



Health  
Canada

Santé  
Canada

*Your health and  
safety... our priority.*

*Votre santé et votre  
sécurité... notre priorité.*

Re-evaluation Decision

RVD2020-02

# Folpet and Its Associated End-use Products for Agricultural Uses

*Final Decision*

*(publié aussi en français)*

**23 January 2020**

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

Publications  
Pest Management Regulatory Agency  
Health Canada  
2720 Riverside Drive  
A.L. 6607 D  
Ottawa, Ontario K1A 0K9

Internet: [canada.ca/pesticides](https://canada.ca/pesticides)  
[hc.pmra.publications-arla.sc@canada.ca](mailto:hc.pmra.publications-arla.sc@canada.ca)  
Facsimile: 613-736-3758  
Information Service:  
1-800-267-6315 or 613-736-3799  
[hc.pmra.info-arla.sc@canada.ca](mailto:hc.pmra.info-arla.sc@canada.ca)

**Canada** 

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

Catalogue number: H113-28/2020-2E (print version)  
H113-28/2020-2E-PDF (PDF version)

© Her Majesty the Queen in Right of Canada, as represented by the Minister of Health Canada, 2020

All rights reserved. No part of this information (publication or product) may be reproduced or transmitted in any form or by any means, electronic, mechanical, photocopying, recording or otherwise, or stored in a retrieval system, without prior written permission of Health Canada, Ottawa, Ontario K1A 0K9.

## Table of Contents

Re-evaluation Decision .....	1
Outcome of Science Evaluation .....	2
Regulatory Decision for Agricultural Products containing Folpet .....	2
Risk Mitigation Measures .....	2
Next Steps .....	4
Other Information .....	4
Science Evaluation Update .....	5
1.0 Revised Health Risk Assessment .....	5
1.1 Toxicology Assessment for Folpet .....	5
1.2 Dietary Exposure and Risk Assessment .....	5
1.3 Occupational and Non-Occupational Exposure and Risk Assessment .....	5
1.3.1 Non-Occupational Exposure and Risk Assessment .....	5
1.3.2 Occupational Exposure and Risk Assessment .....	5
1.4 Aggregate Exposure and Risk Assessment .....	6
1.5 Incident Reports .....	6
2.0 Environmental Risk Assessment .....	6
3.0 Value Assessment .....	7
4.0 Conclusion of Science Evaluation .....	7
List of Abbreviations .....	8
Appendix I Registered Agricultural Folpet Products in Canada <sup>1</sup> .....	9
Table 1 Products Requiring Label Amendments .....	9
Appendix II Comments and Responses .....	10
1.0 Comments Related to the Health Risk Assessment .....	10
1.1 Toxicology .....	10
1.1.1 Comments related to developmental toxicology .....	10
1.1.2 Comment related to the establishment of toxicological reference values .....	13
1.2 Comments Related to Occupational Exposure .....	15
1.2.1 Feasibility of the proposed reduced use patterns and REIs .....	15
1.2.2 Protective equipment for postapplication workers .....	15
2.0 Comments Related to the Value Assessment .....	16
2.1 Apples .....	16
2.2 Strawberries .....	16
Appendix III List of Respondents to PRVD2018-05 .....	17
Appendix IV Label Amendments for Products Containing Folpet .....	18
Table 1 Restricted Entry Intervals (REIs) and Pre-Harvest Intervals (PHIs) for Folpet .....	19
Table 2 Maximum Application rates, number of applications and minimum re-treatment interval .....	21
Appendix V Revised Occupational Mixer/Loader/Applicator (MLA) and Postapplication Exposure and Risk Estimates for Folpet .....	29
Table 1 M/L/A Short- to Intermediate-Term Exposure and Risk Assessment for Groundboom Application .....	31
Table 2 M/L/A Short- to Intermediate-Term Exposure and Risk Assessment for Airblast Application .....	33

Table 3	M/L/A Short- to Intermediate-Term Exposure and Risk Assessment for Handheld Application.....	33
Table 4	Occupational Postapplication Risk Assessment for Agricultural Crops.....	35
Appendix VI	References Considered Following Publication of PRVD2018-05 .....	42

## Re-evaluation Decision

Under the authority of the *Pest Control Products Act*, all registered pesticides must be regularly re-evaluated by Health Canada's Pest Management Regulatory Agency (PMRA) to ensure that they continue to meet current health and environmental 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.

Folpet is a fungicide used on a number of food crops such as apples, crab apples, grapes, strawberries, cranberries, and field vegetables, as well as ornamental crops. This document presents the re-evaluation outcome on these agricultural uses. Currently registered products containing folpet for agricultural uses can be found in the Pesticide [Label Search Webpage](#) and in Appendix I.

Folpet is also used as a material preservative in paints and coatings, and vinyl plastics. Health Canada plans to publish a separate document regarding material preservatives for the folpet products. Further details may be found in the published document: Re-evaluation Note REV2018-02, *Approach for the Re-evaluation of Pesticides Used as Preservatives in Paints, Coatings and Related Uses*.

The regulatory approach for the re-evaluation of folpet for agricultural uses was first presented in the Proposed Re-evaluation Decision PRVD2018-05, *Folpet*<sup>1</sup> which underwent a 90 day consultation period ending on 12 June 2018. PRVD2018-05 proposed continued registration of folpet products with mitigation measures such as reduced number of applications, longer re-treatment intervals, increased personal protective equipment (PPE), longer restricted entry intervals, updated aquatic buffer zones, and implementing a water soluble bag formulation for wettable powder formulations. In addition, use on cranberry, cut flowers and azalea stem soak was proposed for cancellation.

Health Canada received comments and data/information relating to the health and value assessments. Respondents are listed in Appendix III. These comments are summarized in Appendix II along with the responses by Health Canada. These comments and new data/information resulted in revisions to the risk assessments (see Science Evaluation Update), and subsequently some changes to the proposed regulatory decision as described in PRVD2018-05. A reference list of information used as the basis for the proposed re-evaluation decision is included in PRVD2018-05, and further information used in the re-evaluation decision is listed in Appendix VI of this document.

---

<sup>1</sup> "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

This document presents the final regulatory decision<sup>2</sup> for this stage of the re-evaluation of folpet, including the required risk mitigation measures to protect human health and the environment. All products containing folpet that are registered for agricultural uses in Canada are subject to this re-evaluation decision.

## **Outcome of Science Evaluation**

Following the consultation on the proposed re-evaluation decision, Health Canada revised the occupational risk assessment based on the comments and information received. As a result, health risks from the current folpet end-use products have been shown to be acceptable for all agricultural uses when used according to the revised label directions with the new mitigation measures, with the exception of risks associated with apples, crab apples, and cranberries on the wettable powder product. In addition, sufficient data were not available to assess the azalea stem soak use, resulting in its cancellation.

Dietary risks were shown to be acceptable and no comments were received pertaining to the dietary risk assessment.

After a review of the available scientific information, folpet and its associated end use products were found to pose an acceptable risk to the environment when used according to the revised label directions.

As an agricultural fungicide, folpet is a valuable pest management tool and contributes to integrated pest management programs on several important crops, including apples, grapes and strawberries, due to its multi-site mode of action and low risk for resistance development.

## **Regulatory Decision for Agricultural Products containing Folpet**

Health Canada has completed this stage of the re-evaluation of folpet. Under the authority of the *Pest Control Products Act*, Health Canada has determined that with required amendments, continued registration of products containing folpet is acceptable. An evaluation of available scientific information found that all agricultural uses of folpet meet current standards for protection of human health and the environment when used according to the revised label directions with the exception of the azalea stem soak use. Label amendments, as summarized below and listed in Appendix IV, are required. No additional data are required.

## **Risk Mitigation Measures**

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

---

<sup>2</sup> “Decision statement” as required by subsection 28(5) of the *Pest Control Products Act*.

## **Human Health**

To protect mixers/loaders and applicators:

- Additional personal protective equipment (PPE) for all products is required
- Cancellation of the azalea stem soak use as adequate data to estimate exposure were not available
- For the wettable powder product:
  - Closed cab tractor for airblast application equipment is required
  - Limit on the amount of product handled per day when using groundboom application equipment
  - Cancellation of the following wettable powder uses: apples, crab apples, and cranberries.

To protect workers entering treated agricultural areas:

- Revision or establishment of restricted-entry intervals (REIs) is required;
- A reduction to the maximum number of applications per season is required for greenhouse and outdoor ornamentals grown for cut flower production, and for tomatoes not grown for processing
- Label statements to clarify the acceptable greenhouse uses of folpet are required.

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 is required.

To ensure potential residues do not occur on crops not registered for use with folpet:

- A rotational plantback interval of 12 months is required for crops not listed for use on folpet labels.

## **Environment**

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

- Additional precautionary standard label statements for runoff mitigation
- Updated storage statements
- Mitigation statements for aquatic organisms
- Field sprayer and airblast application mitigation statements
- Additional label statement to prohibit aerial application
- Updated buffer zones to mitigate environmental risks

Label improvements to meet current standards:

- Updated discharge of effluent statements
- Updated storage statements

## **Next Steps**

To comply with this decision, the required mitigation measures must be implemented on all affected product labels sold by registrants no later than 24 months after the publication date of this decision document. Refer to Appendix I for details on specific products impacted by this decision.

## **Other Information**

Any person may file a notice of objection<sup>3</sup> regarding this decision on folpet within 60 days from the date of publication of this Re-evaluation Decision. For more information regarding the basis for objecting (which must be based on scientific grounds), please refer to the Pesticides section of the Canada.ca website (Request a Reconsideration of Decision) or contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (hc.pmra.info-arla.sc@canada.ca).

The relevant test data on which the decision is based (as referenced in PRVD2018-05 and this document) are available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa). For more information, please contact the PMRA's Pest Management Information Service.

---

<sup>3</sup> As per subsection 35(1) of the *Pest Control Products Act*.



# Science Evaluation Update

## 1.0 Revised Health Risk Assessment

### 1.1 Toxicology Assessment for Folpet

The toxicological assessment for folpet was previously conducted and summarized in PRVD2018-05. A series of comments was received from the technical registrant regarding the findings in the rabbit developmental toxicity studies, notably concerning the presence of malformations. One comment was received from an end-use product registrant regarding the target margins of exposure established by the PMRA for occupational exposure. Overall, the review of these comments did not result in a change in the reference values established for the human health risk assessment of PRVD2018-05. Detailed responses to comments are located in Appendix II.

### 1.2 Dietary Exposure and Risk Assessment

Dietary risks were shown to be acceptable in PRVD2018-05. No comments specific to the dietary risk assessment were received. There were no changes to the dietary risk assessment.

### 1.3 Occupational and Non-Occupational Exposure and Risk Assessment

The occupational and non-occupational (residential) assessments for folpet were previously conducted and published in PRVD2018-05.

#### 1.3.1 Non-Occupational Exposure and Risk Assessment

In PRVD2018-05, risks were shown to be acceptable for application of commercial-class products on trees in residential areas. The risk assessment was updated to reflect the studies and information submitted during the consultation period. This did not result in any changes in the risk conclusions.

#### 1.3.2 Occupational Exposure and Risk Assessment

In PRVD2018-05, the PMRA had proposed removal of cranberries and ornamentals grown for cut flower production (greenhouse, outdoor) from commercial-class product labels due to unacceptable risks for postapplication workers. Calculated restricted-entry intervals (REIs) were not considered to be agronomically feasible for these crops and cancellation was proposed to mitigate these risks. To mitigate risks for other crops, it was proposed to restrict the number of applications allowed per season and to establish or lengthen REIs. Risks were also not shown to be acceptable for the majority of crops listed on the wettable powder label.

During the PRVD consultation period, additional information and studies were received from the registrant and grower groups. This included dermal absorption studies, as well as use information from growers, crop specialists, and grower groups. These data and information were incorporated into the revised assessment to the extent possible, and were important in refining the occupational risk assessment.

As a result of the information and studies submitted during the consultation period, the outcome of the occupational risk assessment and mitigation proposed in PRVD2018-05 was revised as follows:

- The agricultural uses proposed for cancellation, except for azalea stem soak, are now acceptable for continued registration on at least one product label, provided the updated use pattern and mitigation measures are followed.
- For the wettable powder product only, risks were not shown to be acceptable for apples, crab apples and cranberries, and therefore these crops will be removed from the wettable powder product label. However, apples, crab apples and cranberries are listed crops on the water dispersible granular product, and folpet application to these crops will continue to be available to users.
- The personal protective equipment (PPE) requirements for some mixer/loader/applicator scenarios, REIs, and the number of applications for most crops have been updated.

Health Canada's responses to specific comments are in Appendix II. Details of the revised occupational risk assessment are presented in Appendix V.

In PRVD2018-05, the azalea stem soak use was proposed for cancellation as adequate data to estimate exposure were not available. As no comments or data were submitted for this use during the PRVD comment period, this use will be cancelled.

#### **1.4 Aggregate Exposure and Risk Assessment**

In PRVD2018-05, aggregate risks were shown to be acceptable. As there were no changes to the dietary and non-occupational risk conclusions, there were no changes to the aggregate risk conclusions.

#### **1.5 Incident Reports**

No additional human, domestic animal or environmental incidents involving folpet were received since PRVD2018-05.

### **2.0 Environmental Risk Assessment**

Environmental risk assessment and conclusion were presented in PRVD2018-05. No comments specific to the environmental risk assessment were received. There were no changes to the environmental risk assessment.

### **3.0 Value Assessment**

Folpet is a valuable tool for the management of foliar and root diseases on a number of greenhouse and outdoor ornamentals, a high-value industry. Maintaining high quality and visual appeal is desirable in this sector. Folpet contributes to integrated pest management programs on several important crops due to its multi-site mode of action, low risk for resistance development. Consequently, folpet is used in rotation or as a tank-mix partner with other fungicides, including fungicides that are at high risk for resistance development, and thus help to delay development of resistance. Health Canada has determined that folpet and the associated end use products have acceptable value.

### **4.0 Conclusion of Science Evaluation**

With respect to human health, risks associated with the use of folpet and associated end use products are acceptable when these products are used according to revised label directions with the risk mitigation measures. These mitigation measures are presented in Appendix IV.

The environmental risks associated with the use of folpet and associated end use products are acceptable when used according to revised label directions with the risk mitigation measures outlined in Appendix IV.

Use of folpet is important as a management tool for specific foliar and root diseases on a number of crops where only a limited number of other multi-site fungicides are currently registered.

**List of Abbreviations**

A	applicator
ADI	acceptable daily intake
ARfD	acute reference dose
ATPD	area treated per day
BBCH	phenological growth stage
bw	body weight
CR	chemical-resistant
DA	dermal absorption
DFR	dislodgeable foliar residue
ha	hectare
inhal	inhalation
IT	intermediate-term
kg	kilogram(s)
L	litre(s)
LOAEC	lowest observed adverse effect concentration
LOAEL	lowest observed adverse effect level
mg	milligram(s)
M/L	mixer/loader
M/L/A	mixer/loader/applicator
mg	milligram(s)
MOE	margin of exposure
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
PHI	pre-harvest interval
PMRA	Pest Management Regulatory Agency
PPE	personal protective equipment
PRVD	proposed re-evaluation decision
Reg #	registration number
REI	restricted-entry interval
Resp	respirator
RTI	retreatment interval
ST	short-term
USEPA	United States Environmental Protection Agency
WDG	water dispersible granule
WP	wettable powder formulation

## Appendix I      Registered Agricultural Folpet Products in Canada<sup>1</sup>

**Table 1   Products Requiring Label Amendments**

<b>Registration Number</b>	<b>Marketing Class</b>	<b>Registrant</b>	<b>Product Name</b>	<b>Formulation Type</b>	<b>Active ingredient (% , g/L)</b>
15654	Commercial	Adama Agricultural Solutions Canada Ltd.	Folpan 50WP (Folpet) Fungicide	Wettable powder	50 % a.e.
27733	Commercial	Adama Agricultural Solutions Canada Ltd.	Folpan 80 WDG	Water Dispersable Granules	80%
22040	Technical	Adama Agricultural Solutions Canada Ltd.	Folpan Folpet Technical	Dust or powder	95.9%

<sup>1</sup> as of 18 June 2019, excluding discontinued products or products with a submission for discontinuation

---

## Appendix II      Comments and Responses

In response to the consultation for the folpet proposed re-evaluation decision, PRVD2018-05 written comments were received (respondents' affiliations listed in Appendix III). These comments were considered during the final decision phase of this re-evaluation. Summarized comments and Health Canada's responses to them, are provided below.

### 1.0      Comments Related to the Health Risk Assessment

#### 1.1      Toxicology

##### 1.1.1      Comments related to developmental toxicology.

###### **Comment:**

The registrant indicated that the maternal and developmental NOAEL in the 1985 rabbit developmental toxicity study (PRVD2018-05, PMRA# 1347668) should be 10 mg/kg bw/day rather than the NOAEL of 40 mg/kg bw/day previously established by Health Canada. The registrant cites the following effects at their LOAEL of 40 mg/kg bw/day: decreased maternal bodyweight gain (decreased by 15% from gestation days 7-29) and gravid uterine weight (decreased by 16%), and decreased skeletal ossification and increased extra ribs in fetuses. Furthermore, they contend that the increase in early resorptions and post-implantation loss at the high-dose level of 160 mg/kg bw/day was not statistically significant and likely attributable to maternal bodyweight loss following the onset of dosing.

###### **Health Canada Response:**

With respect to maternal toxicity, it was noted that there was no change in maternal bodyweight gain over the period of treatment (gestation days 7-19) at 40 mg/kg bw/day. However, Health Canada acknowledges that there was a slight, transient weight loss in dams at this dose level at the start of treatment (gestation days 7-9). Accordingly, Health Canada revised the maternal NOAEL to 10 mg/kg bw/day. The slight decrease in gravid uterine weight was not considered treatment-related at 40 mg/kg bw/day but rather reflected a slightly lower number of fetuses per dam.

With respect to developmental toxicity, a treatment-related increase in the incidence of extra ribs of fetuses at 40 mg/kg bw/day was not noted by Health Canada. The decrease in fetal skeletal ossification at 40 mg/kg bw/day was limited to sternebrae 1-4 but occurred on both a fetal and litter basis. Accordingly, Health Canada revised the developmental NOAEL to 10 mg/kg bw/day.

While not statistically significant, the increase in early resorptions and post-implantation loss at the high-dose level of 160 mg/kg bw/day was considered treatment-related by Health Canada. Loss of maternal bodyweight may have been a factor in this observation but a direct effect on the offspring cannot be ruled out.

**Comment:**

The registrant concurs with the maternal and developmental NOAELs established by Health Canada in the 1984 rabbit developmental toxicity study (PRVD2018-05, PMRA# 1347666). However, they question Health Canada's conclusion of evidence of teratogenicity in this study, citing the lack of effect in the 1985 rabbit developmental toxicity study (PRVD2018-05, PMRA#1347668), which was conducted with higher dose levels and examined a similar or greater number of fetuses. The registrant also questions Health Canada's reference to cranial malformations other than hydrocephalus.

**Health Canada Response:**

The lack of treatment-related malformations in the 1985 study does not negate the findings in the 1984 rabbit developmental study. Furthermore, the increased resorptions in the 1985 study may have masked teratogenic potential. It is also noted that the duration of dosing was longer in the 1984 study compared to the 1985 study, thus increasing the likelihood of maternal stress-mediated malformations. Health Canada concurs with the registrant that the other cranial findings (domed skull and enlarged, irregular-shaped fontanelle) are not independent observations, but are rather the consequences of hydrocephaly (severe dilation of the lateral brain ventricles).

**Comment:**

The registrant concurs with the maternal and developmental NOAELs and LOAELs established by Health Canada in the 2006 rabbit developmental toxicity study (PRVD2018-05, PMRA# 2359930). However, they contend that the fetal lens anomalies observed at the high-dose level of 60 mg/kg bw/day are attributable to effects on fetal maturation as a consequence of maternal toxicity. The registrant purports that the maternal toxicity at the high-dose level precludes a meaningful evaluation of developmental effects.

**Health Canada Response:**

Health Canada concurs that there is significant maternal toxicity at the high-dose level of 60 mg/kg bw/day, but does not agree that this is sufficient reason to discount the lens malformations. It was noted that there were three dams at this dose level with greater weight loss than the two dams with the fetuses having lens malformations; none of these three dams had fetuses with major abnormalities. No maternal deaths or treatment-related abortions were noted at the high-dose level and there was an adequate number of fetuses available for examination. Consequently, the assessment of developmental toxicity at the high-dose level was valid and the high-dose effects could not be dismissed.

**Comment:**

The registrant indicates that the incidence of hydrocephaly in a 1985 rabbit developmental toxicity study with pulse-dosing (PRVD2018-05, PMRA# 1347667) [2/378 (0.5%) fetuses, 2/58 (3.4%) litters] was lower than the incidence seen in the 1984 study [3/63 live fetuses (4.8%), 2/11 (18.2%) litters] at the same dose level of 60 mg/kg bw/day. This, coupled with the absence of hydrocephaly in the 2006 and the other 1985 developmental toxicity studies, leads the registrant to conclude that the hydrocephaly finding is incidental rather than treatment-related.

The registrant contends that the pulse-dosing study does not indicate a susceptible window of organogenesis for folpet, in contrast to what would be anticipated with a classic teratogen, since only one incidence of hydrocephaly occurred following each treatment period of gestation days 10-12 or 16-18.

**Health Canada Response:**

As indicated in PRVD2018-05, the malformations may be secondary to maternal toxicity as opposed to a direct teratogenic effect. This would explain the lower incidence of hydrocephaly in the 1985 pulse-dosing study, as less exposure occurred resulting in lower maternal toxicity than in the 1984 study. It would also explain the lack of a susceptible window of organogenesis, as folpet does not exhibit the features of a classic teratogen. As reported in their 2012 Scoping Document for Registration Review, the USEPA also considered the hydrocephaly in the rabbit developmental toxicity study to be treatment-related.

**Comment:**

The registrant provided newly summarized historical control data for hydrocephaly, and marked or extreme dilation of the lateral brain ventricles, from the same laboratory that conducted the 1984 and 1985 (pulse-dosing) studies with the same source of rabbits. Historical control data from 87 studies conducted between 1980 and 1991 indicated the occurrence of hydrocephaly in 14/9470 fetuses (0.15%), with a range of 0-3/study, and in 13/1307 litters (0.99%), with a range of 0-2/study. Furthermore, the registrant stated that over half of historical control incidences occurred in 13 studies conducted in the time between the 1984 and 1985 (pulse-dosing) studies (7/1341 fetuses, 6/193 litters) suggesting a higher prevalence of this malformation at the time of conduct, thus supporting this as an incidental finding.

**Health Canada Response:**

The historical control data confirms hydrocephaly as an uncommon observation. In 85 studies (excluding the 1984 and 1985 [pulse-dosing] studies), 73 studies had no incidence of hydrocephaly, 11 studies had a single incidence and one study had an incidence of three fetuses (in two litters). In the 1984 study, hydrocephaly was observed in four fetuses (three live, one dead) from three litters at 60 mg/kg bw/day and in one fetus at 20 mg/kg bw/day. Coupled with the two additional incidences of hydrocephaly seen in the 1985 pulse-dose study at 60 mg/kg bw/day, the data suggests that the finding is treatment-related rather than incidental.

**Comment:**

The registrant notes that there is little consistency in the nature of malformations seen in developmental toxicity studies of captan and folpet. They further note that maternal dosing with folpet results in fetal exposure entirely to phthalimide, which did not result in treatment-related malformations in a rabbit developmental toxicity study. The dose rate in the phthalimide rabbit developmental toxicity [30 mg/kg bw/day (molecular weight 147.1)] is stated to be the molar equivalent of the 60 mg/kg bw/day (molecular weight 296.6) dose of folpet tested in the 1984 and 1985 (pulse-dosing) studies.



---

**Health Canada Response:**

Consistent malformations are not expected between captan and folpet, given Health Canada's contention these are likely mediated via maternal toxicity. As noted in PRVD2018-05, the PMRA acknowledges that the fetus would be primarily exposed to phthalimide and other metabolites; however, given the absence of developmental data on other metabolites, the folpet studies are relevant in that these studies would consider exposure to all mammalian metabolic degradates including phthalimide.

**Comment:**

The registrant acknowledges Health Canada's determination that the malformations in the rabbit developmental toxicity studies with folpet are not a direct teratogenic effect but rather are secondary to maternal toxicity. They conclude that some observed effects, including lens malformation, delayed ossification and post-implantation loss, are considered a consequence of maternal toxicity.

**Health Canada Response:**

As discussed above, Health Canada agrees that the lens malformation, delayed ossification and post-implantation loss are likely secondary to maternal stress and toxicity.

**Overall Health Canada response to comments related to developmental toxicity:**

Overall, the review of the comments relating to the available developmental toxicity studies for folpet did not result in any changes to the reference values previously established for the human health risk assessment as presented in PRVD2018-05. While the maternal and developmental NOAELs in one of the 1985 rabbit developmental toxicity studies (PRVD2018-05, PMRA# 1347668) was updated to 10 mg/kg bw/day, no change is required to the reference values that utilize developmental toxicity, namely the acute reference dose (ARfD), acceptable daily intake (ADI) and aggregate assessment for females 13-49 years of age as well as for the dermal scenario (all durations), as these were based on a NOAEL of 10 mg/kg bw/day from another developmental toxicity study.

**1.1.2 Comment related to the establishment of toxicological reference values****Comment:**

The registrant indicated "while it is possible to ascertain the toxicological endpoints from the current PRVD document, specific endpoints are lacking for a complete understanding of the Health Canada assessment such as additional safety factors used in the occupational assessment".

**Health Canada Response:**

The toxicological reference values for the occupational risk assessment and accompanying rationales were provided on pages 17-18 of the PRVD. These values are further elaborated upon below.

For the dermal reference values for all durations of exposure, it was not possible to use a route-specific study. The available repeat-dose dermal toxicity study was not designed to assess developmental toxicity, which was identified as a potential endpoint of concern following oral administration of folpet, thus necessitating the use of an oral study. The NOAEL of 10 mg/kg bw/day from an oral developmental toxicity study in rabbits was selected for the dermal risk assessment based on the occurrence of malformations in fetuses from rabbits exposed to folpet during pregnancy. The concern was tempered by the presence of maternal toxicity. For occupational assessment, a target margin of exposure (MOE) of 300 was established consisting of uncertainty factors of 10-fold for interspecies extrapolation, 10-fold for intraspecies variability and a 3-fold factor for the seriousness of the endpoint, namely fetal malformations. As individuals exposed occupationally could include pregnant women, there is the potential for indirect exposure of the fetus. Accordingly, the 3-fold factor for seriousness of the endpoint, as discussed in the *Pest Control Products Act* Hazard Characterization section of the PRVD, was applied, consistent with the approaches outlined in SPN2008-01: The Application of Uncertainty Factors and the *Pest Control Products Act* Factor in the Human Health Risk Assessment of Pesticides.

For the inhalation reference values, the point of departure from the route-specific study was protective of developmental toxicity concerns, enabling the use of the route-specific study. A 28-day inhalation toxicity study with folpet in rats was available with a LOAEC of 5.2 µg/L (1.4 mg/kg bw/day) based on laryngeal lesions and, in males, an increase in lung weight. No NOAEC was established in this study. Target MOEs for all durations included uncertainty factors of 10-fold for interspecies extrapolation, 10-fold for intraspecies variability, and a 3-fold uncertainty factor for the lack of a NOAEC. As the 28-day study was of relevant duration for a short-term inhalation risk assessment, no further factors were required, resulting in a total target MOE of 300 for this scenario.

Given the irritant nature of folpet, increased duration of exposure is expected to result in progressive toxicity to the respiratory tract. This was further supported by the observation of progressive toxicity with increasing duration of exposure observed in repeat-dose inhalation toxicity studies conducted with captan, which like folpet, is metabolized to the highly irritating thiophosgene. As no repeat-dose inhalation studies were available of longer duration with folpet, it was necessary to apply an additional uncertainty factor to account for effects that may be attributable to sustained, prolonged exposure. Consequently, additional uncertainty factors of 3-fold and 10-fold were applied to the intermediate- and long-term inhalation risk assessments, respectively, to account for potential durational toxicity. Thus, the target MOEs for the intermediate- and long-term inhalation risk assessments were 1000 and 3000, respectively.

Overall, no changes to the reference values outlined in PRVD2018-05 were warranted on the basis of the comments received.

---

## 1.2 Comments Related to Occupational Exposure

### 1.2.1 Feasibility of the proposed reduced use patterns and REIs

**Comment:**

Grower groups commented that the reduced use pattern and REIs proposed in the PRVD are not feasible for strawberries and apples.

**Health Canada Response:**

The postapplication risk assessment has been revised based on updated dermal absorption values and use information, as discussed in Appendix V. As a result, shorter REIs and a greater number of applications can be supported.

The REI for strawberry harvesting continues to be longer than what grower groups indicated was feasible for Botrytis Gray Mould control. The risk assessment has been refined to the extent possible with the data available for folpet. As discussed below in response to question 1.2.2, further mitigation of risk with personal protective equipment (PPE) is not possible. Please also refer to question 2.2 for the value assessment of folpet REIs on strawberry.

### 1.2.2 Protective equipment for postapplication workers

**Comment:**

Grower groups suggested that personal protective equipment (PPE) could be a practical approach to mitigate postapplication worker exposure.

**Health Canada Response:**

Studies that are currently used to estimate postapplication worker exposure are based on workers wearing long-sleeved shirts, long pants, socks and footwear. It is also understood that many postapplication workers may wear gloves for personal comfort, or phytosanitary reasons. However, there is no reliable data to indicate the degree of protection that various types of gloves may provide to postapplication workers, or conversely, the extent that gloves may enhance exposure under certain conditions (see below).

Before Health Canada can estimate risk to workers wearing gloves or other PPE, worker exposure studies comparable to those currently used by Health Canada are required. Studies that are currently used are discussed further in the Regulatory Proposal PRO2014-14, *Updated Agricultural Transfer Coefficients for Assessing Occupational Postapplication Exposure to Pesticides*. Most, if not all, studies conducted by the Agricultural Reentry Task Force, submitted by registrants, or available in the scientific literature and used to determine Health Canada's TCs did not include gloves as a basis to estimate exposure with gloves. Gloves may have been worn in some of the studies, but they functioned as dosimeters to measure hand exposure without gloves, rather than exposure as a result of protection from the glove. In addition, some available studies suggest that exposure actually increases when wearing gloves (Brouwer, 2000; Boman et al., 2005; Garrigou et al., 2011; Graves et al., 1995; Keifer, 2000; Rawson et al., 2005).

---

## **2.0 Comments Related to the Value Assessment**

### **2.1 Apples**

#### **Comment:**

Comments from the Apples Growers of Ontario and the Canadian Horticultural Council were received in response to the proposed reduction in the number of applications per year from six to three, and the establishment of a restricted-entry interval (REI) of 21 days for hand thinning. Apple growers support reducing the number of applications to three assuming alternative Group M fungicides continue to be registered. However, growers are strongly opposed to the 21-day REI for hand thinning. Most fungicides are protectant and not curative, and for apple scab control, folpet needs to be applied every 7-10 days. While chemical thinners are available, hand thinning is frequently used in addition, and can overlap with the folpet application schedule.

#### **Health Canada Response:**

Consideration of comments and new information resulted in a revision to the risk assessment, re-instating up to six applications of folpet per season, and reducing the REI to six days for hand thinning.

### **2.2 Strawberries**

#### **Comment:**

Comments from the Berry Growers of Ontario and the Canadian Horticultural Council were received in response to the proposed reduction in the number of applications per year from six to one, and the establishment of a restricted-entry interval (REI) of 12 days for hand harvesting. Each year, Ontario production of strawberries in general increases, particularly for day neutral (all season) types. A single application per season is insufficient to provide adequate disease control. An REI of 12 days for hand harvesting is impractical for day neutral strawberries, which are harvested every 3 days throughout the summer.

#### **Health Canada Response:**

Consideration of comments and new information resulted in revision to the risk assessment, re-instating up to six applications per season and reducing the REI to eleven days for hand harvesting. While this will not permit the use of folpet around strawberry harvest, folpet may still be used before and after harvest season to protect the plants from leaf spot disease.

---

**Appendix III      List of Respondents to PRVD2018-05**

<b>Category</b>	<b>Respondent</b>
<b>Agricultural Associations</b>	Berry Growers of Ontario Ontario Apple Growers Canadian Horticulture Council
<b>Registrant</b>	Adama Agricultural Solutions Canada Ltd.

---

## **Appendix IV      Label Amendments for Products Containing Folpet**

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

### **I.      LABEL AMENDMENTS FOR TECHNICAL GRADE ACTIVE INGREDIENTS CONTAINING FOLPET**

The following label amendments are required on the folpet technical product label under the appropriate sections:

#### **PRIMARY PANEL**

Amend the signal word and hazard statement on the primary display panel from:

“Caution-Poison, Causes eye irritation” to WARNING- POISON, EYE IRRITANT, POTENTIAL SKIN SENSITIZER”

#### **SECONDARY PANEL**

The following statements are required:

#### **PRECAUTIONS**

Add:

“May be fatal if inhaled.”

“Avoid inhaling/breathing dusts or sprays.”

“Causes eye irritation. Do not get in eyes.”

“Potential skin sensitizer.”

#### **ENVIRONMENTAL PRECAUTIONS**

Add:

“TOXIC to small wild mammals and aquatic organisms”

“DO NOT discharge effluent containing this product into sewer systems, lakes, streams, ponds, estuaries, oceans or other waters.”

### **LABEL AMENDMENTS FOR COMMERCIAL CLASS END-USE PRODUCT CONTAINING FOLPET**

The following label amendments are required on the folpet product labels under the appropriate sections:

#### **Cancelled Uses**

Azalea stem soak and any other reference to this use must be removed from all commercial class product labels

Apples, crab apples and cranberries and any other reference to these uses must be removed from all wettable powder product labels

**A. LABEL AMENDMENTS FOR WATER DISPERSABLE GRANULE AND WETTABLE POWDER FORMULATIONS OF FOLPET**

**PRECAUTIONS**

The following table must be added to the labels under **PRECAUTIONS**. Remove any crops from the table that are cancelled or not registered on that specific product label.

**Table 1 Restricted-entry Intervals (REIs) and Pre-Harvest Intervals (PHIs) for Folpet**

Crop	Postapplication Activity	REI/PHI (days)
Apples	Harvesting (hand, mechanical)	1
	Hand thinning fruit	6
	All other activities	12 hours
Crab apples	Harvesting (hand, mechanical)	1
	Hand thinning fruit	3
	All other activities	12 hours
Grape	Hand harvesting, training/tying, leaf pulling by hand	3
	Mechanical harvesting	1
	Hand turning and girdling (table/raisin grapes only)	35
	All other activities	12 hours
Cucumber, pumpkin, melon, squash	Hand harvesting, mechanically-assisted harvesting, training, tying, turning	11
	Hand set/ hand line irrigation related activities involving foliar contact	22
	All other activities	12 hours
Tomato- for processing	Mechanical harvesting	1
	Scouting	2
	Hand set/ hand line irrigation related activities involving foliar contact	22
	All other activities	12 hours
Tomato- not for processing	Hand harvesting, training, tying	16
	Mechanical harvesting, scouting	1

Crop		Postapplication Activity	REI/PHI (days)
		Hand set/ hand line irrigation related activities involving foliar contact	22
		All other activities	12 hours
Strawberry		Hand harvesting	11
		All other activities	12 hours
Cranberry		Harvesting (hand, mechanical)	30
		Scouting	4
		All other activities	12 hours
Ornamentals* grown for cut flower production			
Carnation, zinnias, snapdragon, rose, aster, china aster, chrysanthemum, iris	Greenhouse	Hand harvesting, hand pruning, disbudding	48
		All other activities	12 hours
Carnation, zinnias, snapdragon, rose, aster, china aster, chrysanthemum, iris	Outdoor	Hand harvesting, hand pruning, disbudding	16
		Hand set/ hand line irrigation related activities involving foliar contact	8
		All other activities	12 hours
Ornamentals* NOT grown for cut flower production			
Poinsettia	Greenhouse	All activities	12 hours
Carnations, marigold, zinnias, snapdragon, roses, asters, china asters, phloxes, chrysanthemums, iris	Greenhouse, outdoor	Hand set/ hand line irrigation related activities involving foliar contact	13
		All other activities	12 hours

\*Only for use on ornamental specified on this label

## ENVIRONMENTAL PRECAUTIONS

### Add:

“Toxic to small wild mammals and 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.”



**DIRECTIONS FOR USE**

Scientific names must be added to all diseases.

**Add under a ‘Crop Rotation’ sub header:** “A rotational plantback interval of 12 months for crops not listed on the label.”

**Maximum application rates, maximum number of applications and minimum re-treatment intervals**

The labels must be modified so that the maximum application rate, maximum number of applications, minimum application interval (RTI) and application directions on the label match those specified in Table 2 for each crop currently registered on the label.

**Table 2 Maximum Application rates, number of applications and minimum re-treatment interval**

Crop		Maximum Application Rate(s)	Maximum Number of Applications	Minimum RTI (Days)
Apples		3.0 kg ai/ha	6	10
Crab apples			4	10
Grape		1.0 kg ai/ha	6 total ‘dead arm’: 2 per season All other diseases: 4 per season	10
Cucumber, pumpkin, melon, squash		4.0 kg ai/ha	6	7
Tomato- for processing			6	7
Tomato- not for processing			3	7
Strawberries		2.0 kg ai/ha	6	7
Cranberry		2.6 kg ai/ha	2	10
Ornamentals* grown for cut flower production				
Carnation, zinnia, snapdragon, rose, aster, china aster, chrysanthemum, iris	Greenhouse	1.0 kg ai/1000 L or 1.0 kg ai/ha	1	-
Carnation	Outdoor		2	14
Zinnia, snapdragon			2	3
Rose, aster, china aster, chrysanthemum, iris			2	7
Ornamentals* NOT grown for cut flower production				
Poinsettia	Greenhouse	1.13 kg ai/1000 L or 1.13 kg ai/ha	2	10
Carnation			6	14
Marigold, zinnia, snapdragon			6	3

Crop		Maximum Application Rate(s)	Maximum Number of Applications	Minimum RTI (Days)
Rose, aster, china aster, phlox, chrysanthemum	Greenhouse, outdoor	1.0 kg ai/1000 L or 1.0 kg ai/ha	6	7
Iris			4	7

\*Only for use on ornamentals specified on this label

Under Directions for Use:

Add:

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.

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.

**DO NOT APPLY** using aerial application equipment.

Spot treatments using hand-held equipment **DO NOT** require a buffer zone.

The buffer zones specified in the sections B and C 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.”

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.

The buffer zones for this product can be modified based on weather conditions and spray equipment configuration by accessing the Buffer Zone Calculator found on the Drift Mitigation page of the Canada.ca web site.

---

**STORAGE**Add:

“To prevent contamination store this product away from food or feed.”

**DISPOSAL**Add:

1. Empty bag thoroughly into spray tank.
2. Make the empty bag unsuitable for further use.
3. Dispose of the bag in accordance with provincial requirements.
4. For further information on the disposal of unused, unwanted product contact the manufacturer or the provincial regulatory agency.
5. Contact the manufacturer and the provincial regulatory agency in case of a spill, and for clean-up of spills.

**B. LABEL AMENDMENTS SPECIFIC TO WATER DISPERSIBLE GRANULE (WDG) FORMULATION** (*Reg. No. 27733*)

**PRIMARY PANEL**Remove:

“For commercial use only. This product is not to be used in and around homes or other residential areas such as parks, schools, public buildings, playing fields or any other areas where the general public including children could be exposed.”

Add:

“**DO NOT** use in residential areas. Residential areas are defined as sites where bystanders including children may be potentially exposed during or after spraying. This includes around homes, school, parks, playgrounds, playing fields, public buildings or any other areas where the general public including children could be exposed.”

**PRECAUTIONS**Remove:

“Wear long-sleeved shirt, long pants, chemical resistant gloves and goggles during mixing, loading, application, clean-up and repair activities. Applicator must wear either a respirator with NIOSH/MSHA/BHSE approved organic-vapour-removing cartridge with a prefilter approved for pesticides or a NIOSH/MSHA/BSHE approved canister approved for pesticides when handling open bags during filling operation.”

Add:

“During mixing, loading, application, clean-up and repair, wear a long-sleeved shirt, long pants, chemical-resistant gloves, goggles, socks and shoes, and a respirator with a NIOSH-approved organic-vapour-removing cartridge with a prefilter approved for pesticides OR a NIOSH-approved canister approved for pesticides. Gloves are not required during application within a closed cab.”

When applying using mechanically-pressurized handgun, also wear coveralls.

When applying using open cab airblast application equipment, also wear coveralls and chemical-resistant headgear. Chemical-resistant headgear includes Sou'Wester hat, chemical-resistant rain hat or large brimmed waterproof hat and hood with sufficient neck protection."

Remove:

"**DO NOT** enter or allow worker entry into treated areas within 24 hours of application."

Add:

"**DO NOT** enter or allow worker entry into treated areas during the restricted entry intervals (REIs) specified in the following table."

Add:

REI and PHI table (Table 1), excluding 'roses, asters, China asters, phloxes' from the "crop" descriptions as these ornamentals are not listed on the WDG product label

## **DIRECTIONS FOR USE**

Remove:

"For commercial use only. This product is not to be used in and around homes or other residential areas such as parks, schools, public buildings, playing fields or any other areas where the general public including children could be exposed."

Add:

"**DO NOT** use in residential areas. Residential areas are defined as sites where bystanders including children may be potentially exposed during or after spraying. This includes around homes, school, parks, playgrounds, playing fields, public buildings or any other areas where the general public including children could be exposed."

Remove:

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

Add:

"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."

Remove:

"FIELD TOMATOES"

Replace with:

“TOMATOES -for processing”;

“TOMATOES –not for processing”

The directions for use are the same for both, with the exception of an additional statement added to “TOMATOES –for processing”: “Mechanical harvesting only. **DO NOT** hand harvest processing tomatoes.”

Add:

“**DO NOT** apply in greenhouses, except on greenhouse grown ornamentals.”

Remove the pre-harvest interval statement from all crops, if present:

“Do not apply within ‘x’ day(s) of harvest.” The ‘x’ represents the number of days specified in this statement, which varies between crops.

Add:

“Buffer Zones:

Spot treatments using hand-held equipment **DO NOT** require a buffer zone.

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 (groundboom)	Cucumber, melon, pumpkin, squash, processed and non-processed tomato		40	5	3	2
	Cranberry		35	4	3	1
	Strawberry		25	3	2	1
	Chrysanthemum, carnation, iris, marigold, zinnia, snapdragon		15	2	1	1
Airblast	Apple, crabapple	Early growth stage	60	35	30	20
		Late growth stage	50	25	20	10
	Grape	Early growth stage	50	25	15	10
		Late growth stage	40	15	10	4

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.

The buffer zones for this product can be modified based on weather conditions and spray equipment configuration by accessing the Buffer Zone Calculator found on the Drift Mitigation page of the Canada.ca web site.”

### C. LABEL AMENDMENTS SPECIFIC TO WETTABLE POWDER (WP)

FORMULATION (*Reg. No. 15654*)

#### PRECAUTIONS

Add:

“During mixing, loading, application, clean-up and repair, wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes, and a respirator with a NIOSH-approved organic-vapour-removing cartridge with a prefilter approved for pesticides OR a NIOSH-approved canister approved for pesticides.”

“When applying using mechanically-pressurized handgun, also wear coveralls.”

“When applying using airblast equipment, use a closed cab. A closed cab must have both a physical barrier and respiratory protection (i.e. dust/mist filtering and/or vapour/gas purification system). The closed cab must have a chemical-resistant barrier that totally surrounds the occupant and prevents contact with pesticides outside the cab. Respirators, and chemical-resistant gloves are not required during application within the closed cab.”

“When applying using groundboom application equipment, **DO NOT** handle more than [20 kg ai to be reported as a product equivalent value] per person per day. These restrictions are in place to minimize exposure to individual applicators. Application may need to be performed over multiple days or using multiple applicators.” As indicated by the square brackets above, the active ingredient amount in this statement (i.e. 20 kg a.i.) is to be converted into the corresponding amount of product by the registrant.

“**DO NOT** enter or allow worker entry into treated areas during the restricted entry intervals (REIs) specified in the following table.”

Add REI and PHI table (Table 1), excluding the rows for apples, crabapples, and cranberries, as these uses will be removed from the WP product label.

#### DIRECTIONS FOR USE

Add:

“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.”

Add:

“**DO NOT** apply in greenhouses, except on greenhouse grown ornamentals”

Remove:

“TOMATOES”

Replace with:

“TOMATOES -for processing”;

“TOMATOES –not for processing”

The directions for use are the same for both, with the exception of an additional statement added to “TOMATOES –for processing”: “Mechanical harvesting only. **DO NOT** hand harvest processing tomatoes.”

Add to the use instructions for ‘field tomatoes - for processing’:

“Mechanical harvesting only. **DO NOT** hand harvest processing tomatoes.”

Remove the pre-harvest interval statement from all crops, if present:

“Do not apply within ‘x’ day(s) of harvest.” The ‘x’ represents the number of days specified in this statement, which varies between crops.

For label clarification, in accordance with the Regulatory Directive: Chemigation (DIR93-13), under ‘DIRECTIONS FOR USE’- the product label must be amended as follows:

Add:

“**DO NOT** apply this product by chemigation or through any type of irrigation system

Spot treatments using hand-held equipment **DO NOT** require a buffer zone.

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 (groundboom)	Cucumber, melon, pumpkin, squash, processed and non-processed tomato		40	5	3	2
	Grape, strawberry, rose, aster, China aster, phloxes, chrysanthemum, carnation, iris, marigold, zinnia, snapdragon		25	3	2	1
Airblast	Grape	Early growth stage	55	30	25	15
		Late growth stage	45	20	15	5

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.

The buffer zones for this product can be modified based on weather conditions and spray equipment configuration by accessing the Buffer Zone Calculator found on the Drift Mitigation page of the Canada.ca web site.”



---

## **Appendix V      Revised Occupational Mixer/Loader/Applicator (MLA) and Postapplication Exposure and Risk Estimates for Folpet**

Details and tables for the revised risk assessment are included in this appendix. Please refer to PRVD2018-05 for additional information.

### **Dermal Absorption**

In PRVD2018-05, the dermal absorption value of 20% was selected for all scenarios based on a weight-of-evidence approach using available dermal absorption studies (a human in vivo study, three rat in vivo studies, and a rat and human in vitro study), as well as the physical/chemical properties of folpet, and observations from toxicology studies.

Following the publication of PRVD2018-05, the following studies were submitted to the PMRA: a triple pack of dermal absorption studies consisting of a rat in vivo, rat in vitro, and human in vitro study, a rat and human in vitro study, and a human in vitro study conducted using dried residues. An additional human in vitro study conducted using dried residues was available in the literature. The entire database of folpet dermal absorption studies was considered in the selection of dermal absorption values for folpet.

The available dermal absorption studies allowed for consideration of activity- specific dermal absorption values for workers performing different activities who would be exposed to different concentrations of folpet and different states of the diluted spray solution (e.g. mixers/loaders would be exposed to the end-use product, applicators would be exposed to the diluted spray solution, postapplication workers would be exposed to dry diluted spray residues). Since the percent dermal absorption depends on the concentration of folpet on the skin, and whether liquid or dry residues are present, different dermal absorption values were determined for mixers/loaders, applicators, and postapplication workers.

For agricultural commercial-class products, a dermal absorption value of 1% was selected for workers mixing/loading end-use products based on the results of the high dose group from the human in vitro study in the triple pack conducted with the water dispersible granule (WDG) product. A dermal absorption value of 20% was selected for applicators based on the results of the low dose group from the human in vitro study in the triple pack conducted with the WDG product, as well as the results from the low dose groups from the available rat in vivo studies considered for PRVD2018-05.

For postapplication scenarios following application of agricultural commercial-class products, the dried residue dermal absorption studies were considered. The use of dried residues in dermal absorption studies was recently tested across ten different agrochemicals. For each of those agrochemicals, including folpet, it was observed that dermal absorption from dried residues was less than the equivalent dose of the aqueous spray solution, regardless of formulation type or active ingredient when tested in vitro under the same study conditions (26-88% lower). For folpet, dermal absorption was 82% lower from the dried residues than the equivalent liquid dose in this study.

Based on the highest dermal absorption value from the available folpet human in vitro dried residue studies, the dermal absorption value of 10% was selected for agricultural postapplication scenarios. Selection of this value was considered to be acceptable given the comparison of dermal absorption between liquid and dried residues at the same dose and the extent of data available for folpet, including an acceptable triple pack.

The dermal absorption values selected for folpet are considered to be protective, given the conservatism in how the supporting data were interpreted.

### **Occupational Mixer/Loader/Applicator Risk Assessment**

Occupational mixer/loader/applicator risk assessments were updated to incorporate the dermal absorption value specific for mixers/loaders. The dermal absorption value specific to applicators is the same as that used in PRVD2018-05. Refer to Tables 1-4 in this Appendix for the updated risk assessments. Risks were shown to be acceptable when the dermal, inhalation, and combined risk assessments for the scenario were shown to be acceptable.

In the revised assessment risks were shown to be acceptable for mixers/loaders and applicators, when mitigation measures were considered, for all crops on the WDG product label and most crops on the wettable powder (WP) product label. For the WP product, risks were not shown to be acceptable for apples, crab apples, and cranberries. These uses will be removed from the WP product label. These uses are currently listed on the WDG product and application of folpet on these crops will continue to be available to users.

### **Occupational Postapplication Risk Assessment**

The occupational postapplication risk assessments were updated to incorporate the dermal absorption value specific for postapplication workers. Crop-specific use information provided by growers during the PRVD consultation period and updates to the use of dislodgeable foliar residue (DFR) data were also incorporated. Details are discussed below. Refer to Table 4 in this Appendix for the updated risk assessments.

For grapes, the postapplication risk assessment was updated to include DFR data from the chemical-specific avocado DFR study. In the PRVD, default peak DFR and daily dissipation rate values were used to estimate foliar residues for grapes while the avocado DFR study was used for apples and crab apples. When determining whether a DFR study is appropriate for a given crop, a variety of factors are considered. As the application equipment, crop morphology, foliage type, and application regime in the avocado DFR study are representative of the use of folpet on grapes in Canada, it was considered appropriate to use this study to estimate grape DFR in the revised risk assessment.

For cranberries, use information specific to scouting was submitted to the PMRA. This information was considered along with cranberry use information submitted to the PMRA for other active ingredients, Canadian crop profiles and integrated pest management manuals, as well as the Agricultural Re-entry Task Force grower survey. Based on this information, although professional scouts may work a full day, they spend a short amount of time in contact with treated foliage as they refrain from walking through the cranberry field in order to avoid crop damage.

Therefore, a scouting scenario with a 4 hour daily exposure duration was included in the risk assessment for cranberries. Although this is a reduction from the standard 8 hour duration, it was considered to be sufficiently protective given other conservatisms in the risk assessment, such as:

- The cranberry scouting transfer coefficient is determined based on surrogate crops (corn, dry peas). Due to differences in crop morphology (crop height, foliage density), higher dermal exposure per hour is expected when contacting foliage when scouting these crops compared to cranberries.
- Maximum rate and minimum retreatment interval were assumed.
- The dermal absorption value, although refined for postapplication workers, is conservative (for example, it includes all residues in the stratum corneum as part of the absorbed dose).
- Folpet is not applied before bloom. The greatest contact with foliage during scouting is considered to be during sweep net scouting which typically occurs before bloom.

This risk assessment also considers other activities that farm workers may do in addition to scouting in one day in cranberry fields. REIs were calculated for these separate activities.

Given the conservatisms and considerations discussed above, risks were considered to be acceptable for scouting in cranberries at the calculated REIs of 4 and 10 days for the WDG and WP products, respectively, when the daily exposure duration of 4 hours is used in the risk assessment.

**Table 1 M/L/A Short- to Intermediate-Term Exposure and Risk Assessment for Groundboom Application**

Form	Crop	A	App Rate	ATPD <sup>a</sup>	MOE					Combined MOE <sup>b e</sup> Target = 300	
					Dermal <sup>b</sup> Target = 300	Inhal (ST) <sup>c</sup> Target = 300		Inhal (IT) <sup>d</sup> Target = 1000		No Resp	Resp <sup>f</sup>
						No Resp	Resp <sup>f</sup>	No Resp	Resp <sup>f</sup>		
Open M/L, Open Cab- both wearing single layer, CR gloves											
WDG	Strawberry	Farmer	2.0 kg ai/ha	8 ha	6650	N/A	35400	N/A	35400	N/A	6480
		Custom		26 ha	2050		10900		10900		2000
	Cucumber, Squash, Tomato	Farmer	4.0 kg ai/ha	4 ha	6650		35400	35400	6480		
		Pumpkin, Melon		Farmer	5 ha		5320	28300	28300	5190	
	Outdoor Veggies	Custom		26 ha	1020		5440	5440	997		
	Flowers	Both	1.0 kg ai/ha	26 ha	4090		21800	21800	3990		
	Cranberry	Both	2.6 kg ai/ha	26 ha	1570		8370	N/A	1530		
WP	Strawberry	Farmer	2.0 kg ai/ha	8 ha	4200	122	1220	122	1220	724	2840
		Custom		26 ha	1290	38	377	38	377	223	873
	Cucumber, Squash, Tomato	Farmer	4.0 kg ai/ha	4 ha	4200	122	1220	122	1220	724	2840
		Pumpkin, Melon		Farmer	5 ha	3360	98	980	98	980	579
	Outdoor	Custom		26 ha	646	19	188	19	188	111	436

Form	Crop	A	App Rate	ATPD <sup>a</sup>	MOE					Combined MOE <sup>b e</sup> Target = 300	
					Dermal <sup>b</sup> Target = 300	Inhal (ST) <sup>c</sup> Target = 300		Inhal (IT) <sup>d</sup> Target = 1000			
						No Resp	Resp <sup>f</sup>	No Resp	Resp <sup>f</sup>	No Resp	Resp <sup>f</sup>
	Veggies										
	Flowers	Both	1.0 kg ai/ha	26 ha	2580	75	754	75	754	445	1750
	Cranberry	Both	5 kg ai/ha	26 ha	517	15	151	N/A		89	349
	Max amount handled <sup>g</sup>	20 kg ai/ha			3360	N/A	980	N/A	980	N/A	2270
Open M/L, Closed Cab- both wearing single layer, CR gloves. Respirator for M/L only											
WP	Strawberry	Farmer	2.0 kg ai/ha	8 ha	6650	124	1230	124	1230	784	3790
		Custom		26 ha	2040	38	379	38	379	241	1160
	Cucumber, Squash, Tomato	Farmer	4.0 kg ai/ha	4 ha	6650	124	1230	124	1230	784	3790
		Pumpkin, Melon		Farmer	5 ha	5320	100	986	100	986	627
	Outdoor Veggies	Custom		26 ha	1020	19	190	19	190	121	583
	Flowers	Both		1.0 kg ai/ha	26 ha	4090	77	758	77	758	482
	Cranberry	Both	5 kg ai/ha	26 ha	818	15	152	N/A		96	466
	Max amount handled <sup>g</sup>	20 kg ai/ha			5320	N/A	986	N/A	986	N/A	3030

Shaded cells indicate where the MOE was not greater than or in range of the target MOE and risks were not shown to be acceptable. Risks must be acceptable for the dermal, inhalation (ST, IT), and combined risk assessments for the scenario to have acceptable risks.

Form = formulation; WP = wettable powder; WDG = water dispersible granule; A = applicator; ATPD = area treated per day; App Rate= application rate; Inhal = inhalation; M/L = mixer/loader; ST = short-term; IT = intermediate-term; No resp = without respirator; Resp = with respirator; CR = chemical-resistant; Single layer = long sleeved shirt, long pants; N/A = not applicable; outdoor veggies = cucumber, squash, pumpkin, melon, tomato; MOE = margin of exposure

<sup>a</sup> ATPD values are refined where possible. These are the same values as PRVD2018-05.

<sup>b</sup> NOAEL of 10 mg/kg bw/day from an oral rabbit development study and a target MOE of 300.

<sup>c</sup> Inhalation NOAEL of 1.4 mg/kg bw/day from a rat inhalation study and a short-term target MOE of 300.

<sup>d</sup> Inhalation NOAEL of 1.4 mg/kg bw/day from a rat inhalation study and an intermediate-term target MOE of 1000. Intermediate-term inhalation exposure was assessed for crops where more than three applications are possible.

<sup>e</sup> Combined MOE = NOAEL/ (dermal exposure + inhalation exposure), as both the dermal and inhalation exposure could contribute to the oral endpoint.

<sup>f</sup> Respirators were included in the assessment for WDG formulation as they are currently on the label. Respirators were not included with closed cabs, as the protection factor is already accounted for in the closed scenario and would be a double counting of protection. For scenarios where there was closed cab, 'resp' column indicates where a respirator was assumed only for open mixing/loading component.

<sup>g</sup> The maximum amount that could be handled where risks are shown to be acceptable.

**Table 2 M/L/A Short- to Intermediate-Term Exposure and Risk Assessment for Airblast Application**

Form	Crop	App Rate	ATPD <sup>a</sup>	MOE						Combined MOE <sup>b c</sup>	
				Dermal <sup>b</sup> Target = 300	Inhal (ST) <sup>c</sup> Target = 300		Inhal (IT) <sup>d</sup> Target = 1000		Target = 300		
					No Resp	Resp <sup>f</sup>	No Resp	Resp <sup>f</sup>	No Resp	Resp	
Open M/L wearing single layer, CR gloves; Open Cab wearing coveralls over single layer, CR hat (application only), CR gloves											
WDG	Apples, crabapples	3.0 kg ai/ha	20 ha	401	N/A	1850	N/A	1850	N/A	389	
		2.4 kg ai/ha (typical)		501		2310		2310		487	
	Grapes	1.0 kg ai/ha		1200		5540		5540		1170	
	Cranberries	2.6 kg ai/ha		463		2130		2130		449	
WP	Apples, crabapples	2.0 kg ai/ha	20 ha	750	43	429	43	429	218	602	
	Grapes	1.0 kg ai/ha		1500	86	858	86	858	435	1200	
	Cranberries	5.0 kg ai/ha		300	17	172	17	172	87	241	
Open M/L wearing single layer, CR gloves; Closed Cab wearing single layer, CR gloves, no respirator											
WP	Apples, crabapples	2.0 kg ai/ha	20 ha	1460	49	452	49	452	284	1010	
	Grapes	1.0 kg ai/ha		2930	99	903	99	903	568	2010	
	Cranberries	5.0 kg ai/ha		585	20	181	N/A		114	403	

Shaded cells indicate where the MOE was not greater than or in range of the target MOE and risks were not shown to be acceptable. Risks must be acceptable for the dermal, inhalation (ST, IT), and combined risk assessments for the scenario to have acceptable risks.

Form = formulation; WP = wettable powder; WDG = water dispersible granule; ATPD = area treated per day; App Rate = application rate; Inhal = inhalation; M/L = mixer/loader; ST = short-term; IT = intermediate-term; No resp = without respirator; Resp = with respirator; CR = chemical-resistant; Single layer = long sleeved shirt, long pants; N/A = not applicable; MOE = margin of exposure

<sup>a</sup> ATPD values are refined where possible. These are the same values as PRVD2018-05.

<sup>b</sup> NOAEL of 10 mg/kg bw/day from an oral rabbit development study and a target MOE of 300.

<sup>c</sup> Inhalation NOAEL of 1.4 mg/kg bw/day from a rat inhalation study and a short-term target MOE of 300.

<sup>d</sup> Inhalation NOAEL of 1.4 mg/kg bw/day from a rat inhalation study and an intermediate-term target MOE of 1000. Intermediate-term inhalation exposure was assessed for crops where more than three applications are possible.

<sup>e</sup> Combined MOE = NOAEL/ (dermal exposure + inhalation exposure), as both the dermal and inhalation exposure could contribute to the oral endpoint.

<sup>f</sup> Respirators were included in the assessment for WDG formulation as they are currently on the label. Respirators were not included with closed cabs, as the protection factor is already accounted for in the closed scenario and would be a double counting of protection. Respirators were also not included with closed mixing/loading (WSP). For scenarios where there was closed cab, 'resp' column indicates where a respirator was assumed only for open mixing/loading component.

**Table 3 M/L/A Short- to Intermediate-Term Exposure and Risk Assessment for Handheld Application**

Form	Crop	App Equip	App Rate (g ai/L)	ATPD <sup>a</sup>	MOE					Combined MOE <sup>be</sup>	
					Dermal <sup>b</sup> Target = 300	Inhal (ST) <sup>c</sup> Target = 300		Inhal (IT) <sup>d</sup> Target = 1000		Target = 300	
						No Res <sup>p</sup>	Resp <sup>f</sup>	No Res <sup>p</sup>	Resp <sup>f</sup>	No Res <sup>p</sup>	Resp <sup>f</sup>
Open M/L, wearing single layer, CR gloves, applicators wearing single layer, CR gloves											
WDG	Strawberry	Man PHW	1.0	150 L	28000	N/A	162,000	N/A	162,000	N/A	27,400
		Backpack			4890		118,000		118,000		4860
	Cranberry	Man PHW	1.3		21,600		124,000		N/A		21,000
		Backpack			3760		91,000				3740

Form	Crop	App Equip	App Rate (g ai/L)	ATPD <sup>a</sup>	MOE					Combined MOE <sup>be</sup>	
					Dermal <sup>b</sup> Target = 300	Inhal (ST) <sup>c</sup> Target = 300		Inhal (IT) <sup>d</sup> Target = 1000		Target = 300	
						No Res p	Resp <sup>f</sup>	No Res p	Resp <sup>f</sup>	No Res p	Resp <sup>f</sup>
	Poinsettia	Man PHW	1.125		24900		144,000		N/A		24,300
		Backpack			4350		105,000				4320
	Other Flowers	Man PHW	1.0		28000		162,000		162,000		27,400
		Backpack			4890		118,000		118,000		4860
WP	Strawberry	Man PHW	1.0	150 L	27,500	7360	N/A	7360	N/A	18,100	N/A
		Backpack			4870	6310		6310		4400	
	Cranberry	Man PHW	2.5		11,000	2950		N/A		7220	
		Backpack			1950	2520				1760	
	Poinsettia	Man PHW	1.125		24,400	6550		N/A		16,000	
		Backpack			4330	5610				3910	
	Other Flowers	Man PHW	1.0		27,500	7360		7360		18,100	
		Backpack			4870	6310		6310		4400	
	Open M/L wearing single layer, CR gloves, applicators wearing coveralls over single layer, CR gloves										
WDG	Strawberry	Mech PHG	1.0	3800 L	427	N/A	1940	N/A	1940	N/A	415
	Cranberry		1.3		329		1490		N/A		319
	Poinsettia		1.125		380		1720		N/A		369
	Other Flowers		1.0		427		1940		1940		415
WP	Strawberry	Mech PHG	1.0	3800 L	424	142	1420	142	1420	299	407
	Cranberry		2.5		170	57	569	N/A		120	163
	Poinsettia		1.125		377	126	1260	N/A		266	362
	Other Flowers		1.0		424	142	1420	142	1420	299	407
	Max amount handled <sup>g</sup>		5.3 kg ai/day <sup>g</sup>	304	N/A	1020	N/A	1020	N/A	292	
Open M/L wearing single layer, CR gloves, applicators wearing CR coveralls over single layer, CR gloves											
WP	Cranberry	Mech PHG	2.5	3800 L	227	57	569	N/A		146	215

Shaded cells indicate where the MOE was not greater than or in range of the target MOE and risks were not shown to be acceptable. Risks must be acceptable for the dermal, inhalation (ST, IT), and combined risk assessments for the scenario to have acceptable risks.

Form = formulation; WP = wettable powder; WDG = water dispersible granule; App Equip = application equipment; ATPD = area treated per day; App Rate = application rate; Inhal = inhalation; M/L = mixer/loader; ST = short-term; IT = intermediate-term; No resp = without respirator; Resp = with respirator; Man PHW = manually-pressurized handwand; Mech PHG = mechanically pressurized handgun; CR = chemical-resistant; PPE = personal protective equipment; Single layer = long sleeved shirt, long pants; N/A = not applicable; MOE = margin of exposure

<sup>a</sup> Default ATPD values were used. These are the same values as PRVD2018-05.

<sup>b</sup> NOAEL of 10 mg/kg bw/day from an oral rabbit development study and a target MOE of 300.

<sup>c</sup> Inhalation NOAEL of 1.4 mg/kg bw/day from a rat inhalation study and a short-term target MOE of 300.

<sup>d</sup> Inhalation NOAEL of 1.4 mg/kg bw/day from a rat inhalation study and an intermediate-term target MOE of 1000. Intermediate-term inhalation exposure was assessed for crops where more than three applications are possible.

<sup>e</sup> Combined MOE = NOAEL/ (dermal exposure + inhalation exposure), as both the dermal and inhalation exposure could contribute to the oral endpoint.

<sup>f</sup> Respirators were assumed for WDG formulations as they are already on the label.

<sup>g</sup> The maximum amount that could be handled where risks are shown to be acceptable.

**Table 4 Occupational Postapplication Risk Assessment for Agricultural Crops**

Crop	Rates <sup>a</sup> (kg ai/ha)	# of Apps <sup>b</sup>	RTI (days)	Activity	TC <sup>c</sup> (cm <sup>2</sup> /hr)	Day 0 DFR <sup>d</sup>	Day 0 MOE <sup>e</sup> (Target = 300)	REI <sup>f</sup> (days)
<b>Greenhouse Ornamentals</b>								
Poinsettia	1.13	2	10	Non-cut flower: all activities	230	5.04	<b>862</b>	12 hours
Carnations	1.0	6	14	Cut flower: hand harvesting, hand pruning, disbudding	4000	7.72	<b>32</b>	96
				Non-cut flower: all activities Cut flower: container moving, pinching, hand pruning (low height), hand weeding, plant support/staking, scouting, transplanting	230		<b>563</b>	12 hours
Marigolds, zinnias, snapdragons	1.0	6	3	Cut flower: hand harvesting, hand pruning, disbudding	4000	12.7	<b>20</b>	118
				Non-cut flower: all activities Cut flower: container moving, pinching, hand pruning (low height), hand weeding, plant support/staking, scouting, transplanting	230		<b>343</b>	12 hours
Roses, asters, china asters, phloxes, chrysanthemums	1.0	6	7	Cut flower: hand harvesting, hand pruning, disbudding	4000	10.4	<b>24</b>	109
				Non-cut flower: all activities Cut flower: container moving, pinching, hand pruning (low height), hand weeding, plant support/staking, scouting, transplanting	230		<b>419</b>	12 hours
Irises	1.0	4	7	Cut flower: hand harvesting, hand pruning, disbudding	4000	7.96	<b>31</b>	98
				Non-cut flower: all activities Cut flower: container moving, pinching, hand	230		<b>546</b>	12 hours



Crop	Rates <sup>a</sup> (kg ai/ha)	# of Apps <sup>b</sup>	RTI (days)	Activity	TC <sup>c</sup> (cm <sup>2</sup> /hr)	Day 0 DFR <sup>d</sup>	Day 0 MOE <sup>e</sup> (Target = 300)	REI <sup>f</sup> (days)	
				pruning (low height), hand weeding, plant support/staking, scouting, transplanting					
All cut flowers	1.0	1	N/A	Cut flower: hand harvesting, hand pruning, disbudding	4000	2.5	100	48	
				Cut flower: container moving, pinching, hand pruning (low height), hand weeding, plant support/staking, scouting, transplanting	230		1739	12 hours	
				Irrigation (non-handset), mechanical weeding	No TC <sup>g</sup>	12 hours			
Fruit Trees									
Apples	3.0 (WDG)	6	10	Thinning fruit by hand	3000	1.83	182	6	
				Hand harvesting	1400		390	12 hours	
				Hand pruning, scouting, training	580		940		
				Transplanting	230		2370		
				Hand weeding, propping, orchard maintenance	100		5460		
				Mechanical weeding, mechanical harvesting, irrigation (non-hand set), frost control, spreading bins	No TC <sup>g</sup>	12 hours			
Apples	2.0 (WP)	6	10	Thinning fruit by hand	3000	1.22	273	3	
				Hand harvesting	1400		584	12 hours	
				Hand pruning, scouting, training	580		1410		
				Transplanting	230		3560		
				Hand weeding, propping, orchard maintenance	100		8180		
				Mechanical weeding, mechanical harvesting, irrigation (non-hand set), frost control, spreading bins	No TC <sup>g</sup>	12 hours			
Fruit and Ornamental Trees									
Crabapples	3.0 (WDG)	4	10	Thinning fruit by hand	3000	1.57	213	3	
				Hand harvesting	1400		456	12 hours	
				Hand pruning, scouting, training	580		1100		
				Transplanting	230		2780		
				Hand weeding, propping, orchard maintenance	100		6390		
				Handset/handline irrigation	1750	Only applicable for ornamental crabapple use. However, this does not occur in crabapples			
				Mechanical weeding, mechanical harvesting,	No TC <sup>g</sup>	12 hours			



Crop	Rates <sup>a</sup> (kg ai/ha)	# of Apps <sup>b</sup>	RTI (days)	Activity	TC <sup>c</sup> (cm <sup>2</sup> /hr)	Day 0 DFR <sup>d</sup>	Day 0 MOE <sup>e</sup> (Target = 300)	REI <sup>f</sup> (days)
				irrigation (non-hand set), frost control, spreading bins				
Crabapples	2.0 (WP)	4	10	Thinning fruit by hand	3000	1.04	319	12 hours
				Hand harvesting	1400		684	
				Hand pruning, scouting, training	580		1650	
				Transplanting	230		4170	
				Hand weeding, propping, orchard maintenance	100		9580	
				Mechanical weeding, mechanical harvesting, irrigation (non-hand set), frost control, spreading bins	No TC <sup>g</sup>	12 hours		
Grapes								
Grapes- dead arm	1.0	2	10	Postapplication exposure is expected to be low as foliage is minimal (before BBCH 13) <sup>h</sup> and residues on foliage will likely dilute as the leaves grow				12 hours
Grapes- black rot, downy mildew	1.0	4	10	Table/raisin grapes only: girdling, turning	19300	0.52	99	35
				Hand harvesting, tying/training, leaf pulling by hand	8500		225	3
				Scouting, hand weeding, hand pruning, propagating, bird control, trellis repair	640		2990	12 hours
				Transplanting	230		8330	
				Handset/handline irrigation	1750	Handline irrigation does not occur in grapes (PMRA, 2016d)		
				Mechanical harvesting, mechanical weeding, mechanical leaf pulling, burn down, ditching, mechanical pruning, irrigation (non-hand-set)	No TC <sup>g</sup>	12 hours		
Berries								
Strawberry	2.0	6	7	Hand harvesting	1100	9.47	96	11
				Transplanting	230	Activity occurs before pesticide application		
				Scouting	210	9.47	503	12 hours
				Hand weeding, canopy management	70		1510	
				Mechanical weeding, irrigation (non-hand-set)	No TC <sup>g</sup>	12 hours		
		1	N/A	Hand harvesting	1100	5.00	182	5
				Scouting	210		952	12 hours
				Hand weeding, canopy management	70		2860	
Cranberry	5.0 (WP)	2	10	Hand harvesting (raking)	1100	16.9	54	16
				Scouting- 8 hour duration			108	10
				Scouting- 4 hour duration				

Crop	Rates <sup>a</sup> (kg ai/ha)	# of Apps <sup>b</sup>	RTI (days)	Activity	TC <sup>c</sup> (cm <sup>2</sup> /hr)	Day 0 DFR <sup>d</sup>	Day 0 MOE <sup>e</sup> (Target = 300)	REI <sup>f</sup> (days)
	2.6 (WDG)			Transplanting	230	Activity occurs before pesticide application		
				Hand pruning (shears), hand weeding	70	16.9	847	12 hours
				Mechanical harvesting (flooding), mechanical weeding, ditching, frost control, sanding, irrigation (non-hand-set)	No TC <sup>g</sup>	12 hours		
				Hand harvesting (raking)	1100	8.77	104	10
				Scouting- 8 hour duration			207	4
				Scouting- 4 hour duration				
				Hand pruning (shears), hand weeding	70		1630	12 hours
				Mechanical harvesting (flooding), mechanical weeding, ditching, frost control, sanding, irrigation (non-hand-set)	No TC <sup>g</sup>	12 hours		
				Field Vegetable Crops				
Cucumbers, pumpkin, melons, squash	4.0	6	7	Hand harvesting, mechanically-assisted harvesting, training, turning (pumpkin, melon only)	550	18.9	96	11
				Transplanting	230	Activity occurs before pesticide application		
				Scouting, hand weeding, thinning fruit, hand pruning (melons only)	90	18.9	587	12 hours
				Handset/handline irrigation	1750		30	22
				Mechanical weeding, irrigation (non-hand set), fertilizing	No TC <sup>g</sup>	12 hours		
Tomatoes (for processing)	4.0	6	7	Hand harvest <sup>i</sup>	1100	18.9	48	17
				Handset/handline irrigation	1750		30	22
				Transplanting	230	Activity occurs before pesticide application		
				Scouting	210	18.9	251	2
				Hand weeding	70		754	12 hours
				Irrigation (non-hand-set), mechanical weeding, mechanical harvesting	No TC <sup>g</sup>	12 hours		
Tomatoes (not for processing)	4.0	6	7	Hand harvest, tying/training	1100	18.9	48	17
				Handset/handline irrigation	1750		30	22
				Transplanting	230	Activity occurs before pesticide application		
				Scouting	210	18.9	251	2
				Hand weeding, hand pruning	70		754	12 hours
				Irrigation (non-hand-set)	No TC <sup>g</sup>	12 hours		
		3	7	Hand harvest, tying/training	1100	17.1	53	16

Crop	Rates <sup>a</sup> (kg ai/ha)	# of Apps <sup>b</sup>	RTI (days)	Activity	TC <sup>c</sup> (cm <sup>2</sup> /hr)	Day 0 DFR <sup>d</sup>	Day 0 MOE <sup>e</sup> (Target = 300)	REI <sup>f</sup> (days)
				Handset/handline irrigation	1750		33	21
				Scouting	210		279	1
				Hand weeding, hand pruning	70		966	12 hours
Outdoor Ornamentals								
Carnation	1.0	6	14	Cut flower: hand harvesting, hand pruning, disbudding	4000	3.24	77	13
				Handset/handline irrigation	1750		176	6
				Non-cut flower: all activities Cut flower: container moving, pinching, hand pruning (low height), hand weeding, plant support/staking, scouting, transplanting	230		1340	12 hours
				Non-hand-set irrigation	No TC <sup>g</sup>		12 hours	
Carnation		2	14	Cut flower: hand harvesting, hand pruning, disbudding	4000	3.07	81	12
				Handset/handline irrigation	1750		186	5
				Non-cut flower: all activities Cut flower: container moving, pinching, hand pruning (low height), hand weeding, plant support/staking, scouting, transplanting	230		1415	12 hours
				Non-hand-set irrigation	No TC <sup>g</sup>		12 hours	
Marigold, Zinnias, Snapdragons		6	3	Cut flower: hand harvesting, hand pruning, disbudding	4000	7.84	32	21
				Handset/handline irrigation	1750		73	13
				Non-cut flower: all activities Cut flower: container moving, pinching, hand pruning (low height), hand weeding, plant support/staking, scouting, transplanting	230		555	12 hours
				Non-hand-set irrigation	No TC <sup>g</sup>		12 hours	
Marigold, Zinnias, Snapdragons	2	3	Cut flower: hand harvesting, hand pruning, disbudding	4000	4.32	58	16	
			Handset/handline irrigation	1750		132	8	
			Non-cut flower: all activities Cut flower: container moving, pinching, hand pruning (low height), hand	230		1006	12 hours	

<b>Crop</b>	<b>Rates<sup>a</sup></b> (kg ai/ha)	<b># of Apps<sup>b</sup></b>	<b>RTI</b> (days)	<b>Activity</b>	<b>TC<sup>c</sup></b> (cm <sup>2</sup> /hr)	<b>Day 0 DFR<sup>d</sup></b>	<b>Day 0 MOE<sup>e</sup></b> (Target = 300)	<b>REI<sup>f</sup></b> (days)
Roses, asters, china asters, phloxes, chrysanthemums		6	7	weeding, plant support/staking, scouting, transplanting				
				Non-hand-set irrigation	No TC <sup>g</sup>	12 hours		
				Cut flower: hand harvesting, hand pruning, disbudding	4000	4.73	<b>53</b>	17
				Handset/handline irrigation	1750		<b>121</b>	9
				Non-cut flower: all activities Cut flower: container moving, pinching, hand pruning (low height), hand weeding, plant support/staking, scouting, transplanting	230		<b>918</b>	12 hours
				Non-hand-set irrigation	No TC <sup>g</sup>	12 hours		
Roses, asters, china asters, phloxes, chrysanthemums		2	7	Cut flower: hand harvesting, hand pruning, disbudding	4000	3.70	<b>68</b>	14
				Handset/handline irrigation	1750		<b>155</b>	6
				Non-cut flower: all activities Cut flower: container moving, pinching, hand pruning (low height), hand weeding, plant support/staking, scouting, transplanting	230		<b>1176</b>	12 hours
				Non-hand-set irrigation	No TC <sup>g</sup>	12 hours		
Irises		4	7	Cut flower: hand harvesting, hand pruning, disbudding	4000	4.54	<b>55</b>	16
				Handset/handline irrigation	1750		<b>126</b>	8
				Non-cut flower: all activities Cut flower: container moving, pinching, hand pruning (low height), hand weeding, plant support/staking, scouting, transplanting	230		<b>957</b>	12 hours
				Non-hand-set irrigation	No TC <sup>g</sup>	12 hours		
Irises	1.0	2	7	Cut flower: hand harvesting, hand pruning, disbudding	4000	3.70	<b>68</b>	14
				Handset/handline irrigation	1750		<b>155</b>	6
				Non-cut flower: all activities Cut flower: container moving, pinching, hand pruning (low height), hand weeding, plant	230		<b>1176</b>	12 hours

Crop	Rates <sup>a</sup> (kg ai/ha)	# of Apps <sup>b</sup>	RTI (days)	Activity	TC <sup>c</sup> (cm <sup>2</sup> /hr)	Day 0 DFR <sup>d</sup>	Day 0 MOE <sup>e</sup> (Target = 300)	REI <sup>f</sup> (days)
				support/staking, scouting, transplanting				
				Non-hand-set irrigation	No TC <sup>g</sup>		12 hours	

Shaded cells indicate those calculated MOEs that are not greater than or within range of the target MOE of 300 on the day of the last application and risks are not shown to be acceptable.

Apps = applications; RTI = Re-treatment Interval; DFR = Dislodgeable Foliar Residue; REI = Restricted Entry Interval; MOE = margin of exposure; WDG = water dispersible granule; WP = wettable powder

<sup>a</sup> Maximum listed label rates expressed in kilograms a.i./hectare for both wettable powder and water dispersible granule, unless otherwise specified.

<sup>b</sup> Maximum number of applications per season. When calculated REIs were not agronomically feasible at the maximum number of applications per season, postapplication exposure was calculated with a reduced number of applications per season.

<sup>c</sup> Transfer coefficients (TC) are from the PMRA Agricultural TC memo using Agricultural Re-entry Task Force Data.

<sup>d</sup> Day 0 DFR = Dislodgeable Foliar Residues on Day 0 after application. Dislodgeable foliar residue values for field crops were calculated using the peak DFR of 25% of the application rate and 10% dissipation per day. For greenhouse ornamental crops, the default peak of 25% of the application rate and dissipation rate of 2.3% per day was used. For fruit trees and grapes, actual DFR data from the avocado DFR study was used; therefore, the REI days were limited by the days that were sampled in the DFR study.

<sup>e</sup> Dermal MOE on Day 0 = NOAEL / (DFR<sub>Day 0</sub> x Transfer Coefficient x 8 hr x 10% dermal absorption / 80 kg). MOE on day 0 after application; based on the NOAEL of 10 mg/kg bw/day from the oral rabbit developmental toxicity study, target MOE of 300 for all durations.

<sup>f</sup> Day at which the dermal exposure results in an MOE greater than or within range of the target MOE (300) and risks are shown to be acceptable. For fruit trees and grapes, the potential REI day was limited by the available sampling days in the avocado DFR study.

<sup>g</sup> Not considered to be a hand labour activity. Postapplication worker risks are acceptable provided the minimum 12 hour REI is followed.

<sup>h</sup> BBCH = phenological development stage of a plant. BBCH 13 is when the third leaf unfolds and foliage is minimal.

<sup>i</sup> Hand harvesting was included the postapplication risk assessment, but is not routinely conducted in processing tomatoes as the plants are mechanically harvested.

## Appendix VI      References Considered Following Publication of PRVD2018-05

Note that the following includes only references that were not previously considered in PRVD2018-05.

### A. Information Considered in the Toxicological Risk Assessment

#### A.1 List of Studies/Information Submitted by Registrant

PMRA	Reference
2936948	2018, Folpet: Response to Proposed Re-evaluation Decision by Health Canada, DACO: 4.8
1347668	1985. Folpan: Teratology Study in the Rabbit. DACO: 4.5.3

#### A.2 Additional Published Information Considered

PMRA	Reference
3008067	2012, US Environmental Protection Agency. Folpet: Human Health Risk Scoping Document in Support of Registration Review, November 28, 2012. DACO 12.5.4.

### B. Information Considered in the Updated Occupational and Residential Exposure Assessment

#### B.1 List of Studies/Information Submitted by Registrant

PMRA	Reference
2936951	2016, In vitro percutaneous absorption of Folpet, from transferred dried surface residue, through human skin, DACO: 5.8
2936949	2006, 14C-FOLPET COMPARISON OF THE IN VITRO DERMAL ABSORPTION USING HUMAN AND RAT SKIN WITH THE IN VIVO DERMAL ABSORPTION IN THE MALE RAT, DACO: 5.8
2936950	2009, Folpet: Folpet 80 WG - In Vitro Absorption through Human and Rat Epidermis Using [14C- Radiolabelled]-Folpet, DACO: 5.8
2572743	2014, Agricultural Handler Exposure Scenario Monograph: Open Cab Airblast Application of Liquid Sprays, DACO: 5.3,5.4
2259317, 2259318	Dennis R. Klonne et. al., 1999, Determination of Dermal and Inhalation Exposure to Reentry Workers During Scouting in Dry Peas, DACO: 5.6
2259311	Dennis R. Klonne, et. al., 1999, Determination of Dermal and Inhalation Exposure to Reentry Workers During Scouting in Sweet Corn, DACO: 5.6
2259299, 2366020	Randy Thompson, 1998, Agricultural Worker Crop Contact from Reentry Activities Performed in the United States and Canada: Grower Results, DACO: 5.12

## B.2 Additional Published Information Considered

Reference
Aggarwal, M., Fisher, P., Kluxen, F.M., Maas, W., Morgan, N., Parr-Dobrzanski, R., Strupp, C., Wiemann, C. 2019. Assessing in vitro dermal absorption of dry residues of agrochemical sprays using human skin within OECD TG 428. <i>Reg. Toxicol. Pharmacol.</i> 106:55–67.
Agricultural and Agri-food Canada, 2015. Crop Profile for Cranberry in Canada, 2013. Second Edition. Published 2015. Accessed April 30, 2019: <a href="http://publications.gc.ca/site/eng/9.629965/publication.html">http://publications.gc.ca/site/eng/9.629965/publication.html</a>
Agricultural and Agri-food Canada, 2000. Integrated Pest Management for Cranberries in Western Canada. A guide to identification, monitoring, and decision-making for pests and diseases. December 2000.
Brouwer, D.H., de Vreede, S.A.F., Meuling, W.J.A., van Hemmen, J.J. 2000. Determination of the efficiency for pesticide exposure reduction with protective clothing: a field study using biological monitoring. Chapter 5 In: <i>Assessment of Occupational Exposure to Pesticides in Dutch Bulb Culture and Glasshouse Horticulture</i> . Doctoral Thesis of D.H. Brouwer. pp.158-179.
Désert, M., Ravier, S., Gille, G., Quinapallo, A., Armengaud, A., Pochet, G., Savelli, J.L., Wortham, H., Quivet, E. 2018. Spatial and temporal distribution of current-use pesticides in ambient air of Provence-Alpes-Côte-d’Azur Region and Corsica, France. <i>Atmospheric Environment</i> . 192:241-256
European Commission. 2018a. Draft Renewal Assessment Report. Folpet. Volume 3- B.5 (PPP)- Folpan 80 WDG. 2018/03. Published.
European Commission. 2018b. Draft Renewal Assessment Report. Folpet. Volume 3- B.5 (PPP)- Folpet 80 WG. 2018/03. Published.
Garrigou, A., Baldi I., Le Frious P., Anselm R., Vallier M. 2011. Ergonomic contribution to chemical risks prevention: an ergotoxicological investigation of the effectiveness of coverall against plant pest risk in viticulture. 42: 321-330.
Graves, C.J., Edwards, C., Marks R. 1995. The effects of protective occlusive gloves on stratum corneum barrier properties. <i>Contact Derm</i> 33: 183-187.
Keifer, M.C., 2000. Effectiveness of Interventions in Reducing Pesticide Overexposure and Poisonings. <i>American Journal of Preventive Medicine</i> . 18 (4S); 80-89.
Le Duc, I., Turcotte, C., Allard, F. 2004. Integrated Pest Management. Eastern Canada Cranberry IPM Manual. Accessed April 30, 2019: <a href="http://publications.gc.ca/collections/Collection/H114-10-2004E.pdf">http://publications.gc.ca/collections/Collection/H114-10-2004E.pdf</a>
Mahn, D., Dittl, T., Kummer, L. Undated. SCOUTING AND CONTROLLING CRANBERRY INSECTS. University of Wisconsin. Accessed April 30, 2019: <a href="https://fruit.wisc.edu/wp-content/uploads/sites/36/2011/05/Scouting-and-Controlling-Cranberry-Insects.pdf">https://fruit.wisc.edu/wp-content/uploads/sites/36/2011/05/Scouting-and-Controlling-Cranberry-Insects.pdf</a>
Raherison, C., Baldi, I., Pouquet, M., Berteaud, E., Moesch, C., Bouvier, G., Canal-Raffin, M. 2019. Pesticides Exposure by Air in Vineyard Rural Area and Respiratory Health in Children: A pilot study. <i>Environ Res.</i> Feb;169:189-195.

Sandler, H.A. 2008. Integrated Cranberry Pest Management. In Sandler, H.A. and Demoranville, C.J. Editors. 2008. Cranberry Production: A Guide for Massachusetts. UMass Publication CP-08. Accessed April 30, 2019:  
<http://www.umass.edu/cranberry/downloads/CP-08.pdf>

Rawson, B.V., Cocker, J., Evans, P.G. Wheeler, J.P. and Akrill, P.M. 2005. Internal contamination of Gloves: routes and Consequences. Am. Occup. Hyg. 49 (6): 535-541.