Re-evaluation Decision RVD2016-02

Carbaryl

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Re-evaluation Decision for Carbaryl

After a thorough re-evaluation of the insecticide carbaryl, Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is granting continued registration of certain products containing carbaryl for sale and use in Canada.

An evaluation of available scientific information found that, under the revised conditions of use:

- Certain uses of carbaryl products have value in Canada and do not pose unacceptable risks to human health or the environment. These uses include commercial products applied in agricultural, non-crop and forestry settings, other than those noted below. As a requirement for continued registration of these carbaryl uses, new risk reduction measures are required. No additional data are requested at this time.

- Certain uses of carbaryl must be removed from the current carbaryl labels because they are not supported by the technical registrant. These uses are as follows and were not included in the risk assessment:

    - Indoor pest control uses including greenhouses, residences, food and feed handling establishments and barns and livestock production areas
    - Aerosol products
    - Agricultural dust uses
    - Bran bait application to residential garden
    - Livestock for food
    - Livestock for non-food
    - Companion animals
    - Granular bait products for ornamental gardens
    - Applications by hand, spoon and bellygrinder

- Certain products or uses pose risks of concern to human health and do not meet Health Canada's current standards for human health protection. As a result, the following products or uses will be cancelled:

    - All domestic class products
    - Commercial application of carbaryl in residential settings including ornamentals, vegetable gardens and fruit trees in residential areas
    - All turf applications in commercial and residential areas, including lawns, sod farms and golf courses
    - Various crops (alfalfa, apples (insecticide use), apricot, barley, broccoli, Brussels sprouts, cabbage, cauliflower, cherries, clover, corn (sweet & field), grapes, kale, oats, peach, pears, peppers, plums, prunes, rye, snapbeans (hand harvest only), strawberries, sweet white lupin, wheat); and
    - Balsam fir, spruce, farm woodlots, municipal parks and rights-of-way for control of spruce budworm.

The PMRA's pesticide re-evaluation program considers potential risks as well as the value of pesticide products to ensure they meet modern standards established to protect human health and the environment. Regulatory Directive DIR2001-03, *PMRA Re-evaluation Program*, presents the details of the re-evaluation activities and program structure. Re-evaluation draws on data from registrants, published scientific reports, information from other regulatory agencies, and any other relevant information available.

The regulatory approach for the re-evaluation of carbaryl was first presented in Proposed Re-evaluation Decision PRVD2009-14, *Carbaryl*[1]. This Re-evaluation Decision[2] describes this stage of PMRA's regulatory process for the re-evaluation of carbaryl and summarizes the Agency's decision and the reasons for it.

Comments received during the consultation process were taken into consideration. These comments and new data/information resulted in revisions to some parts of the risk assessments, however, did not result in substantial changes to the proposed regulatory decision as described in PRVD2009-14. Appendix I of this document summarizes comments received and provides the PMRA's response.

To comply with this decision, the following implementation timelines must be followed. Registrants of end-use products containing carbaryl will be informed of the specific requirements affecting their product registration(s) and of the regulatory options available to them.

1) Label changes: The required mitigation measures (Appendix V) must be implemented on all commercial product labels sold by registrants as soon as possible but no later than 24 months after the publication date of this document.

2) Domestic products: The last sale of all domestic products by Registrants and Retailers is 12 months and 24 months following the publication date of this document, respectively. The registration of these products will expire 36 months following the publication date of this document (Appendix VI).

3) Water soluble packaging requirements: An application to register a new product in water soluble packaging is required within 24 months following the publication date of this document (Appendix VI).

What Does Health Canada Consider When Making a Re-evaluation Decision?

The key objective of the *Pest Control Products Act* is to prevent risks of concern to people and the environment from the use of pest control products. Health or environmental risk is considered of no concern if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its conditions or proposed conditions of registration.[3] The Act also requires that products have

1 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act.*
2 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act.*
3 "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act.*

value[4] when used according to the label directions. Requirements of continued registration may include special precautionary measures on the product label to further reduce risk.

To reach its decisions, the PMRA applies hazard and risk assessment methods as well as policies that are rigorous and modern. These methods consider the unique characteristics of sensitive populations subgroups in both humans (for example, children) and organisms in the environment (for example, those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties present when predicting the impact of pesticides. For more information, please refer to the following sections of the Pesticides and Pest Management portion of the Health Canada website at healthcanada.gc.ca/pmra:

- Protecting Your Health and the Environment
- Pesticide Registration Process
- Pesticide Risk Reduction Program

What is Carbaryl?

Carbaryl is a broad spectrum Resistance Management Group 1A (carbamate) insecticide. In Canada, it is registered to control a wide range of arthropod pests including beetles, moths, fleas, flies, lice, mites, sawflies, crickets, earwigs, grasshoppers, millipedes, sow bugs, thrips, ticks and cockroaches. It is also registered for use in apple thinning.

Carbaryl is used on both agricultural and non-agricultural sites including feed crops, industrial oil seed and fibre crops, livestock, greenhouse tobacco seedlings, companion animals, structures, forestry, food crops, turf, lawns and ornamentals. It is applied by both ground and aerial equipment.

Health Considerations

Can Approved Uses of Carbaryl Affect Human Health?

Carbaryl is unlikely to affect human health when used according to the revised label directions, which include additional risk-reduction measures.

Potential exposure to carbaryl may occur through the diet (food and water), by applying the product or by entering treated sites. When assessing health risks, two key factors are considered: the dose at which no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers).

[4] "Value" as defined by subsection 2(1) of the *Pest Control Products Act*: "the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (a) efficacy; (b) effect on host organisms in connection with which it is intended to be used; and (c) health, safety and environmental benefits and social and economic impact".

Toxicology studies on laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose at which no effects are observed. The health effects noted in animals occur at doses more than 100-times higher (and often much higher) than levels to which humans are normally exposed when carbaryl products are used according to label directions.

The acute toxicity of carbaryl ranged from moderate to high via the oral route of exposure. It was of low acute toxicity via the dermal and inhalation routes of exposure. Carbaryl was mildly irritating to eyes, but non-irritating to skin and not a skin sensitizer.

Registrant-supplied short, and long term (lifetime) animal toxicity tests, as well as information from the published scientific literature were assessed for the potential of carbaryl to cause neurotoxicity, immunotoxicity, chronic toxicity, cancer, reproductive and developmental toxicity, and various other effects. The most sensitive endpoints for risk assessment included effects on the nervous system. In addition, there was evidence that young animals were more sensitive than adult animals to carbaryl toxicity as demonstrated by the effects on the nervous system at lower levels than adults. Longer-term dosing with carbaryl resulted in tumors of the blood in mice.

Only those uses where exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Risks in Residential and Other Non-Occupational Environments

Residential uses of carbaryl on turf, ornamentals, fruit trees and vegetable gardens are of concern. These uses will be cancelled.

Carbaryl is registered for use on turf, and on residential ornamental and vegetable gardens. Estimates of exposure using turf transferable residue data and dislodgeable foliar data, as well as carbaryl specific biomonitoring data did not achieve the target margin of exposure (MOE) and/or aggregate risk index for adults and children for all postapplication exposure scenarios and some application scenarios, and are therefore of concern. Risks of concern remained even after consideration of all feasible mitigation measures.

As a result, all residential uses of carbaryl must be cancelled. This includes cancellation of all domestic-class products and commercial applications in residential areas. Applications on turf, golf courses, ornamentals, vegetable gardens and fruit trees in residential areas will not be permitted. Residential areas are defined as sites where bystanders including children could be exposed during or after application. This includes homes, schools, public buildings or any other areas where the general public including children could be exposed.

As described in PRVD2009-14, carbaryl is currently registered in use scenarios that could potentially include Pick-Your-Own (PYO) operations. When the updated use refinements, product discontinuations and risk mitigation measures are taken into account, aggregate exposure for PYO patrons is not of concern.

Cancer risks are not of concern to any residential population for the remaining uses of carbaryl.

Occupational Risks from Handling Carbaryl

Mixer/Loader/Applicator

The majority of risks for mixers, loaders and applicators are not of concern provided additional mitigation measures are followed.

Occupational risk assessments from handling carbaryl consider exposure to workers who mix, load, and apply the pesticide. Most uses for agricultural scenarios have margins of exposure that are not of concern, provided that engineering controls or personal protective equipment are used. These measures are needed to minimize potential exposure and protect workers' health.

All non-cancer risk estimates for lawn care operators applying carbaryl to residential turf, as well as for golf course and sod farm workers applying carbaryl, did not reach the target margin of exposure and/or aggregate risk index for broadcast treatments, even with maximum personal protective equipment and engineering controls, and are therefore of concern. These uses must be cancelled.

Risks of concern were identified in PRVD2009-14 for agricultural workers using hand held equipment. However, with the updated use refinements, product discontinuations and risk mitigation measures taken into account, occupational risk from the use of hand held equipment is no longer of concern.

The mixer/loader/applicator risk assessment for carbaryl was revised for tobacco and canola, based on new data and updated use information provided by registrants and stakeholders during the comment period for PRVD2009-14. Mitigation options proposed by registrants and stakeholders were also carefully considered. These data and the revised risk assessment are presented in Appendix III. With the risk mitigation, the exposure during mixing, loading and applying for tobacco and canola reach target MOEs and are not of concern.

For other uses, while the additional information resulted in a more accurate risk assessment and more refined mitigation measures for certain uses, the overall risk conclusions did not change significantly from those presented in PRVD2009-14. As occupational mixer/loader/applicator risks of concern for certain uses could not be addressed, the following uses must be cancelled:

> alfalfa, barley, broccoli, Brussels sprouts, cabbage, cauliflower, cherries, clover, oats, pears, peppers, plums, rye, strawberries and wheat.

Cancer risks are not of concern to mixers, loaders or applicators for the remaining uses of carbaryl.

Postapplication Workers

Most occupational postapplication risks are not of concern based on revised label directions. Risks for certain uses could not be mitigated and must be cancelled.

Post–application risk assessments consider exposure to workers entering treated areas. The postapplication risk assessment for carbaryl was revised based on new data and updated use information provided by registrants and stakeholders during the comment period for PRVD2009-14. Mitigation options proposed by registrants and stakeholders were also carefully considered. These data and the revised risk assessment are presented in AppendixIV.

Target MOEs for certain uses of carbaryl are achieved when revised conditions of use and risk reductions measures, such as increased restricted-entry intervals (REIs), are considered. The revised conditions of use are presented in Appendix V. The uses acceptable for continued registration are:

> Asparagus and asparagus ferns, beans, beet (root/top), blueberries, bran bait applications (non-residential), cane berries, canola, carrots, celery, choke cherries, cranberries, cucumbers, ditch banks, eggplants, forests and woodlots, green ash, high value trees, horseradish, kohlrabi, leafy vegetables, melons, ornamental trees, parsnips, peas, potatoes, pumpkins, rutabaga (root), salsify (root/top), snapbeans (mechanical harvest), squash, trap trees, tobacco, tomatoes and turnip (root/top).

For other uses, while the additional information resulted in an exposure assessment that may more accurately reflect typical use conditions, the overall risk conclusions did not change significantly from those presented in PRVD2009-14. As postapplication risks of concern could not be addressed through agronomically feasible REIs, the following uses must be cancelled:

> alfalfa, apples (for insect control), apricot, barley, broccoli, Brussels sprouts, cabbage, cauliflower, cherries, clover, corn (sweet & field), grapes, kale, oats, peach, pears, plums, prunes, rye, snapbeans (hand harvest only), strawberries, sweet white lupin, wheat, balsam fir, spruce, farm woodlots, municipal parks and rights-of-way for control of spruce budworm.

Cancer risks are not of concern to postapplication workers for the remaining uses of carbaryl.

The use of carbaryl for apple thinning is unlikely to be of concern for postapplication workers when used in accordance with the revised label directions.

The risk assessment for the apple thinning use was revised and refined based on updated use information, revised application rates, and other information provided by registrants and stakeholders. Information on modern apple orchard production indicated that the majority of apple orchards have transitioned to high density plantings (or are in the process of transitioning). Postapplication exposure to workers is expected to be lower with high density trellis plantings than with standard trees. Revised conditions of use for apple thinning have been developed as follows to reflect use in high density apple orchards as well as for standard orchard plantings:

For orchards that have transitioned to high density trellis production architecture (for example, spindle or super spindle trees):

- Maximum seasonal rate of 1.5 kg a.i./ha and an REI of 14 days for hand thinning

For orchards that have not transitioned to high density trellis production architecture (for example, dwarf, semi-dwarf and full sized trees):

- Maximum seasonal rate of 1 kg a.i./ha and an REI of 17 days for hand thinning

Additional label amendments described in Appendix V must also be implemented as required.

Residues in Food and Water

Dietary risks from food and water are not of concern when risk reduction measures are implemented.

Reference doses define levels to which an individual can be exposed over a single day (acute) or lifetime (chronic) and expect no adverse health effects. Generally, dietary exposure from food and water is not of concern if it is less than 100% of the acute reference dose or chronic reference dose (acceptable daily intake). An acceptable daily intake is an estimate of the level of daily exposure to a pesticide residue that, over a lifetime, is believed to have no significant harmful effects.

Human exposure to carbaryl was estimated from residues in treated crops and drinking water, including the most highly exposed sub-populations (for example, infants and children one to six years old). Data from the Canadian Food Inspection Agency, the United States Department of Agriculture Pesticide Data Program (USDA PDP), field trials, processing factors and percent crop treated (%CT) were used to estimate residue levels. As well, information on drinking water was used to estimate both the acute and chronic (non-cancer and cancer) aggregate exposures and risks.

Short term (acute), long term (chronic) and lifetime cancer exposure estimates were determined for different sub-populations representing different ages, genders and reproductive status. The maximum degree of refinement possible, based on all available information, was used in both the non-cancer and cancer dietary assessments.

As noted in PRVD2009-14, aggregate dietary exposure to carbaryl (that is, from food and drinking water) represented 2% of the chronic reference dose, while the lifetime cancer risk estimate was 7×10^{-8} for the general population. As a result, chronic and cancer risks were not of concern. However, the acute aggregate dietary exposure estimate for carbaryl was 117% and 393% of the acute reference dose for the general population and all infants, respectively, when using drinking water inputs based on modelling data. This represented a potential risk of concern for acute dietary exposure.

The acute aggregate dietary assessment in PRVD2009-14 was updated to reflect the revised use pattern. Previously the drinking water assessment included carbaryl applications to turf. However, since the use of carbaryl on residential turf, golf courses and sod farms is to be cancelled due to residential and occupational risk concerns, the drinking water modelling is now based on carbaryl applications to field crops. As a result, the revised acute aggregate dietary exposure for carbaryl is 41% of the acute reference dose for the general population, and ranges from 31 to 107% for the various population subgroups. The highest exposure at 107% occurs for all infants and is not of concern due to conservative (high-end) assumptions in the exposure assessment, attributable primarily to the use of water modelling data to estimate drinking water exposures.

The *Food and Drug Act* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). While pesticide MRLs are specified through the evaluation of scientific data under the *Pest Control Products Act*, the MRLs for carbaryl were established under the *Food and Drugs Act.* Each MRL value defines the maximum concentration in parts per million (ppm) of a pesticide allowed in/on certain foods. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

MRLs for carbaryl are currently specified for a wide range of commodities (MRL database http://pr-rp.hc-sc.gc.ca/mrl-lrm/index-eng.php). Where no specific MRL has been established, a default MRL of 0.1 ppm applies, which means that pesticide residues in a food commodity must not exceed 0.1 ppm.

The MRLs for barley, oats and rye will be revoked following the cancellation of the associated uses in Canada. As there are no American tolerances or Codex MRLs for these uses, this action will not impact trade.

Environmental Considerations

What Happens When Carbaryl is Introduced into the Environment?

When used according to the revised label directions, carbaryl is not expected to pose risk of concern to the environment.

When carbaryl is released into the environment some of it can be found in soil and surface water. Carbaryl is quickly broken down by soil microbes and by chemical reaction in water and is not expected to persist in the environment. Although laboratory studies indicate that carbaryl is mobile in soil, field studies suggest carbaryl is broken down quickly and is unlikely to reach groundwater.

Under controlled laboratory conditions, carbaryl can be toxic to some non-target species, such as bees, beneficial insects, birds, wild mammals, aquatic invertebrates and fish. If carbaryl is used at labelled application rates without any risk reduction measures, it has the potential to cause adverse effects in the organisms listed above. Therefore, mitigation measures are required in order to reduce potential exposure of non-target organisms and reduce environmental risks.

When carbaryl is used in accordance with the revised label and the required risk reduction measures are applied, the resulting environmental risk posed by carbaryl is considered to be acceptable.

Value Considerations

What is the Value of Carbaryl?

Carbaryl contributes to insect pest management in agriculture, forestry and ornamental production in Canada.

In Canada, carbaryl is used extensively and is integral to the management of insect pests in many crops, forestry and ornamental production. It is the only registered active ingredient in Canada for the control of certain insect pests.

Carbaryl contributes to sustainable pest management by playing an important role in prevention of the development of insecticide resistance when used in rotation with insecticides of different modes of action.

Carbaryl is also used to thin apples. The thinning of developing fruit is a critical step in the economical production of apples as it results in larger apples of higher quality. Of the registered chemicals for apple thinning, carbaryl is considered the most versatile and effective thinning agent for growers to use. Carbaryl is used alone or in combination with one of the following:

- naphthalene acetic acid (NAA) marketed as Fruitone-N; or
- benzyladenine (BA) marketed as Accel, MaxCel and Cilis.

Incident Reports

As of 30 July 2015, the Incident Reporting Program has received 49 human, 79 domestic animal and 13 environment incidents for carbaryl. Most incidents were minor in severity. All but a few of the human and domestic animal incidents involved the use of domestic class products. The discontinuation of such uses should reduce the occurrence of future incidents involving carbaryl. There was one major environment incident in which fish were killed when water that was used to extinguish a chemical warehouse fire was released into a nearby stream. The remaining environment incidents were minor in severity and involved plant damage or honeybee mortality. Honeybee mortality was reported in five of the incidents; however, other chemical active ingredients in addition to carbaryl were also reported.

Organisation for Economic Co-operation and Development Status of Carbaryl

Canada is part of the Organisation for Economic Co-operation and Development (OECD), which provides a forum in which governments of member countries can work together to share experiences and seek solutions to common problems.

As part of the re-evaluation of an active ingredient, the PMRA takes into consideration of recent developments and new information on the status of the active ingredient in other jurisdictions, including OECD member countries.

Carbaryl is currently registered in some OECD countries, including the United States, Australia and New Zealand.

The European Commission prohibited the use of carbaryl as a plant protection product in 2007 for health and environmental reasons. Therefore, pursuant to subsection 17(2) of the *Pest Control Products Act*, the PMRA has initiated a special review of pest control products containing carbaryl based on the 2007 European Commission decision (REV2013-06). The PMRA will publish its proposed special review decision once completed.

Measures to Minimize Risk

Registered pesticide product labels include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law. Appendix II lists all current products containing carbaryl. Further risk-reduction measures are required to address potential risks of concern identified in this assessment (Appendices V and VI). The following key risk-reduction measures are required.

Key Risk-Reduction Measures

Human Health

After consideration of all possible mitigation measures, the following uses must be cancelled due to residential and/or occupational risk concerns:

- All domestic class products
- Commercial application of carbaryl in residential settings including ornamentals, vegetable gardens and fruit trees in residential areas
- All turf applications in commercial and residential areas, including sod farms and golf courses
- Various crops (alfalfa, apples (for insect control), apricot, barley, broccoli, Brussels sprouts, cabbage, cauliflower, cherries, clover, corn (sweet & field), grapes, kale, oats, peach, pears, peppers, plums, prunes, rye, snapbeans (hand harvest only), strawberries, sweet white lupin, wheat, Balsam fir, spruce, farm woodlots, municipal parks and rights-of-way for control of spruce budworm.

For all other uses, to protect mixer/loader/applicators using commercial products, additional mitigation measures such as personal protective equipment and engineering controls are required. All carbaryl products currently registered as wettable powders must be packaged in water soluble packaging.

For all other uses, to protect workers entering treated sites, revised restricted-entry intervals as well as revised application frequencies and intervals are to be added to product labels.

For the apple thinning use, revised conditions of use include minimizing the application rate, updated REIs, and label recommendations to reduce exposure, such as the use of chemical-resistant gloves during hand-thinning.

Precautionary statements to avoid drift to areas of human habitation or areas of human activity are to be added to product labels.

The Toxicological Information section on labels is to be updated to include additional information about symptoms and treatment for over-exposure.

Environment

- Precautionary statements include statements to reduce runoff and revised spray buffer zones for non-target aquatic habitats.
- Changes to application timing, including restriction of application during bloom for some crops, are required as a result of the pollinator risk assessment.

What Additional Scientific Information is Being Requested?

No data are required under section 12 of the *Pest Control Products Act*.

Other Information

Any person may file a notice of objection[5] regarding this decision on carbaryl within 60 days from the date of publication of this Re-evaluation Decision. For more information regarding the basis for objecting (which must be based on scientific grounds), please refer to the Pesticides and Pest Management portion of Health Canada's website (Request a Reconsideration of Decision, or contact the PMRA's Pest Management Information Service.

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

List of Abbreviations

ARfD	acute reference dose
ARI	aggregate risk index
ARTF	Agricultural Re-entry Task Force
ASAE	American Society of Agricultural Engineers
BChE	brain acetylcholinesterase
BMD	benchmark dose
BMD_{10}	benchmark does associated with a 10% response
$BMDL_{10}$	lower confidence limit on the benchmark dose associated with a 10% response
bw	body weight
ChE	acetylcholinesterase
cm	centimetre(s)
cm^2	centimetres squared
cont'd	continued
%CT	percent crop treated
d	day(s)
DA	dermal absorption
DACO	data code
DFR	dislodgeable foliar residue
EC_{50}	exposure concentration to 50% (a concentration causing 50% adverse effects in the test population
EChE	erythrocyte acetylcholinesterase
EEC	expected environmental concentration
EPA	Environmental Protection Agency
et al	and others
GD	gestation day
ha	hectare
kg	kilogram
km	kilometre(s)
L	litre(s)
LC_{50}	lethal concentration to 50% (a concentration causing 50% mortality in the test population
LOAEL	lowest observed adverse effect level
M/L	mixer/loader
M/L/A	mixer/loader/applicator
mg	milligram(s)
mm	millimetre(s)
MOE	margin of exposure
MRL	maximum residue limit
NAFTA	North American Free Trade Agreement
NOAEL	no observed adverse effect level
OECD	Organisation for Economic Co-operation and Development
PCA	percent cropped area
pH	-log10 hydrogen ion concentration
PMRA	Pest Management Regulatory Agency
PND	post-natal day

PPE	personal protective equipment
ppm	part per million
PRVD	proposed re-evaluation decision
PYO	pick your own facilities
Q^*_1	lifetime cancer risk estimate
r.a.n.	repeat as necessary
REI	restricted entry interval
REV	Re-evaluation Note
SA	surface area
SU	Suspension
TC	transfer coefficient
TRR	total radioactive residues
TTR	turf transferable residues
USEPA	United States Environmental Protection Agency
UV	ultraviolet/visible spectrum
WBC	white blood cells
WP	wettable powder formulation
WSP	water soluble packaging

Appendix I Comments and Responses

1.0 Comments Related to the Health Risk Assessments

1.1 Toxicology

Comment:
For the dermal endpoint selected for occupational and residential risk assessment, the registrant supported the use of benchmark dose (BMD) modelling to establish the point of departure. However, the BMD values were considered too conservative based on the results from oral and dermal dosing in a pharmacokinetic (PK) study. In the PK study rats were administered a single dose of radiolabelled carbaryl and the total radioactive residues (TRR) in erythrocytes and brain were assessed. The registrant proposed that systemic levels of carbaryl associated with the oral dose of 1.08 mg/kg bw used in the PK study would not produce any significant cholinesterase inhibition, as this dose was below the $BMDL_{10}$ (lower confidence limit on the benchmark dose associated with a 10% response) values of 1.13 and 2.02 mg/kg bw for pups and adults, respectively, in an acute oral comparative cholinesterase study. Since the peak total TRR levels in brain or erythrocytes following dermal exposure of 103 mg/kg bw radiolabelled carbaryl were below the levels following an oral dose of 1.08 mg/kg bw radiolabelled carbaryl, the registrant suggested that a dermal exposure of 103 mg/kg bw carbaryl for 10 hours (the exposure duration in the PK study) would not produce significant cholinesterase inhibition.

The PMRA applied a 3-fold uncertainty factor to the dermal endpoint for the protection of infants and children. The registrant proposed reducing this to 1.8, reflecting that the BMD_{10} (benchmark dose associated with a 10% response) for brain cholinesterase inhibition in PND (post-natal day) 11 pups was 1.8 fold lower than PND 97 adults in the comparative cholinesterase study. This would reduce the target margin of exposure for the dermal risk assessment of all durations from 300 to 180. The registrant considered that the single bolus dose administered in the comparative cholinesterase study likely overestimated any cholinesterase inhibition that might occur following indirect prenatal exposure. Carbaryl was also rapidly metabolized with no parent compound detected in plasma at any time point after oral dosing in the PK study, thus the registrant contended that indirect prenatal exposure was likely negligible. Consequently, an uncertainty factor of 1.8 was considered adequate by the registrant for protection of infants and children.

PMRA Response:
The peak total TRR by the oral route did exceed that by the dermal route in the PK study, and the oral PK dose of 1.08 mg/kg bw was lower than the oral $BMDL_{10}$s of 1.13 and 2.02 mg/kg bw for pups and adults, respectively. However, the PK study assessed TRR in erythrocytes and brain tissue, not the endpoint of concern (cholinesterase activity). The registrant's comment presumed that TRR in erythrocytes and brain tissue were related to the extent of cholinesterase inhibition, but their relationship had not been established. It is unclear how TRR in erythrocytes or brain tissue following dermal exposure related to cholinesterase activity in these compartments. This uncertainty in the relationship between TRR and cholinesterase inhibition, as well as other limitations, were discussed by the United Sates Environmental Protection Agency Federal Insecticide, Fungicide, and Rodenticide Act Science Advisory Panel in 2004.

A recent paper (PMRA #1968927) investigated the relationship between carbaryl levels in brain and plasma and cholinesterase inhibition. Carbaryl levels in individual brain and plasma samples from 3 previous acute gavage studies in male rats were compared to their brain and erythrocyte cholinesterase activities at about 40 minutes post-dosing. A first order exponential decay function with an asymptote described the relationship between carbaryl levels in the brain and brain cholinesterase activity, and carbaryl levels in plasma and erythrocyte cholinesterase activity. The study authors noted that this relationship was likely valid for time periods closely approximating that used in the studies; the relevance of this information to the slower peak associated with dermal exposure is unclear. In support of the time-sensitivity of this relationship, carbaryl was not detected in the plasma of some or all rats by 2 hours post-dosing in an acute gavage time-course study (0.5 to 24 hours post-dosing; carbaryl in the brain was not assessed). A noteworthy finding from this paper was that there were no differences in the amount of carbaryl in plasma or brain between the age groups (post-natal days 11, 21 and 97). In other words, carbaryl levels in the brain or plasma are not equivalent to cholinesterase inhibition, given that PND 11 pups were more sensitive than adults to ChE inhibition. The higher sensitivity of the young to carbaryl cannot be explained by higher levels of brain carbaryl.

The registrant suggested that the 103 mg/kg bw used in the acute dermal component of the PK study must be a NOAEL (no observed adverse effect level) for short-term dermal exposure. This was based on lower TRR in brain and erythrocytes from this dermal dose, relative to those measured from an oral dose comparable to that of the $BMDL_{10}$s for BChE (brain acetylcholinesterase) and EChE (erythrocyte acetylcholinesterase) inhibition[6] from an acute oral dose of carbaryl. This assumed that total TRR are equivalent to the amount of carbaryl, and that the total TRRs in Figures 1 and 2 of registrant's comments from the other radiolabelled metabolites (1-naphthol and *N*-hydroxymethyl carbaryl) in the PK study did not contribute significantly to the extent of cholinesterase inhibition. Given that age-related differences in PK were not observed in the recent literature study, reliance on the PK information to refine the dermal toxicity endpoint is not supported.

In addition, while the oral component of the PK study was considered acceptable, there was uncertainty regarding the data from the dermal route due to concerns with study methodology. The dermal dose was applied in an acetone/water solution on a waterproof band-aid, exposed to air to evaporate the acetone prior to exposure to skin. There was uncertainty whether residual acetone/water remained on the band-aid, which may have affected the absorption. A greater uncertainty was the amount available for absorption, since residual carbaryl left on the removed bandaid and on the skin was not measured after study termination. In addition, the band-aid upon which the dose was applied was 1 inch by 2 inches (equivalent to 12.9 cm^2, or approximately 3% of the total body surface area[7]). The dermal exposure may have been underestimated due to the small surface area (while this is not a repeated dose dermal toxicity study, OECD guideline 410 recommends 10% of the body surface area be covered.) As such, the toxicity of carbaryl by the dermal route could be underestimated.

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6 The PMRA determines the $BMDL_{20}$ (not a $BMDL_{10}$) for EChE inhibition.

7 From the study, the male Sprague-Dawley rat was on average 277 g or 242 g, for the low or high dose dermal exposures, respectively. For a 200-299 g rat, the total body surface is about 394 cm^2. (PMRA document number 2309078)

The 4-week dermal toxicity study in rats demonstrated that a dermal dose of 103 mg/kg bw exceeded a NOAEL (PMRA document number 1526156). There was BChE inhibition in both sexes (15% in males, 24% in females with statistical significance), as well as transient EChE inhibition in males on days 5 - 19 (15 to 21% inhibition with statistical significance), and decreased body weight gain in males (12%) at the highest dose of 100 mg/kg bw/day. There was also decreased BChE activity (15% with statistical significance) in males at the LOAEL of 50 mg/kg bw/day, with a resultant NOAEL of 20 mg/kg bw/day. Thus this study provided empirical evidence that the NOAEL for short-term dermal exposure should not be 103 mg/kg bw/day. The $BMDL_{10}$ of 35.5 mg/kg bw/day was selected as a point of departure, rather than the NOAEL of 20 mg/kg bw/day. The higher sensitivity to carbaryl by the oral route than the dermal route was reflected in the higher dermal $BMDL_{10}$ of 35.5 mg/kg bw/day, relative to the oral $BMDL_{10}$ of 1-2 mg/kg bw.

The registrant suggested refinement of the 3-fold uncertainty factor for the protection of infants and children in the target Margin of Exposure for dermal risk assessment. Based on the acute oral comparative cholinesterase study, the BMD_{10} ratio of brain cholinesterase inhibition for adults (2.55 mg/kg bw) versus PND11 pups (1.48 mg/kg bw) was 1.72, clearly identifying that the directly exposed young were more sensitive to carbaryl. Refinement of the uncertainty factor was not undertaken, because there was limited confidence in the robustness of this BMD_{10} ratio as being representative of the sensitivity of all young populations. There was uncertainty that BMD modelling was sufficiently robust to refine a risk assessment for this purpose, because even with the same data, BMD values can differ based on the model selected and the parameters selected within a model. There was also uncertainty as to how this ratio might change if brain cholinesterase activity was sampled at other times after dosing. In the comparative cholinesterase study in rats, cholinesterase activity was assessed at 40 minutes after dosing, based on stated time-to-peak effects in PND 17 and adult rats, with no time-to-peak information presented for PND 11 pups. It was also unknown how the BMD_{10} ratio would be altered if other age groups were tested. Furthermore, the BMD_{10} ratio was from an oral study and it was unknown whether this ratio would be reflective of differences in sensitivity by the dermal route. Thus there was insufficient confidence that reducing the margin of exposure (MOE) based on the BMD_{10} ratio was protective of potential sensitivity in a young population.

The PMRA agreed that administration via a bolus dose may overestimate the exposure level expected in a fetus or neonate, but the extent of overestimation is unclear. The PMRA also agreed that the metabolism of carbaryl after an oral dose was rapid in the PK study, with relatively slower metabolism by the dermal route. Carbaryl in the brain was not tested by the dermal route in the PK study, but it would be expected to also reach the brain at a different rate than the oral route. However, rapid metabolism by the oral route may not necessarily equate to negligible exposure to the fetus or neonate. While the parent compound was not detected in plasma in the PK study by either the single oral or dermal exposure, carbaryl was observed in plasma and brain tissue in acute toxicity studies in male rats with higher single oral doses of carbaryl. Thus fetal brains could be indirectly exposed to carbaryl above negligible levels by the dermal or oral route. The pharmacokinetics of carbaryl in the fetal brain and consequent pharmacodynamic effects of cholinesterase inhibition in fetuses remained unclear. Therefore it

was considered appropriate to use a 3-fold uncertainty factor to protect infants and children in the dermal risk assessment.

1.1.1 Refinement of the 3-fold Uncertainty Factor to 1.8-fold

Comment:
The registrant suggested refinement of the 3-fold uncertainty factor for database deficiency, applied to the dermal toxicity endpoint to address potential sensitivity of the young via the dermal route. The registrant considered that a 1.8-fold uncertainty factor would be more appropriate to address post-natal sensitivity to carbaryl, based on the relative BMD_{10} for brain cholinesterase inhibition in adults relative to postnatal (PND) 11 pups in an acute oral comparative cholinesterase study.

PMRA Response:
Refinement of the 3-fold uncertainty factor was not undertaken, because there was limited confidence in this BMD_{10} ratio as being representative of the sensitivity of all young populations. There was uncertainty that BMD modelling was sufficiently robust to refine a risk assessment for this purpose, because even with the same data, BMD values can differ based on the model selected and the parameters selected within a model. There was also uncertainty as to how this ratio might change if brain cholinesterase activity was sampled at other times after dosing. In the comparative cholinesterase study in rats, cholinesterase activity was assessed at 40 minutes after dosing, based on stated time-to-peak effects in PND 17 and adult rats, with no time-to-peak information presented for PND 11 pups. It was also unknown how the BMD_{10} ratio would be altered if other age groups were tested. Furthermore as the dermal toxicity study was conducted solely in adults, but the BMD_{10} ratio was from an oral study, it was unknown whether this ratio would be reflective of sensitivity by the dermal route. Given these uncertainties, it was considered appropriate to use a 3-fold uncertainty factor to protect for potential sensitivity of fetuses and nursing infants in the dermal risk assessment.

1.1.2 Intraspecies Differences in Neurodevelopment

Comment:
The registrant proposed refinement of the 3-fold uncertainty factor applied to the dermal post-occupational risk assessment, based on the differences in neurodevelopment between the neonatal rat up to PND 21and the human infant.

PMRA Response:
The human and rat neurodevelopmental timelines provided by the registrant, based on comparative brain morphology, suggested that early brain development took longer to develop in rats, relative to humans. However, the sensitivity of PND 11 rats relative to adults demonstrated in a comparative cholinesterase assay was still considered relevant to humans and should be taken into account in the risk assessment. If not considered a manifestation of post-natal sensitivity due to differences in neurodevelopment, the effect would be considered as evidence of potential pre-natal (for example, perinatal) sensitivity, rather than no sensitivity at all.

1.1.3 No Fetal Sensitivity to Brain Cholinesterase Effects in Sufficient and Available Studies

Comment:
The registrant considered that there was sufficient information available to address outstanding concerns regarding exposure to the fetus and no additional data was required to address these concerns.

PMRA Response:
It was agreed that overall the carbaryl reproduction, developmental and developmental neurotoxicity studies did not indicate fetal sensitivity. There was a limited developmental study in the mouse wherein offspring had increased resorptions and variations in the absence of maternal toxicity, as well as malformations at maternally toxic levels, but these effects were not replicated in another dietary and gavage mouse prenatal developmental toxicity study. However, with the exception of one rabbit developmental toxicity study (which showed that maternal cholinesterase inhibition occurred at lower levels than the fetal effects observed), and one limited rat developmental neurotoxicity study (the NIEHS/NTP study discussed below), none of the reproduction, developmental or developmental neurotoxicity studies included cholinesterase measurements. No sensitivity of the prenatal young was observed in the NIEHS/NTP developmental neurotoxicity study, but it was hampered by lack of detail (including unknown levels of cholinesterase inhibition, unknown number of pups examined). As such, the potential for prenatal and lactational sensitivity of the young was not adequately addressed in the database.

The registrant submitted 4 published and 1 unpublished references that pertained to prenatal exposure to carbaryl. The unpublished NIEHS/NTP study was not available in its completed study form, but the synopsis of this study in USEPA HIARC reports for carbaryl (PMRA document numbers 1572726 and 2308493) indicated that brain cholinesterase (BChE) inhibition was similar in dams and fetuses on gestation day (GD) 19, after repeated oral exposure to dams from gestation days 14 to 18. This was previously taken under consideration in the PMRA re-evaluation of carbaryl, for although it suggested that prenatal sensitivity was not of concern, there were insufficient animals (one dam and two fetuses per time point) and lack of study details (including extent of change, study methodology of how and when animals were tested for BChE inhibition) to decisively exclude the concern for prenatal sensitivity of the young. Three published studies also demonstrated that oral exposure to dams on GD18, or after repeated daily oral exposure from GD11 to GD23, did not increase BChE inhibition in fetal rats, in comparison to pregnant dams (PMRA document numbers 2308483, 2308491 and 2308485). Together, these studies indicated that prenatal exposure was possible through placental transfer. They suggested that sensitivity was not of concern, but the data quality of these studies was such that there was limited confidence in their conclusions. The particular concerns are the lack of detail (including unknown number of dams and/or fetuses examined, time after dosing and pup delivery that BChE activity was assessed in dams, or time after dosing that fetal brains were extracted for BChE activity).

An autoradiographic study in pregnant Sprague-Dawley rats and Swiss mice also demonstrated that placental transfer was possible in rodents (PMRA document number 2308487). The radioactivity from an oral dose of 10 mg/kg bw radiolabelled carbaryl was distributed to the brain (and other organs) much faster in fetal rats (detected by 0.5 hours post-dosing) than in mice (not detected at 0.5 or 1 hour post-dosing, but detected at 5 hours post-dosing). This study did not elucidate whether fetuses were more or less sensitive, as dams were not similarly autoradiographed.

If further information is submitted for these studies to enhance their robustness, or if a new study to address prenatal exposure is submitted, it may be possible to reconsider the sensitivity of the prenatal young. However, the sensitivity of the post-natal young via lactational transfer was still unclear. There were no studies available examining the effect of carbaryl on BChE or erythrocyte (EChE) inhibition in nursing pups. Without further data, postnatal sensitivity via lactational transfer cannot be excluded. With the given database, the current 3-fold uncertainty factor for database deficiency applied to the dermal risk assessment was considered to be appropriate.

The registrant also submitted references to 4 published studies pertaining to post-natal sensitivity of directly-dosed young. These studies investigated EChE and BChE inhibition after acute or repeated oral doses of carbaryl in young and/or adult rats, and/or the mechanism in post-natal sensitivity. Two of these references pertained to the acute comparative cholinesterase study which provided evidence of post-natal sensitivity of the young to ChE inhibition (PMRA document numbers 1533160 and 2308498); this study data was used in the carbaryl re-evaluation.

Another study determined the carbaryl levels in the brain and plasma of the rats in the acute comparative cholinesterase study, as well as three other acute and repeated dose cholinesterase studies, and related them to the extent of ChE inhibition in these tissues (PMRA #2308494). The post-natal sensitivity of the young to BChE and EChE inhibition in these studies were not due to differences in carbaryl levels in the brain, as levels were comparable irrespective of age. The mechanism behind post-natal sensitivity to carbaryl was further investigated in an *in vitro* pharmacokinetic study that determined pharmacokinetic parameters (AChE IC50, Km, Vmax) of brain cholinesterase in mixtures of carbaryl and whole brain homogenates of rats ranging in age from PND 4 to 90 (PMRA document number 2309077). The post-natal sensitivity of the young was not attributed to intrinsic developmental differences in BChE sensitivity, based on similar Km, and relatively lower Vmax and higher IC50 in the young. While informative, the data from these studies do not elucidate the mechanism behind the post-natal sensitivity of the young to ChE inhibition, nor do they affect the reference doses selected for the risk assessment of carbaryl.

1.2 Comments Related to Residential and Occupational Exposure

Comments recommended that the occupational and residential mixer/loader/applicator and postapplication risk assessments be revised based on: updated use information, updated crop groupings, revised application rates, revised postapplication activities, updated transfer

coefficients, revised application intervals and frequencies, and revised dermal absorption estimates.

The PMRA has revised the occupational mixer/loader/applicator risk assessment in accordance with comments received to the greatest extent possible. The mixer/loader/applicator risk assessments for canola, tobacco and orchard crops were revised based on updated application rates and use information; the results of the revised risk assessment are presented in Appendix II. The mixer/loader/applicator risk assessments for all other uses are as described in PRVD2009-14, as there were no further updates to the information used in these risk assessments.

Due to the risks of concern for certain uses, personal protective equipment and engineering controls are required to mitigate risk. The personal protection equipment required for each crop use is intended to protect against the greatest potential exposure.

The postapplication risk assessments for a number of crops were revised based on: updated use information, updated crop groupings, revised application rates, revised postapplication activities, updated transfer coefficients, and revised application intervals and frequencies. The results of the revised risk assessments are presented in AppendixIV. The postapplication risk assessments for all other uses are as described in PRVD2009-14. The postapplication risk assessment for turf was revised based on updated use information. The results of the revised risk assessment are presented in AppendixIV.

Specific comments are addressed below.

1.2.1 Comments relating to the Human Health Risk Assessment for Agricultural Uses

Comment:
Stakeholders requested that updated transfer coefficients (TCs) based on the Agricultural Re-entry Task Force (ARTF) data be used in the risk assessments, rather than the TCs in USEPA Policy 3.1.

PMRA Response:
The PMRA has analyzed the detailed comments for transfer coefficients (TCs) that could be amended and incorporated these refinements into an updated risk assessment. Where applicable, the PMRA has reviewed the ARTF database and proposed clustering schemes, determined the most appropriate TC, and conducted new postapplication risk assessments. The refinement of the TCs resulted in reduced restricted-entry intervals (REIs) for some crops, but increased REIs for other crops. Refer to Appendix IVfor the results of the revised risk assessment.

Comment:
Multiple stakeholders have proposed use pattern refinements based on revisions to label language, such as dividing crop groupings, limiting particular times of application, or clarification of spray rates.

PMRA Response:
The PMRA has examined the specific comments to identify any refinements that are deemed both agronomically feasible and suitable for label amendments. In the interest of providing clear and consistent end-use product labels, it was not possible to divide crop groupings or specify application timings for certain uses. However, efforts were made to ensure that all the applicable recommended refinements were taken into account. Spray rate clarifications provided by stakeholders during the PRVD2009-14 consultation were confirmed and applied as necessary.

Changes made to the use pattern (such as revised spray rates or the separation of crop groupings) are presented in detail in Appendix IIIand AppendixIV, where the revised risk assessments for mixer/loader/applicators and postapplication workers are provided.

Comment:
Stakeholders have proposed several clarifications or new restrictions regarding the number of applications permitted per year or crop cycle.

PMRA Response:
Bayer CropScience indicated that the maximum number of applications for all registered commercial commodities was three per year (with the exception of chokecherry shelterbelts at once per year), with a 7-10 day interval unless otherwise stated (Bayer, 2007b). However, due to the limited number of dislodgeable foliar residue (DFR) studies available, it was necessary to assess some crops according to the number of applications and application intervals described in the DFR studies. Appendix V lists the number of applications and application intervals per crop.

Comment:
Registrants requested refinement of the dermal toxicity endpoint based on consideration of oral and dermal pharmacokinetic data, as well as a refinement of the dermal absorption value based upon the carbaryl *in vitro* human and rat dermal absorption study. Specifically, the registrants proposed that based on a comparison of the rat and human dermal absorption in the *in vitro* dermal absorption study (Dick, 2001), rat skin is approximately 2.8 times more permeable than human skin at low concentrations. The dermal absorption between the rat *in vivo* study (Cheng, 1995) and the rat *in vitro* (Dick, 2001) was also compared. The registrants concluded that the overall consistency between the *in vivo* and *in vitro* dermal penetration studies for carbaryl supports adjustment of the BMD values from the 28-day dermal study by a factor of 2.8, to account for the difference in permeability between rat and human skin. This was considered by the registrants to be supported by the North American Free Trade Agreement (NAFTA) dermal absorption policy on the use of *in vitro* dermal penetration data in risk assessment, noting that a critical point in the NAFTA policy for the use of *in vitro* data is the demonstrated consistency between *in vitro* and *in vivo* data.

PMRA Response:
Since the occupational and residential risk assessment was based on a dermal toxicity study in rats, a dermal absorption value for carbaryl was not required. In the comment above, the registrant is proposing adjusting the dermal toxicological point of departure, or bench mark dose, based on differences between rats and humans.

Adjustment of the bench mark dose (BMD) values by a factor of 2.8 to account for the differences in permeability between rat and human skin is not supported by the PMRA. An adjustment of the BMD could also be considered an adjustment for the interspecies uncertainty factor, specifically the toxicokinetic factor. For such an adjustment to be made, a large amount of data conducted under similar conditions is required to refine the toxicokinetic factor, which accounts for the absorption, transport, metabolism and transformation, sequestration and excretion of the chemical. The PMRA does not agree that the results from one *in vitro* study alone, which was not conducted under similar conditions as the dermal toxicology study, would be sufficient to refine the default uncertainty factor for toxicokinetics.

The NAFTA Dermal Absorption Group position paper on the *Use of In Vitro Dermal Absorption Data in Risk Assessment* outlines that when the *in vitro* animal technique is shown to be a good predictor of animal *in vivo* data (in other words, a ratio close to 1), the human *in vitro* data are likely to be a good predictor of human dermal absorption when conducted under the same conditions. This is also referred to as the 'triple pack approach.' This paper also discusses a number of 'minimal standards' which should be considered when applying the triple pack approach. These include: same dose/duration regimen, guideline studies (i.e., no major limitations), reproducibility of *in vitro* results, and consideration of regional variability in human skin.

Consideration of the triple pack approach to adjust dermal toxicological points of departure was not the mandate of the NAFTA Dermal Absorption Working Group. The intent of the position paper and the triple pack approach was to provide guidance on determining dermal absorption for exposure assessments when the toxicology reference dose is based on an oral study.

The PMRA did, however, review the dermal absorption data available for carbaryl, as this was required for the cancer risk assessment, as well as any assessments based on toxicological points of departure from non-dermal studies.

The dermal absorption values cited by the registrant in their comments do not include skin bound residues. Since the studies were terminated at 24 hours, characterization of the fate of the skin bound residues is not possible and, thus, skin bound residues were included in the PMRA estimate of dermal absorption, as per the USEPA Health Effects Test Guidelines USEPA, 1998.

The *in vitro* and *in vivo* studies cited by the registrant were previously reviewed and did not meet the criteria as per the NAFTA position paper. As shown in Table 1.2.1, the studies do not result in a ratio close to 1 when dermal absorption values are compared, nor did they meet the minimal standards outlined in the position paper, as the doses (medium, high) and exposure durations differ between the two studies. In addition, the formulations in the two studies are not the same; formulants have been shown to affect dermal penetration (Bronaugh and Franz, 1986).

Table 1.2.1 Comparison of Dermal Absorption (DA) Values for In Vivo and In Vitro Studies

Rat *In Vivo* DA (Cheng, 1995)			Rat *In Vitro* DA (Dick, 2001)	
Dose ($\mu g/cm^2$)	**DA w/SBR**		**Dose** ($\mu g/cm^2$) **(actual dose)**	**DA w/SBR (8 h)**
	10 h	**24 h**		
35.6	21.1%	34.0%	36	28.1%
403	10.8%	27.9%	470	37.8%
3450	2.5%	4.0%	4495	5.9%

w/SBR = with skin bound residues; actual dose = actual amount applied (versus nominal dose)

Comment:
The postapplication risk assessment for trees and shrubs should have applied the initial Dislodgable Foliar Residue (DFR) of 3.4% of the application rate on olives from the available DFR data.

PMRA Response:
The PMRA did review the ARTF olive study and did consider it for use in the assessment of ornamentals (trees, shrubs) and fruit trees, since the application equipment, formulation and tree canopy would be similar. The initial DFR of 3.4% of the application rate was not used in the assessment, as it was much lower than what was seen for other crops, potentially due to the morphology of olive trees, differences in foliage type, or the spacing in the olive grove. Therefore, the default DFR value of 20% of the initial application rate was used. The 9.8% daily dissipation as measured in the study was used for the risk assessment. As noted in the comments, this value is similar to the default dissipation of 10% per day.

Comment:
The registrant indicated that the six tree crops grouped together need to be separated based on existing label directions, since these six crops have different application rates, preharvest intervals, and spray schedules that can affect the DFRs.

PMRA Response:
The PMRA has examined the label directions to ensure that those crops that have different application rates are evaluated separately. Spray schedules on the label and preharvest intervals have no impact on the DFR values calculated; the determined DFR values are based on the parameters of the DFR studies used, which in turn are imposed on the affected use pattern. For those uses where default values were used instead of study values, the PMRA did take into consideration label directions concerning application frequencies and intervals. Pre-harvest intervals were only taken into consideration for those use scenarios where the PHI precluded certain postapplication intervals.

Comment:
The registrant believes that hand line irrigation should not be considered for tree crops because carbaryl is a foliar spray and irrigation lines do not run through the foliage; irrigation would either be overhead or drip, and any hand labour activities would not involve foliar contact. Therefore, an REI would not be relevant to irrigation.

PMRA Response:
As indicated by the registrant, overhead and drip irrigation systems are commonly used in newer orchards. However, since hand line irrigation is common in older orchards and still in use for certain tree varieties, there is still a need to address the exposure incurred during hand line irrigation. Although an airblast application is directed at the foliage of fruit trees, it is assumed that some spray residue would come into contact with a hand-line irrigation system. In addition, some foliar contact may occur during hand-line irrigation depending on the variety and developmental stage of the trees. The amount of foliar contact incurred in fruit tree orchards while using hand line irrigation is difficult to determine, due to the variety of orchard production systems, the tree spacing for each crop, the variety of irrigation systems used, and a lack of information on the extent of use of various irrigation systems within orchards. Since it has been determined that foliar contact may occur during the use of hand line irrigation in some orchard crops, an REI for hand line irrigation in tree crops is indeed required to address any risks of concern (See Appendix IV for details).

Comment:
The 8 hour workday assumed in the postapplication risk assessment should be refined to reflect field conditions and specific tasks.

PMRA Response:
The PMRA does not have sufficient information to reduce the number of hours for specific postapplication activities. The information available to the PMRA indicates that 8 hours is an appropriate estimate of work day duration for agricultural workers. This value may in fact underestimate actual work day duration, as discussed below; however, it is considered to be a suitable estimate for use in regulatory risk assessments. The question of workday duration was addressed by a USEPA Federal Insecticide, Fungicide, and Rodenticide Act Science Advisory Panel, which endorsed the use of 8 hours (2008).

The 8 hour duration is based on a grower survey (Thompson, 1998) and a United States Department of Labor report (USDL, 2005) from the National Agricultural Worker Survey. These were considered to be the best available data. The Science Advisory Panel concurred with the USEPA's scientific analysis that these datasets were adequate to establish a workday duration of 8 hour for generic dermal exposure assessment.

Further, the Panel agreed that the use of the 8 hour workday duration represents a large proportion of the exposure distribution profile, but does not adequately reflect exposures at the 90th or 95th percentiles of the distribution following a single day exposure. The data presented by the USEPA suggested that the use of the central tendency of 8 hours for workday duration resulted in an estimated dermal exposure that fell at the 65th percentile, underestimating exposure for 35% of the population. The Panel stated that the USEPA's estimates fell short of being "high end" estimates of exposure.

Comment
Consider reducing REIs based on a 90% exposure reduction for the use of chemical resistant gloves.

PMRA Response:
The PMRA acknowledges that gloves are often worn during postapplication activities for some crops. Gloves are typically worn as protection (for example, thorns) or to prevent the transmission of microorganisms from the worker to the plant commodity. However, the type of glove worn may not be chemical resistant, and the level of chemical protection afforded by the gloves worn by postapplication workers is unknown. While the use of chemical resistant gloves and other exposure reduction practices are recommended, the consideration of PPE as mitigation for postapplication workers in the risk assessment is not appropriate for regulatory purposes. Moreover, gloves are usually not worn in hot weather, and delicate tasks such as hand thinning often cannot be adequately performed while wearing gloves.

Comment:
Different carbaryl formulations have different maximum application rates and the REIs should be set based on the application rates for each formulation.

PMRA Response:
In the interest of clarity and consistency, one REI is recommended based on the formulation associated with the greatest worker exposure. This approach ensures that the risks of concern are addressed for all workers, regardless of the formulation used. In addition, it prevents REI disparity among labels for the same use.

1.2.2 Comments Relating to the Human Health Risk Assessment for Turf Use

Comment:
Stakeholders have suggested that the risk assessment should be refined in terms of workday duration (golf courses) and reduced transfer coefficients (all turf).

PMRA Response:
The PMRA agrees that the duration of 4 hours could be applicable to the postapplication risk assessment for golf course turf (greens and tees only) treated with carbaryl, based on the information submitted by the registrant. The postapplication risk assessment for golf course workers could be refined to reflect this by decreasing the anticipated hours worked per day from 8 to 4. However, a duration of 4 hours is applicable to greens and tees only, and does not adequately address postapplication exposure on the entire golf course. Given that some of the

pest pressures related to carbaryl use require broadcast applications to turf, a label statement would be required limiting the use of carbaryl to greens and tees. In the absence of this label statement, the duration of 8 hours must be retained (see Table IV.3 of Appendix IV).

The transfer coefficient (TC) supplied in the comments from the registrant (758 cm^2/hr) is not used by the PMRA. The ARTF golf course worker study (ARTF 057) was closely reviewed by the PMRA and the Standard Operating Procedure for turf was revised based on this ARTF study. The TC of 3500 cm^2/hr was considered appropriate for use in the risk assessment to calculate golf course worker exposure, since this is the arithmetic mean of all replicates for all activities. This value represents a composite TC of all activities a worker may be performing throughout the day.

The registrant suggested revising the TC for golf course workers performing mowing, watering, cup changing, repairing irrigation, and miscellaneous grooming activities from 3500 cm^2/hr to 758 cm^2/hr. The registrant has also previously expressed concern over the large difference between the geometric mean and the arithmetic mean of the data set and suggested that one replicate (IR8) with an unusually high TC for the lower leg should be excluded as an outlier. The validity of this request was considered.

The high TC (75,910 cm^2/hr) comes from a worker performing irrigation repair. These workers are likely to get wet and to kneel on the ground, leading to increased residue transfer, so one of these workers having a higher exposure on their lower legs is not necessarily unusual.

The total dermal exposure for this worker (IR8) is 1594 µg/kg. The next highest exposure value for irrigation workers is 1402 µg/kg. The total dermal exposure for all replicates in the data set ranges from 40.9 µg/kg to 3222 µg/kg. This implies that exposure for this worker was not exceptionally high. The Transferable Turf Residue (TTR) value for this worker (IR8) is 0.021 µg/cm^2, which is low. The high TC is a result of a relatively high exposure values combined with a low TTR value. However, some of the other replicates had TTR values lower than this one (TTR values ranged from 0.014 to 2.8 µg/cm^2 with an arithmetic mean of 0.62 µg/cm^2).

As such, PMRA does not accept the rationale to exclude either the high exposure from one monitoring unit, or the low exposure from another. For this reason, the PMRA does not agree that the IR8 replicate should be excluded as an outlier, and maintains that the TC of 3500 cm^2/hr is appropriate for use in the risk assessment for golf course workers performing mowing, watering, cup changing, repairing irrigation, and miscellaneous grooming activities.

The arithmetic mean of the TC was used, since the TC is a composite TC representing many activities that would occur during the course of a day. Therefore, the average value of all these activities is most appropriate. In addition, as the arithmetic mean of the TTR values were used, it was considered appropriate to couple these values with the arithmetic mean of the TC.

When using the TC of 3500 cm^2/hr for all golf course activities, the calculated restricted-entry intervals are considered to be agronomically unfeasible for certain postapplication activities (See Table IV.3 of Appendix IV). Although a number of comments received from stakeholders highlight the importance of the use of carbaryl on turf, the risks of concern identified for both mixer/loader/applicators and postapplication workers cannot be further mitigated.

To separate turf activities and assign different TCs for each activity reduces confidence in each TC, as the number of replicates is low for each individual activity and there is high variability in the exposure estimates. In addition, a worker would do many tasks throughout the day. Having separate REIs for each activity is not practical. Therefore, the composite TC of 3500 cm^2/hr was considered appropriate to represent the various tasks a worker would do throughout the day. The resulting exposure estimates, MOEs and REIs are presented in Table IV.3 of Appendix IV. The golf course and sod farm REIs are considered to be agronomically unfeasible, based on the revised and refined risk assessment. These uses will be cancelled as a result of the worker and postapplication risks of concern.

Comment:
Consider adding spot and border treatments as a label statement for residential turf uses.

PMRA Response:
The spot application use directions, as suggested by the registrant, are appropriate for ants and possibly cutworms and fall armyworm. However, to effectively control European chafer, Japanese beetle, leatherjackets, chinch bugs and sod webworms, the entire lawn would typically need to be treated, since the damage from these pests is not concentrated into one small area as it is for ants. Therefore, spot and border treatments for residential turf are not considered to be appropriate methods to mitigate residential exposure.

1.2.3 Comments Relating to the Human Health Risk Assessment for Apple Thinning

Comment:
The registrant has proposed a number of significant label changes with regards to the carbaryl apple thinning use. The registrant believes the resulting label will provide growers clearer "directions for use" that will result in flexibility for apple growers to select application rates, PPE and agronomically feasible REIs.

PMRA Response:
The postapplication risk assessment for all apple activities has been updated in accordance with the revised use pattern (See Tables IV.1 and IV.2 of Appendix IV). The risk assessment was revised and refined based on updated use information, revised application rates and other information provided by registrants and stakeholders. Notwithstanding the high level of refinement, risks of concern to workers involved with hand thinning following the use of carbaryl as a chemical thinning agent remain. As a result, revised conditions of use have been developed to minimize the risk to workers:

For orchards that have transitioned to high density trellis production architecture (for example, spindle or super spindle trees):

- Maximum seasonal rate of 1.5 kg a.i./ha and an REI of 14 days for hand thinning

For orchards that have not transitioned to high density trellis production architecture (for example, dwarf, semi-dwarf and full sized trees):

- Maximum seasonal rate of 1.0 kg a.i./ha and an REI of 17 days for hand thinning

The use of chemical-resistant gloves may further reduce potential exposure. The updated postapplication risk assessment is based on the unmodified orchard thinning transfer coefficient of 3000 cm^2/hr and a $BMDL_{10}$ of 35.5 mg/kg bw/day. The TC used likely over-estimates dermal postapplication exposure for high-density trellis orchards. However, the degree of over-estimation cannot be quantified.

1.3 Comments Relating to the Dietary Risk Assessment

The acute aggregate dietary (in other words, food plus water) assessment was updated to reflect the revised use pattern. Previously, the drinking water assessment was based on carbaryl application to turf. However, since the use of carbaryl on residential turf, golf courses and sod farms is to be cancelled due to residential and occupational risk concerns, the drinking water modelling is now based on carbaryl application to field crops (two applications of 3.0 kg a.i./ha) assuming an 8-day interval between applications. The full distribution of drinking water estimated environmental concentrations (EECs) was incorporated into the residue file. As a result, the acute aggregate dietary exposure for carbaryl is 41% of the acute reference dose for the general population, and ranges from 31 to 107% for the various population subgroups (see Table 1.3 below). The highest exposure at 107% occurs for all infants and is not of concern due to use of certain conservative (that is, high-end) assumptions in the exposure assessment, attributable primarily to the use of water modelling data to estimate drinking water exposures.

Table 1.3 Acute Aggregate Dietary Exposure and Risk

Sub-population	Acute Aggregate Dietary (food and drinking water) Exposure (99.9th percentile exposure)	
	Exposure (mg/kg bw/day)	% ARfD [a]
General population	0.004497	41
All infants	0.011788	107
Children 1-2 years	0.007795	71
Children 3-5 years	0.006580	60
Children 6-12 years	0.004651	42
Youth 13-19 years	0.003371	31
Adults 20-49 years	0.004236	39
Adults 50+ years	0.003685	33
Females 13-49 years	0.004424	40

[a] ARfD (Acute Reference Dose) = 0.011 mg/kg bw ($BMDL_{10}$ = 1.13 mg/kg bw and Composite Adjustment Factor of 100)

Comment:
While monitoring data may be considered as a lower bound of the peak environmental concentration, monitoring data of surface water bodies are not necessarily representative of drinking water concentrations. Monitoring data from drinking water sources in Canada as presented in Table 2 in Appendix XVII (of the PRVD2009-14) show a peak concentration of 0.005 ppb. In the drinking water monitoring study conducted by Bayer CropScience, for high use locations in the United States, the peak concentration was 0.16 ppb, which would be a reasonable upper bound on a peak carbaryl concentration in drinking water in the United States.

PMRA Response:
The PMRA considers monitoring data from surface waters in its drinking water assessments because some Canadians do not obtain their drinking water from treatment facilities. The PMRA has considered and included the monitoring study provided by the registrant into its drinking water assessment, and notes that the maximum concentrations detected were 0.181 µg/L. The PMRA considers monitoring data from the United States, given the extensive monitoring programs that exist in the United States. The PMRA notes that monitoring data from the United States Geological Survey's National Water Quality Assessment Program indicate that concentrations of carbaryl in surface water were as high as 33.5 µg/L in agricultural land use areas, 45.2 µg/L in mixed land use areas, 5.5 µg/L in urban land use areas, and 16.5 µg/L in other land use areas. These data were also considered in the PMRA's drinking water assessment. A revised peak concentration in drinking water was calculated as 10.6 µg/L.

Although carbaryl monitoring data were considered sufficient for the chronic and cancer dietary risk assessments, in general these data are not considered appropriate for an acute dietary risk assessment. The PMRA notes that water monitoring, as is the case in most available studies for carbaryl, generally involves sampling that is limited in time and space, and thus is unlikely to capture peak concentrations that can occur immediately after use. Since turf uses are to be cancelled, the drinking water assessment was based on other agricultural uses of carbaryl. Based on this drinking water scenario, there are no acute aggregate dietary risks of concern in the updated assessment.

Comment:
Bayer CropScience concurs that use of percent crop area (PCA) would be appropriate for refining modeled drinking water EECs, but believe drinking water monitoring data provide the most realistic estimates of drinking water concentrations for carbaryl. We are, however, proposing to work with PMRA on development of PCA data because of its widespread applicability.

PMRA Response:
Carbaryl is fairly mobile and is unlikely to persist and accumulate in the environment. Water monitoring, as noted previously is unlikely to capture peak concentrations that can occur. This rationale is consistent with the approach taken by the USEPA for carbaryl. The USEPA determined that currently available monitoring studies for carbaryl were limited in the likeliness to capture peak concentrations in the environment, and did not use them to define peak values for carbaryl. As noted above, carbaryl monitoring data were considered sufficient for the chronic and cancer dietary risk assessments, but were not considered appropriate for an acute dietary risk assessment.

PMRA currently uses, on a case-by-case basis, PCAs based on Census of Agriculture data at the consolidated census subdivision level. PCAs based on watersheds which feed drinking water systems might be an improvement on this approach and is being investigated.

Preliminary scoping of the percent crop areas (PCAs) for various crops indicates that the PCAs for carbaryl are relatively large and may not necessarily refine the aggregate acute dietary risk assessment. Since turf uses are to be cancelled, the drinking water assessment was based on other agricultural uses of carbaryl. Based on this drinking water scenario, there are no dietary acute risks of concern in the updated assessment.

2.0 Comments Related to the Environmental Risk Assessments

2.1 Effects on Aquatic Organisms

Comment:
The registrant indicated that the use of a single data point from the most sensitive species is inappropriate and overly conservative for a number of reasons. Additional data on aquatic invertebrates were submitted for consideration to develop a species sensitivity distribution. By considering these data and the two mesocosm studies, the registrant has proposed that 10 µg/L in buffer zone calculations would provide adequate protection for aquatic invertebrates. Although the database for estuarine/marine invertebrates is smaller, the sensitivity of marine/estuarine species is in the same range as freshwater species, and this value of 10µg/L would also be appropriate for marine/estuarine species.

PMRA Response:
The PMRA has reviewed the additional studies submitted by the registrant and the results are as follows:

The mesocosm study by Helm (1993) [8] was conducted at pH 9-10. Carbaryl rapidly hydrolyzes at pH>7 (half-life at pH 8 and 9 is 4 and <1 d, respectively). Given the pH of many aquatic ecosystems is < 9, it was determined that this study is not relevant to environmental conditions.

[8] Helm 1993, Carbaryl (Sevin (R) XLR Plus): Outdoor aquatic microcosm test for environmental fate and ecological effects.

The other mesocosm study (Havens, 1995) confirms that *Daphnia* is more sensitive than smaller cladocerans to the carbamate carbaryl and that cladocerans in general are more sensitive than copepods. It also indicates that the zooplankton at the concentration of 10µg/L of carbaryl is reduced by 50%.

The registrant submitted eight toxicity studies on aquatic invertebrates and two of these studies were conducted in water and six in water/sediment systems. However Schäfers (2002) had already summarised the results of these studies. Consequently, a detailed species sensitivity distribution which takes into account acute toxicity data for relevant exposure scenarios for different freshwater invertebrate species was developed by Schäfers (2002). An HC_5 of 12.7 µg/L was obtained. Schafers proposed an ecologically acceptable concentration of 10 µg/L, and considered it as being sufficiently conservative and representative of all the sensitive aquatic invertebrates. The results from Schäfers (2002) and Havens (1995) were considered by the PMRA in the choice of a toxicity endpoint for the revised risk assessment of freshwater invertebrates.

Available data indicate that the sensitivity of marine invertebrates to carbaryl falls into two groups. Mysid shrimps are most susceptible (1.2-32 µg/L) unlike oysters (> 1000 µg/L). Available toxicity data on marine invertebrates will be used for buffer zone calculations for marine habitats as the use of data from freshwater species would not be appropriate.

Taking all available information into consideration the following aquatic invertebrate's toxicity endpoints were used for the aquatic risk assessment and the revised buffer zone calculations:

- freshwater invertebrates LC_{50}=10 µg ai/L (based on mesocosm study by Havens)
- marine invertebrates $1/2LC_{50}$=3.1 µg ai/L. This is a geometrical mean of toxicity endpoints from two studies on mysid shrimp (LC_{50} of 6.7 and 5.7).

2.2 Aerial Buffer Zone Calculations

Comment:
The registrant disagreed with the water content used in calculating aerial buffer zones (0% based on buffer calculation workbook provided by PMRA), which is not different from content on the product's Statement of Control Specification Form. Swath displacement was not considered in calculating buffer zones by the agency. This is not a realistic assumption.

In addition, the registrant proposed to consider the performance of AGDISP (agricultural dispersal) model in making buffer zone decisions. Research has demonstrated that AGDISP over-predicts deposition and therefore, over-predicts the buffer zones in a great extent.

PMRA Response:
The PMRA had recalculated the no-spray buffer zones resulting from aerial application based on the water content of the formulation. The revised aquatic toxicity endpoints were also used in the buffer zone calculations.

The PMRA agrees that applicators use swath displacement; however, it varies considerably according to meteorological conditions, most notably the wind speed. The 0 m swath displacement in the model input indicates that spray deposition is to the edge of the target area

and as such, the aerial applicators will adjust their off-set flight-line to achieve this deposit. If the PMRA assumed a ½ swath displacement as the standard, then a ½ swath displacement would be prescribed on product labels. In any event, the buffer zone distance would be the ½ swath displacement distance plus the predicted buffer zone value thus it is more appropriate to simply give the buffer zone distance based on a 0 m swath displacement.

The overestimation of no-spray buffer zones in the far field by both AgDrift and AgDISP has been known for some time. There have been numerous discussions, both national and international, regarding this phenomenon but there has been no mechanism to address this issue or agreement on how this issue should be addressed within the model. Modifications to the existing aerial models would be necessary to address the over-prediction in buffer zone distances for aerial application; however, it is not within PMRA's prerogative to bridge the discrepancy between predicted and observed spray deposit or to modify the existing models for any given chemical. In order to be consistent the same approach is needed for all assessments.

2.3 Buffer Zone for Tobacco

Comment:
The most common method of applying carbaryl to tobacco is with a ground boom sprayer. There were no buffer zones for tobacco identified in the re-evaluation document other than for aerial application.

PMRA Response:
Buffer Zones for ground application on tobacco are included in the buffer zone table in Appendix V.

2.4 Buffer Zones for the Use of Carbaryl on Apple

Comment: Many stakeholders indicated that the buffer zones for apple use, especially for apple thinning, are too big and not practical. They also indicated that typical number of application for apple thinning is only once per year.

PMRA Response:
As the PRVD was published in 2009, the buffer zones were calculated according to application rates, numbers and intervals recommended on the label at that time.

Based on use information received during the comment period and the revised application rates for apple thinning (see 1.2.3 of Appendix I in this document), the buffer zones were recalculated and are presented in Appendix V.

2.5 Bee Precaution Statement

The registrant proposed a number of significant changes in the apple thinning section of SEVIN BRAND XLR PLUS CARBARYL INSECTICIDE including the following additional honey bee precautionary statements:

BEE CAUTION: This product is highly toxic to honey bees exposed to direct treatment on blooming crops or weeds. However, field studies have shown that Sevin XLR CARBARYL INSECTICIDE LIQUID SUSPENSION, while toxic to honey bees, is less hazardous than other carbaryl products when direct application to bees is avoided and the spray residues have dried. For maximum honey bee hazard reduction, apply Sevin XLR CARBARYL INSECTICIDE LIQUID SUSPENSION from late evening to early morning or when bees are not foraging. If application must be made during foraging periods, the following precautionary measures should be performed prior to treatment to minimize honey bee kill: notify beekeepers to: (1) confine the honey bees to the hive by covering the colony or screening the entrance; or (2) locate hives beyond honey bee flight range from the treated area. Precautionary measures may be discontinued after spray residues have dried. Leafcutter bees are more sensitive to insecticides than honey bees. Carbaryl applications should be avoided where these bees are foraging.

PMRA Response:

The PMRA does not accept this label amendment. As a result of the pollinator risk assessment, it was determined that the application of carbaryl during bloom should be prohibited for a number of crops in order to reduce pollinator exposure. Additional label statements with respect to pollinators are presented in Appendix V. The label requirements take into consideration the protection of managed bees by prohibiting application during bloom for crops which use managed bees for pollination services. These requirements also consider the protection of non-managed bees by prohibiting application during bloom for crops which present a high likelihood of exposure (for both *apis* and non-*apis* bees). In addition, the label requirements refer to a link which informs users of best management practices during spraying, and these practices will also aid in further reducing exposure.

The wording to be implemented by PMRA will be applicable to all labels and is based on exposure potential for pollinators.

3.0 Comments Pertaining to the Value Assessment

The PMRA received several comments from stakeholders regarding the value of the carbaryl uses in response to PRVD2009-14. The comments were considered for the refinement of the mitigation measures and in the value assessment to identify crops with pest management concerns.

3.1 Use of Carbaryl on Apples

Comments:
Carbaryl is primarily used as an apple thinner and is the primary product used on apples for this purpose. There are no suitable alternative active ingredients to carbaryl for thinning apples, nor are any currently under development.

Carbaryl is also needed for late season control of white apple leafhopper. Endosulfan is the only alternative active ingredient registered to control this pest.

PMRA Response:

The risk assessment for apple thinning was revised and refined based on updated use information, revised application rates and other information provided by registrants and stakeholders (see Section of 1.2.3 of Appendix I of this document). Additional label amendments will also clarify the use of carbaryl and provide growers with the flexibility to apply carbaryl in a manner appropriate to the thinning requirements in their orchard. The revised use directions are provided in Appendix V.

Alternative active ingredients to carbaryl are registered for use in Canada to control white apple leafhopper on apples. These are listed in Table 3.1.

Table 3.1 Registered Commercial Class Alternative Active Ingredients to Carbaryl for the Control of White Apple Leafhopper on Apples as of August 2015

Crop	Pest	Resistance Management Group MoA:[1] Registered alternatives[2]	Comments
Apple	White apple leafhopper	1A: methomyl, oxamyl (non-bearing apples), formetanate hydrochloride	Methomyl is currently under re-evaluation.
		1B: diazinon	As published in REV2013-01 *Diazinon Risk Management Plan*, all uses of diazinon on apples will be phased out 31 December 2016.
		3: cypermethrin, deltamethrin, lambda-cyhalothrin, permethrin	Cypermethrin, deltamethrin, lambda-cyhalothrin and permethrin are currently under re-evaluation. Repeated applications of synthetic pyrethroids may cause secondary pest outbreaks (for example, mites).
		4: acetamiprid, clothianidin, imidacloprid, thiacloprid	Clothianidin and imidacloprid are currently under re-evaluation.
		28: chlorantraniliprole (suppression), cyantraniliprole	
		Other: kaolin clay	

[1] Insecticide and Acaricide Resistance Management Group Numbers based on Regulatory Directive DIR 99-06, *Voluntary Pesticide Resistance Management Labelling based on Target Site/Mode of Action*, with updates from the Insecticide Resistance Action Committee (IRAC) Mode of Action Classification Scheme v7.4, May 2015. Available at http://www.irac-online.org/documents/moa-classification. 1A = acetylcholinesterase inhibitors (carbamates); 1B = acetylcholinesterase inhibitors (organophosphates); 3 = sodium channel modulators; 4 = nicotinic acetylcholine receptor competitive modulators; 28 = ryanodine receptor modulators.

[2] This is a list of registered alternatives, current as of August 2015. The registration status of active ingredients under re-evaluation may change pending the final regulatory decision. For additional information, consult the Pesticides and Pest Management portion of Health Canada's website at http://www.hc-sc.gc.ca/cps-spc/pubs/pest/_decisions/index-eng.php (English) and http://www.hc-sc.gc.ca/cps-spc/pubs/pest/_decisions/index-

fra.php (French) for Re-evaluation Decisions (RVD and RRD documents) and Re-evaluation Notes (REV documents) or http://www.hc-sc.gc.ca/cps-spc/pest/part/consultations/index-eng.php (English) and http://www.hc-sc.gc.ca/cps-spc/pest/part/consultations/index-fra.php (French) for current and past consultation documents including Proposed Re-evaluation Decisions (PRVD and PACR documents) and certain Re-evaluation Notes (REV documents).

3.2 Use of Carbaryl on Turf

Comments:
Carbaryl is registered to control a wide range of insect pests on turf. For some of these pests there are few, if any, registered alternative active ingredients. For certain turf pests (for example, ants, chinch bug, cutworms and sod webworm), carbaryl is necessary for rotation with active ingredients from differing resistance mode of action (MoA) groups.

For the control of leatherjackets (European crane fly), carbaryl is the only active ingredient registered on residential turf and is the main active ingredient used on golf courses and turf farms. There are no biological control agents for the control of this pest.

European chafer is a new pest in British Columbia and is currently confined to turf in Vancouver and adjacent areas. Controlling the pest population in turf will delay the spread of this pest into agricultural production areas.

Carbaryl and chlorpyrifos are the only active ingredients available for the control of later instar grub larvae and mature leatherjacket larvae. Chlorpyrifos is not registered for use in residential areas.

PMRA Response:
The PMRA will cancel carbaryl use on turf due to risk concerns. Several alternative active ingredients to carbaryl (a group 1A insecticide) for control of turf pests are available from a number of resistance management mode of action groups, including the organophosphates (group 1B), synthetic pyrethroids (group 3), nicotinic acetylcholine receptor competitive modulator (group 4), nicotinic acetylcholine receptor allosteric modulators (group 5) and ryanodine receptor modulators (group 28). The registered alternative active ingredients to carbaryl for the control of European chafer, Japanese beetle, leatherjackets and other turf pests are listed in Table 3.2.

The PMRA notes that there are some use limitations to the registered alternative active ingredients including:

- a seasonal maximum limit of one application for each of imidacloprid, clothianidin and chlorantraniliprole;
- the limit of a single application per season for clothianidin and imidacloprid precludes their use to control both the European chafer and leatherjackets on the same turf in a given season, as the timing of application for these pests differ and clothianidin and imidacloprid may not be used on the same area of turf within the same season in order to prevent the development of resistance.

Parasitic nematodes are available for control of both the European chafer and leatherjackets, however, there are limitations to their use. Applicators require substantial knowledge of the pest biology for proper application timing and sufficient irrigation is required following application if effective reduction in pest populations is to be achieved. As nematodes are live organisms, proper handling and storage is required to maintain their viability. Furthermore, reduction in pest populations using nematodes will not prevent damage immediately after application. For turf where there is a very low tolerance for damage (for example, golf greens) the use of nematodes may not be feasible.

For leatherjackets, there are few registered alternatives. As indicated in REV2000-5 *Chlorpyrifos*, chlorpyrifos is limited to use on golf courses, rights of way and other non-residential turf areas. Chlorantraniliprole (MoA group 28) is the only alternative product to carbaryl to rotate with the IRAC MoA group 4 insecticides for insecticide resistance management on residential turf.

European chafer and Japanese beetle may be controlled by a preventative application prior to, or at egg hatch, or by a curative application after egg hatch to control larvae. Alternative active ingredients to carbaryl that may be applied at either timing include clothianidin and chlorantraniliprole. Imidacloprid is registered as a preventative application however it cannot be applied in the same season as clothianidin.

Table 3.2 Registered Commercial Class Alternative Active Ingredients to Carbaryl for the Control of Insect Pests on Turf as of August 2015

Crop	Pest	Resistance Management Group MoA:[1] Registered alternatives[2]	Comments
Turf	European crane fly (leatherjacket)	1B: chlorpyrifos 4: clothianidin, imidacloprid 28: chlorantraniliprole	Clothianidin and imidacloprid are currently under re-evaluation. Chlorpyrifos is applied in the late fall after adults have ceased flying (and the laying of eggs has finished). Chlorpyrifos is used to control the young larvae of the subsequent generation. Chlorpyrifos is registered for use on golf courses, industrial sites, highway medians and sod farms only. Clothianidin may be applied in the fall prior to egg hatch (for control of young larvae) or in the spring to control larger larvae prior to pupation. Clothianidin is registered for one application per year. For resistance management purposes it should not be applied with another group 4