine/marine algae						
Skeletonema costatum	Acute	Cymoxanil technical grade active ingredient	Static, growth inhibition	120-h EC_{50}	>0.92	1169704

Table 7 Risk quotient calculated for earthworms, bees, beneficial insects (predator mites and parasitoids) and terrestrial vascular plants resulting from a worst-case seasonal application scenario of cymoxanil products (3 × 210 g a.i./ha)

Organism	Test species	Exposure	Test substance	Endpoint	Endpoint values	Unit	LOC	EEC	RQ
Earthworm	*E. fetida*	Chronic	End-use product, Cymoxanil 50 WP	8-week NOEC	= 9.6	mg a.i./kg soil	1	0.1 mg a.i./kg soil	= 0.0
Bees/pollinators	*Apis mellifera*	Adult acute contact	Technical grade active ingredient	48-h LD_{50}	> 25.0	µg a.i./bee	0.4	0.5 µg a.i. /bee/day	< 0.0
		Adult acute oral	Technical grade active ingredient	48-h LD_{50}	> 85.6	µg a.i./bee	0.4	6.0 µg a.i. /bee/day	< 0.1
		Adult chronic	Technical grade active ingredient	10-d NOEDD	= 4.6	µg a.i./bee/day	1	6.0 µg a.i. /bee/day	**= 1.3**
		Larvae acute	Technical grade active ingredient	72-h LD_{50}	> 99.3	µg a.i./larva	0.4	2.6 µg a.i. /bee/day	< 0.0
Predatory mites	*Typhlodromus pyri*	Acute (GPT)	Cymoxanil DPX-T3217 60WG	7-d LR_{50}	> 120.0	g a.i./ha	2	301.4 g a.i./ha	**< 2.5**
		Reproduction (GPT)	Cymoxanil DPX-T3217 60WG	14-d ER_{50}	= 56.0	g a.i./ha	1	301.4 g a.i./ha	**= 5.4**
		Acute (ELR refinement)	Cymoxanil 6 + Mancozeb 70WP	7-d LR_{50}	> 384.0	g a.i./ha	1	301.4 g a.i./ha	< 0.8
		Reproduction without aging (ELR refinement)	Cymoxanil 6 + Mancozeb 70WP	14-d ER_{50}	< 384.0	g a.i./ha	1	301.4 g a.i./ha	> 0.8
		Reproduction after aging (ELR refinement)	Cymoxanil 6 + Mancozeb 70WP	14-d ER_{50}	> 384.0	g a.i./ha	1	301.4 g a.i./ha	< 0.8
Parasitoids wasp	*Aphidius rhopalosiphi*	Acute (GPT)	DPX-T3217 60WG	48 h LR_{50}	> 120.0	g a.i./ha	2	301.4 g a.i./ha	**< 2.5**
		Reproduction (GPT)	Cymoxanil 60WG	12-d ER_{50}	> 120.0	g a.i./ha	1	301.4 g a.i./ha	**< 2.5**
		Acute (ELR refinement)	Cymoxanil 50 + Chlorothalonil 375 g/L	48 h LR_{50}	> 324.0	g a.i./ha	1	301.4 g a.i./ha	< 0.9
		Reproduction (ELR refinement)	Cymoxanil 50 + Chlorothalonil 375 g/L	12-d ER_{50}	> 324.0	g a.i./ha	1	301.4 g a.i./ha	< 0.9

Vascular plants	Multiple plant species	Seedling emergence	DPX-T3217 60WG (60% cymoxanil technical grade active ingredient)	28-d ER_{50}	> 720.0	g a.i./ha	1	243.1	g a.i./ha	< 0.7
	Multiple plant species	Vegetative vigour	DPX-T3217 60WG (60% cymoxanil technical grade active ingredient)	28-d ER_{50}	> 720.0	g a.i./ha	1	301.4	g a.i./ha	< 0.8

***** LOC = 1 for all organisms with the following exceptions: LOC = 2 for glass plate tests on *T. pyri* and *A. rhopalosiphi;* LOC = 0.4 for honey bee acute oral and contact exposure (LOC = 0.4). GPT = glass plate test; ELR = extended leaf residues. Bold value indicates that the RQ exceeds the LOC.

Table 8 Estimated daily exposure and risk quotient calculated for birds and mammals resulting from a worst-case seasonal application scenario of cymoxanil products (3 × 210 g a.i./ha), based on estimated mean nomogram residues

Exposure	Toxicity endpoint (mg a.i./kg bw/d)	Food Guild (food item)	Mean nomogram residues							
			On-field		Off-field (airblast drift, 74%)		Off-field (aerial drift, 26%)		Off-field (groundboom drift, 6%)	
			EDE (mg a.i./kg bw)	RQ*	EDE (mg a.i./kg bw)	RQ*	EDE (mg a.i./kg bw)	RQ*	EDE (mg a.i./kg bw)	RQ*
Small Bird (0.02 kg)										
Acute	>2000.0	Insectivore	16.9	0.1	12.5	0.1	4.4	0.0	1.0	0.0
		Granivore (grain and seeds)	1.8	0.0	1.3	0.0	0.5	0.0	0.1	0.0
		Frugivore (fruit)	3.6	0.0	2.7	0.0	0.9	0.0	0.2	0.0
Dietary	947.9	Insectivore	16.9	0.2	12.5	0.1	4.4	0.0	1.0	0.0
		Granivore (grain and seeds)	1.8	0.0	1.3	0.0	0.5	0.0	0.1	0.0
		Frugivore (fruit)	3.6	0.0	2.7	0.0	0.9	0.0	0.2	0.0
Reproduction	14.9	Insectivore	16.9	**1.1**	12.5	0.8	4.4	0.3	1.0	0.1
		Granivore (grain and seeds)	1.8	0.1	1.3	0.1	0.5	0.0	0.1	0.0
		Frugivore (fruit)	3.6	0.2	2.7	0.2	0.9	0.1	0.2	0.0

Exposure	Toxicity endpoint (mg a.i./kg bw/d)	Food Guild (food item)	Mean nomogram residues							
			On-field		Off-field (airblast drift, 74%)		Off-field (aerial drift, 26%)		Off-field (groundboom drift, 6%)	
			EDE (mg a.i./kg bw)	RQ*	EDE (mg a.i./kg bw)	RQ*	EDE (mg a.i./kg bw)	RQ*	EDE (mg a.i./kg bw)	RQ*
Medium Sized Bird (0.1 kg)										
Acute	>2000.0	Insectivore	13.2	0.1	9.8	0.0	4.0	0.0	0.8	0.0
		Granivore (grain and seeds)	1.4	0.0	1.0	0.0	0.4	0.0	0.1	0.0
		Frugivore (fruit)	2.8	0.0	2.1	0.0	0.9	0.0	0.2	0.0
Dietary	947.9	Insectivore	13.2	0.1	9.8	0.1	4.0	0.0	0.8	0.0
		Granivore (grain and seeds)	1.4	0.0	1.0	0.0	0.4	0.0	0.1	0.0
		Frugivore (fruit)	2.8	0.0	2.1	0.0	0.9	0.0	0.2	0.0
Reproduction	14.9	Insectivore	13.2	0.9	9.8	0.7	4.0	0.3	0.8	0.1
		Granivore (grain and seeds)	1.4	0.1	1.0	0.1	0.4	0.0	0.1	0.0
		Frugivore (fruit)	2.8	0.2	2.1	0.1	0.9	0.1	0.2	0.0
Large Sized Bird (1 kg)										
Acute	>2000.0	Insectivore	3.9	0.0	2.9	0.0	0.2	0.0	0.2	0.0
		Granivore (grain and seeds)	0.4	0.0	1.0	0.0	0.0	0.0	0.0	0.0
		Frugivore (fruit)	0.8	0.0	2.1	0.0	0.0	0.0	0.0	0.0
		Herbivore (short grass)	4.4	0.0	2.9	0.0	1.1	0.0	0.3	0.0
		Herbivore (long grass)	2.5	0.0	0.3	0.0	0.6	0.0	0.1	0.0
		Herbivore (Broadleaf plants)	3.8	0.0	0.6	0.0	1.0	0.0	0.2	0.0
Dietary	947.9	Insectivore	3.9	0.0	2.9	0.0	0.2	0.0	0.2	0.0
		Granivore (grain and seeds)	0.4	0.0	1.0	0.0	0.0	0.0	0.0	0.0
		Frugivore (fruit)	0.8	0.0	2.1	0.0	0.0	0.0	0.0	0.0
		Herbivore (short grass)	4.4	0.0	2.9	0.0	1.1	0.0	0.3	0.0
		Herbivore (long grass)	2.5	0.0	0.3	0.0	0.6	0.0	0.1	0.0
		Herbivore (Broadleaf plants)	3.8	0.0	0.6	0.0	1.0	0.0	0.2	0.0
Reproduction	14.9	Insectivore	3.9	0.3	0.2	0.0	0.2	0.0	0.2	0.0
		Granivore (grain and seeds)	0.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0
		Frugivore (fruit)	0.8	0.1	0.0	0.0	0.0	0.0	0.0	0.0

Exposure	Toxicity endpoint (mg a.i./kg bw/d)	Food Guild (food item)	Mean nomogram residues							
			On-field		Off-field (airblast drift, 74%)		Off-field (aerial drift, 26%)		Off-field (groundboom drift, 6%)	
			EDE (mg a.i./kg bw)	RQ*	EDE (mg a.i./kg bw)	RQ*	EDE (mg a.i./kg bw)	RQ*	EDE (mg a.i./kg bw)	RQ*
		Herbivore (short grass)	4.4	0.3	0.3	0.0	1.1	0.1	0.3	0.0
		Herbivore (long grass)	2.5	0.2	0.1	0.0	0.6	0.0	0.1	0.0
		Herbivore (Broadleaf plants)	3.8	0.3	0.2	0.0	1.0	0.1	0.2	0.0
Small Mammal (0.015 kg)										
Acute	≤251.0	Insectivore	9.7	0.4	7.2	0.3	2.5	0.1	0.6	0.0
		Granivore (grain and seeds)	1.0	0.0	0.8	0.0	0.3	0.0	0.1	0.0
		Frugivore (fruit)	2.1	0.1	1.5	0.1	0.5	0.0	0.1	0.0
Reproduction	6.95	Insectivore	9.7	**1.4**	7.2	**1.0**	2.5	0.4	0.6	0.1
		Granivore (grain and seeds)	1.0	0.1	0.8	0.1	0.3	0.0	0.1	0.0
		Frugivore (fruit)	2.1	0.3	1.5	0.2	0.5	0.1	0.1	0.0
Medium Sized Mammal (0.035 kg)										
Acute	≤251.0	Insectivore	8.5	0.3	6.3	0.3	0.5	0.0	0.5	0.0
		Granivore (grain and seeds)	0.9	0.0	0.7	0.0	0.1	0.0	0.1	0.0
		Frugivore (fruit)	1.8	0.1	1.4	0.1	0.1	0.0	0.1	0.0
		Herbivore (short grass)	9.7	0.4	7.2	0.3	2.5	0.1	0.6	0.0
		Herbivore (long grass)	5.5	0.2	4.0	0.2	1.4	0.1	0.3	0.0
		Herbivore (forage crops)	8.4	0.3	6.2	0.2	2.2	0.1	0.5	0.0
Reproduction	6.95	Insectivore	8.5	**1.2**	6.3	0.9	0.5	0.1	0.5	0.1
		Granivore (grain and seeds)	0.9	0.1	0.7	0.1	0.1	0.0	0.1	0.0
		Frugivore (fruit)	1.8	0.3	1.4	0.2	0.1	0.0	0.1	0.0
		Herbivore (short grass)	9.7	**1.4**	7.2	**1.0**	2.5	0.4	0.6	0.1
		Herbivore (long grass)	5.5	0.8	4.0	0.6	1.4	0.2	0.3	0.0
		Herbivore (Broadleaf plants)	8.4	**1.2**	6.2	0.9	2.2	0.3	0.5	0.1

Exposure	Toxicity endpoint (mg a.i./kg bw/d)	Food Guild (food item)	Mean nomogram residues							
			On-field		Off-field (airblast drift, 74%)		Off-field (aerial drift, 26%)		Off-field (groundboom drift, 6%)	
			EDE (mg a.i./kg bw)	RQ*	EDE (mg a.i./kg bw)	RQ*	EDE (mg a.i./kg bw)	RQ*	EDE (mg a.i./kg bw)	RQ*
Large Sized Mammal (1 kg)										
Acute	≤251.0	Insectivore	4.6	0.2	3.4	0.1	0.3	0.0	0.3	0.0
		Granivore (grain and seeds)	0.5	0.0	0.4	0.0	0.0	0.0	0.0	0.0
		Frugivore (fruit)	1.0	0.0	0.7	0.0	0.1	0.0	0.1	0.0
		Herbivore (short grass)	5.2	0.2	3.8	0.2	1.4	0.1	0.3	0.0
		Herbivore (long grass)	2.9	0.1	2.2	0.1	0.8	0.0	0.2	0.0
		Herbivore (Broadleaf plants)	4.5	0.2	3.3	0.1	1.2	0.0	0.3	0.0
Reproduction	6.5	Insectivore	4.6	0.7	3.4	0.5	0.3	0.0	0.3	0.0
		Granivore (grain and seeds)	0.5	0.1	0.4	0.1	0.0	0.0	0.0	0.0
		Frugivore (fruit)	1.0	0.1	0.7	0.1	0.1	0.0	0.1	0.0
		Herbivore (short grass)	5.2	0.7	3.8	0.6	1.4	0.2	0.3	0.0
		Herbivore (long grass)	2.9	0.4	2.2	0.3	0.8	0.1	0.2	0.0
		Herbivore (Broadleaf plants)	4.5	0.6	3.3	0.5	1.2	0.2	0.3	0.0

* **Bold** values indicate that RQ exceeds the LOC; All RQs for acute birds are < the values listed in the table; All RQs for acute mammals are ≥ the values listed in the table

Table 9 Aquatic organisms screening level risk assessment for cymoxanil and IN-KQ960 with highest annual application rate of 3 × 210 g a.i./ha[1]

Organism	Exposure	Test material	Type	Endpoint (mg/L)	EEC (mg/L)	RQ[4]
Freshwater species						
Daphnia magna	Acute	Technical grade active ingredient	48-h EC_{50}	6.1	0.028	0
	Chronic	Technical grade active ingredient	21-day NOEC	0.067	0.028	0.4
	Acute	IN-KQ960[3]	48-h EC_{50}	0.8	0.031	0.1
	Chronic	IN-KQ960[3]	24-day NOEC	0.302	0.031	0.1
Bluegill sunfish *Lepomis macrochirus*	Acute	Technical grade active ingredient	96-h LC_{50}	29	0.028	0
Rainbow trout *Oncorhynchus mykiss*	Acute	Technical grade active ingredient	96-h LC_{50}	61	0.028	0
	Chronic	Technical grade active ingredient	90-day NOEC	<0.031	0.028	>0.9
	Acute	IN-KQ960[3]	96-h LC_{50}	>120	0.031	0
Amphibian[2] (Bluegill sunfish *Lepomis macrochirus*)	Acute	Technical grade active ingredient	96-h LC_{50}	29	0.15	0.1
Amphibian[2] (Rainbow trout *Oncorhynchus mykiss*)	Acute	Technical grade active ingredient	96-h LC_{50}	61	0.15	0
	Chronic	Technical grade active ingredient	90-day NOEC	<0.031	0.15	**>4.8**

Organism	Exposure	Test material	Type	Endpoint (mg/L)	EEC (mg/L)	RQ[4]
freshwater diatom *Navicula pelliculosa*	Acute	Technical grade active ingredient	120-h EC_{50}	0.202	0.028	0.3
Lemna gibba	Acute	Technical grade active ingredient	14-day NOEC	>0.7	0.028	<0.1
Marine species						
Crustacean *Mysidopsis bahia*	Acute	Technical grade active ingredient	96-h LC_{50}	>44.4	0.028	0
	Chronic	Technical grade active ingredient	28-d NOEC	1.7	0.028	0
sheepshead minnow *Cyprinodon variegatus*	Acute	Technical grade active ingredient	96-h LC_{50}	>47.5	0.028	0
	Chronic	Technical grade active ingredient	36-d NOEC	0.0942	0.028	0.3
Marine diatom *Skeletonema costatum*	Acute	Technical grade active ingredient	120-h EC_{50}	>0.916	0.028	<0.1

[1] Uncertainty factors were applied to endpoints for RQ calculation;
[2] Fish were selected as surrogate species for acute and chronic amphibian endpoints, respectively and in 15 cm water depth;
[3] IN-KQ960 EEC was calculated by converting the parent EEC assuming molecular equivalence.
[4] **Bold** values indicate that RQ exceeds the LOC.

Table 10 Risks of cymoxanil end use product, Tanos Fungicide, to aquatic organisms following spray applications at 3 × 210 g a.i./ha using endpoints from the product[1]

Organism	Exposure	Test material	Type	Endpoint value	Screening level assessment (parent only)		Airblast drift (74%)	Aerial drift (26%)	Boom spray drift (6%)
					EEC (mg test material/L)	RQ[5]	RQ[5]	RQ[5]	RQ
Freshwater invertebrates									
Daphnia magna	Acute	End-use product (Tanos Fungicide)	48-h EC_{50} (product)	0.0555 mg product/L	0.112	**4.0**	**3.0**	**1.0**	0.2
			48-h EC_{50} (Cymoxanil a.i.) [4]	0.014 mg a.i./L	0.028	**4.0**	**3.0**	**1.0**	0.2
Fish									
Rainbow trout *Oncorhynchus mykiss*	Acute	End-use product (Tanos Fungicide)	96-h LC50 (product)	0.0287 mg product/l	0.112	**39.0**	**28.9**	**10.1**	**2.3**
			96-h LC50 (Cymoxanil a.i.) ***	0.0072 mg a.i./L	0.028	**38.9**	**28.8**	**10.1**	**2.3**
Amphibian[2]									
Rainbow trout *Oncorhynchus mykiss*	Acute	End-use product (Tanos Fungicide)	96-h LC_{50} (product)	0.0287 mg product/l	0.598	**208.4**	**154.2**	**54.2**	**12.5**
			96-h LC_{50} (Cymoxanil a.i.) ****	0.0072 mg a.i./L	0.150	**208.3**	**154.2**	**54.2**	**12.5**

[1] Uncertainty factors were applied to endpoints for RQ calculation;
[2] Fish were selected as surrogate species for amphibian using EECs in 15 cm water depth;
[3] Runoff EEC were the 24 hr peak concentrations for the acute exposure;
[4] Toxicity endpoint for the end-use product (Tanos™) is expressed based on the amount of cymoxanil technical grade active ingredient. Screening EEC was calculated based on the product use rates using dissipation rate of cymoxanil and then compared to the endpoint on the product basis for RQ calculation;
[5] **Bold** values indicate that RQ exceeds the LOC.

Table 11 Toxic substances management policy considerations - Comparison to TSMP Track 1 Criteria

TSMP Track 1 Criteria	TSMP Track 1 Criterion value		Active Ingredient Endpoints	Transformation Products Endpoints
Toxic or toxic equivalent as defined by the *Canadian Environmental Protection Act*[1]	Yes		Yes	Yes
Predominantly anthropogenic[2]	Yes		Yes	Yes
Persistence[3]	Soil	Half-life ≥ 182 days	4.5 days	2.2–4.4 day for transformation product IN-KQ960 under aerobic conditions
	Water	Half-life ≥ 182 days	3.1 days	Not available
	Sediment	Half-life ≥ 365 days	Not available	Not available
	Air	Half-life ≥ 2 days or evidence of long range transport	1.8 days	Not available
Bioaccumulation[4]	Log $K_{ow} \geq 5$		0.667	Not available
	BCF ≥ 5000		Not available	Not available
	BAF ≥ 5000		Not available	Not available
Is the chemical a TSMP Track 1 substance (all four criteria must be met)?			No, does not meet TSMP Track 1 criteria.	No, does not meet TSMP Track 1 criteria.

[1] All pesticides will be considered toxic or toxic equivalent for the purpose of initially assessing a pesticide against the TSMP criteria. Assessment of the toxicity criterion may be refined if required (in other words, all other TSMP criteria are met).

[2] The policy considers a substance "predominantly anthropogenic" if, based on expert judgement, its concentration in the environment medium is largely due to human activity, rather than to natural sources or releases.

[3] If the pesticide and/or the transformation product(s) meet one persistence criterion identified for one media (soil, water, sediment or air) than the criterion for persistence is considered to be met.

[4] Field data (for example, BAFs) are preferred over laboratory data (for example, BCFs) which, in turn, are preferred over chemical properties (for example, log K_{ow}).

Appendix VIII Water modelling

Table 1 Major fate inputs for the modelling

Fate Parameter	Drinking Water (cymoxanil + 6TPs)	Ecological Water (cymoxanil only)	Ecological Water (cymoxanil + IN-KQ960)
K_{oc} (L/kg)	3.11[1]	23.23[2]	3.11[1]
Aerobic water half-life (d) at 20°C	29.8[3]	3.15[4]	29.8[5]
Anaerobic water half-life life (d) at 20°C	125[6]	1.19[7]	1.20[8]
Photolysis half-life (d) at 40°N	Stable[9]	5.0[10]	8.6[11]
Hydrolysis life (d) at pH 7 and 20°C	Stable[12]	4.77[13]	6.23[14]
Soil half-life (d) at 20°C	6.70[15]	4.50[16]	6.33[17]

1 20th percentile of 8 values for IN-KQ960
2 20th percentile of 5 values for CYO
3 80th percentile of 8 values for the combined residue
4 80th percentile of 8 values for CYO
5 80th percentile of 8 values for the combined residue
6 80th percentile of 8 values for the combined residue
7 80th percentile of 8 values for CYO
8 80th percentile of 8 values for the combined residue
9 Longer of 2 values for the combined residue
10 Longer of 2 values for CYO
11 Longer of 2 values for the combined residue
12 Longest of 3 values for the combined residue
13 Longest of 2 values for CYO
14 Longest of 3 values for the combined residue
15 90th percentile confidence on the mean of 10 values for the combined residue
16 90th percentile confidence on the mean of 10 values for CYO
17 90th percentile confidence on the mean of 10 values for the combined residue

Table 2 Cymoxanil ecological modelling EECs (in µg a.i./L)

Use pattern	Water depth	Water column						Pore water	
		Peak	24 hour	96 hour	21 day	60 day	90 day	Peak	21 day
Raspberry	80 cm	13	12	9.7	4.0	1.7	1.1	0.46	0.28
	15 cm	68	60	50	20	8.4	5.6	-	-
Potato (tank mix)	80 cm	9.0	7.6	5.0	1.4	0.71	0.48	0.34	0.072
	15 cm	48	40	26	7.0	3.5	2.4	-	-
Potato	80 cm	10	8.8	5.7	1.8	0.75	0.50	0.37	0.095
	15 cm	55	47	29	8.8	3.7	2.5	-	-
Field tomato	80 cm	6.9	5.9	3.8	1.2	0.50	0.33	0.25	0.063
	15 cm	37	31	20	5.9	2.5	1.7	-	-

Table 3 Cymoxanil and IN-KQ960 ecological modelling EECs (in µg a.i./L)

Use pattern	Water depth	Water column						Pore water	
		Peak	24 hour	96 hour	21 day	60 day	90 day	Peak	21 day
Raspberry	80 cm	14	13	12	6.6	2.9	2.0	0.53	0.35
	15 cm	75	71	63	33	14	9.6	-	-
Potato (tank mix product)	80 cm	11	9.8	8.1	4.3	2.0	1.4	0.24	0.13
	15 cm	56	52	43	21	10	6.7	-	-
Potato (alone product)	80 cm	14	13	11	4.8	1.9	1.3	0.31	0.15
	15 cm	74	69	56	24	9.3	6.2	-	-
Field tomato	80 cm	9.3	8.7	7.2	3.2	1.3	0.85	0.21	0.10
	15 cm	49	46	38	16	6.2	4.1	-	-

Table 4 EECs (µg a.i./L) for the drinking risk assessment of the combined residue of cymoxanil, IN-U3204, IN-R3273, IN-KP533, IN-T4226, IN-KQ960 and IN-JX915, as parent equivalent

Use pattern	Groundwater (µg a.i./L)		Surface Water (µg a.i./L)	
	Daily[1]	Yearly[2]	Daily[3]	Yearly[4]
three applications of 210 g a.i./ha at intervals of 5 and 20 days	13	13	30	2.8

[1] 90th percentile of daily average concentrations
[2] 90th percentile of 365-day moving average concentrations
[3] 90th percentile of the peak concentrations from each year
[4] 90th percentile of yearly average concentrations

Appendix IX Water monitoring data

Based on available monitoring data, cymoxanil was not detected in any of the samples from either Canadian or United States sources. In general, sampling occurred in use areas throughout the year, corresponding with the use of cymoxanil to control blight in potatoes and tomatoes throughout the growing season.

Groundwater

A total of 19 groundwater samples from Canada (15 samples from New Brunswick) and the United States (4 samples) were analyzed for cymoxanil. Cymoxanil was not detected in any of the samples collected.

Surface water sources relevant for the human health risk assessment

A total of 473 ambient surface water samples from potential drinking water sources in Canada (4 samples from New Brunswick) and the United States (469 samples) were analyzed for cymoxanil residues. Cymoxanil was not detected in any of these samples.

Surface water sources relevant for the aquatic risk assessment

A total of 35 ambient surface water samples that were only relevant to the aquatic ecoscenario risk assessment were analyzed for cymoxanil residues in the United States. Cymoxanil was not detected in any of the samples.

In addition to this data, the 473 samples relevant to human health were all from river or lake sources and are also considered relevant to the aquatic risk assessment. A total of 508 samples relevant to the aquatic ecoscenario were analyzed for cymoxanil in Canada and the United States and none of these samples had detections.

Appendix X Proposed label amendments for products containing cymoxanil

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

1.0 Label Amendments Relating to the Health Risk Assessment

Label Amendments Proposed for END-USE PRODUCTS CONTAINING CYMOXANIL

1. On the principal panel:

   Do not handle more than 35 kg a.i. per day for groundboom application.
   Do not handle more than 52.5 kg a.i. per day for aerial application.

2. Under the Product Specific Precaution for Aerial application:

   Apply the recommended rate in a minimum spray volume of 50 L per hectare.

3. The following PPE is proposed to be included under the **PRECAUTIONS** sections, as applicable:

   For groundboom application
   Wear chemical resistant coveralls over long-sleeved shirt and long pants, goggles or face shield and chemical resistant gloves during mixing, loading, application, cleanup and repair. Wear a respirator with a NIOSH-approved organic-vapour-removing cartridge with a prefilter approved for pesticides, or a NIOSH-approved canister approved for pesticides during all mixing and loading activities.

   For aerial application
   Wear chemical resistant coveralls over long-sleeved shirt and long pants, goggles or face shield and chemical resistant gloves during mixing, loading, cleanup and repair. Wear a respirator with a NIOSH-approved organic-vapour-removing cartridge with a prefilter approved for pesticides, or a NIOSH-approved canister approved for pesticides during all mixing and loading activities.

   For airblast application
   Wear chemical resistant coveralls over long-sleeved shirt and long pants, goggles or face shield and chemical resistant gloves during mixing, loading, application, cleanup and repair. In addition, wear chemical-resistant headgear during open cab airblast application. Chemical-resistant headgear includes Sou'Wester hat, chemical-resistant rain hat or large brimmed waterproof hat and hood with sufficient neck protection. Gloves are not required during application within a closed cab.

4. Under the **USE PRECAUTIONS** section:

   Apply only to agricultural crops when the potential for drift to areas of human habitation and human activity such as houses, cottages, schools and recreational areas is minimal. Take into consideration wind speed, wind direction, temperature inversions, application equipment, and sprayer settings.

5. The following REIs are proposed:

   DO NOT enter or allow worker entry into treated areas to perform postapplication activities during the intervals specified in the following table:

Crop	Postapplication activity	Restricted-entry interval
Potatoes	Hand set/hand line irrigation related activities involving foliar contact	18 days
	Roguing	6 days
	All Other Activities	1 day
Field Tomatoes	Hand set/hand line irrigation related activities involving foliar contact	8 days
	All Other Activities	12 hours
Caneberries	Hand set/hand line irrigation related activities involving foliar contact	11 days
	All Other Activities	9 days

2.0 Label Amendments Relating to the Environmental Risk Assessment

2.1 Label Amendments Proposed for the TECHNICAL GRADE ACTIVE INGREDIENT

1. Under ENVIRONMENTAL PRECAUTIONS, to include (if not currently present):

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

2. Under DISPOSAL, to include (if not currently present):

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

2.2 Label Amendments Proposed for END-USE PRODUCTS CONTAINING CYMOXANIL

1. Under ENVIRONMENTAL PRECAUTIONS

- TOXIC to aquatic organisms. Observe buffer zones specified under DIRECTIONS FOR USE.
- To reduce runoff from treated areas into aquatic habitats avoid application to areas with a moderate to steep slope, compacted soil, or clay.
- Avoid application when heavy rain is forecast.
- Contamination of aquatic areas as a result of runoff may be reduced by including a vegetative strip between the treated area and the edge of the water body.

2. Under DIRECTIONS FOR USE

- As this product is not registered for the control of pests in aquatic systems, **DO NOT** use to control aquatic pests.
- **DO NOT** contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes.

3. Under STORAGE

- Store this product away from food or feed.

4. Under DISPOSAL

General statement for non-recyclable container (in other words, plastic bags/pouches):

- Triple- or pressure-rinse the empty container. Add the rinsings to the spray mixture in the tank.
- Follow provincial instruction for any required additional cleaning of the container prior to its disposal.
- Make the empty container unsuitable for further use.
- Dispose of the container in accordance with provincial requirements.
- For information on disposal of unused, unwanted product, contact the manufacturer or the provincial regulatory agency. Contact the manufacturer and the provincial regulatory agency in case of a spill, and for clean-up of spills.

General statement for recyclable container (for example, plastic bottles):

- **DO NOT** reuse this container for any purpose. This is a recyclable container, and is to be disposed of at a container collection site. Contact your local distributor/dealer or municipality for the location of the nearest collection site. Before taking the container to the collection site:

1. Triple- or pressure-rinse the empty container. Add the rinsings to the spray mixture in the tank.

2. Make the empty, rinsed container unsuitable for further use.

- If there is no container collection site in your area, dispose of the container in accordance with provincial requirements.
- For information on disposal of unused, unwanted product, contact the manufacturer or the provincial regulatory agency. Contact the manufacturer and the provincial regulatory agency in case of a spill, and for clean-up of spills.

5. Under DIRECTIONS FOR USE

- Under BUFFER ZONE

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

2.3 Label Amendments Proposed for CO-FORMULATED PRODUCT OF CYMOXANIL AND FAMOXADONE, PCP Reg. No. 27435

Under DIRECTIONS FOR USE

- Under BUFFER ZONE

    - Field sprayer application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** apply with spray droplets smaller than the American Society of Agricultural Engineers (ASAE S572.1) medium classification. Boom height must be 60 cm or less above the crop or ground.
    - Airblast application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** direct spray above plants to be treated. Turn off outward pointing nozzles at row ends and outer rows. **DO NOT** apply when wind speed is greater than 16 km/h at the application site as measured outside of the treatment area on the upwind side.
    - Aerial application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** apply when wind speed is greater than 16 km/h at flying height at the site of application. **DO NOT** apply with spray droplets smaller than the American Society of Agricultural Engineers (ASAE S572.1) medium classification. Reduce drift caused by turbulent wingtip vortices. Nozzle distribution along the spray boom length MUST NOT exceed 65% of the wing- or rotorspan.

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

Method of Application	Crop		Buffer Zones (metres) Required for the Protection of:			
			Freshwater Habitat of Depths:		Estuarine/Marine Habitat of Depths:	
			Less than 1 m	Greater than 1 m	Less than 1 m	Greater than 1 m
Field sprayer	Potatoes, caneberries		5	1	2	1
	Field tomatoes		5	1	1	1
Airblast	Caneberries	Early growth stage	40	15	25	15
		Late growth stage	30	5	15	5
Aerial	Potatoes	Fixed wing	450	10	25	10
		Rotary wing	225	10	20	10
	Field Tomatoes	Fixed wing	150	10	15	10
		Rotary wing	150	5	15	5

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A. Information Considered in the Chemistry Assessment

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Additional Information Considered

Published Information

PMRA Document Number	Title
3052522	European Food Safety Authority (EFSA). 2017. Conclusion regarding the peer review of the pesticide risk assessment of the active substance cymoxanil.
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