Pest Management Regulatory Agency
Agence de réglementation de la lutte antiparasitaire

Proposed Acceptability for Continuing Registration

PACR2003-06

Re-evaluation of Bensulide

The purpose of this document is to inform the registrant, pesticide regulatory officials and the Canadian public that the Pest Management Regulatory Agency (PMRA) has completed a re-evaluation of bensulide pursuant to Section 19 of the Pest Control Products Regulations. This Proposed Acceptability for Continuing Registration document provides a summary of the data and information reviewed, and the rationale for the proposed regulatory decision.

By way of this document, the PMRA is soliciting comments from interested parties on the proposed regulatory decision for bensulide. The PMRA will accept written comments on this proposal up to 60 days from the date of publication of this document to allow interested parties an opportunity to provide input into the proposed decision. All comments should be forwarded to the Publications Coordinator at the address listed below.

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Publications Coordinator
Pest Management Regulatory Agency
Health Canada
2720 Riverside Drive
A.L. 6605C
Ottawa, Ontario
K1A 0K9

Internet: pmra_publications@hc-sc.gc.ca
www.hc-sc.gc.ca/pmra-arla/
Information Service:
1-800-267-6315 or (613) 736-3799
Facsimile: (613) 736-3798

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Foreword

The re-evaluation of the active ingredient bensulide and the associated end-use products (EPs) registered for use on food and non-food areas has been completed by the Pest Management Regulatory Agency (PMRA). The registrant of the technical active ingredient is Gowan Company.

The PMRA has announced in June 1999 that organophosphate active ingredients, including bensulide, were subject to re-evaluation under authority of Section 19 of the Pest Control Product (PCP) Regulations.[1]

Subsequent to that announcement, Gowan, the primary registrant of bensulide in Canada, indicated that it intended to provide continued support for products containing bensulide on cucumber and turf.

The PMRA has carried out an assessment of available information and has concluded that the use of bensulide and its end-use products on cucumber and turf does not entail an unacceptable risk to human health and the environment pursuant to Section 20 of the PCP Regulations, provided that the proposed mitigation measures described in this document are implemented.

It is proposed that the Food and Drug Regulations be amended so that, with the exception of cucumber, food with quantifiable residues of bensulide cannot be sold in Canada once Canadian use has been phased out, unless additional data to support bensulide residues in imported food are provided.

The PMRA will accept written comments on this proposal up to 60 days from the date of this document to allow interested parties an opportunity to provide input into the proposed re-evaluation decision for these products.

[1] Re-evaluation Document REV2000-01, *Re-evaluation of organophosphate pesticides*

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1.0 Purpose

This document describes the outcome of the Pest Management Regulatory Agency's (PMRA) re-evaluation of the herbicide bensulide and its end-use products (EPs). It includes a human health assessment, an environmental assessment and information on the value of bensulide to pest management in Canada. By way of this document, the Agency is soliciting comments from interested parties on the decisions and mitigation measures proposed.

2.0 General background on re-evaluation

The PMRA is re-evaluating, under Section 19 of the Regulations pursuant to the *Pest Control Products Act* (PCPA), all pesticides, both active ingredients and formulated EPs, that were registered prior to 1995. As outlined in Regulatory Directive DIR2001-03, *PMRA Re-evaluation Program*, a modern scientific approach is used to determine the continuing acceptability of older active ingredients in relation to human health and the environment. Bensulide is under reassessment in the U.S. as a result of the *Food Quality Protection Act* and therefore is being re-evaluated by the PMRA under Program 3. The following components are addressed and considered in this re-evaluation:

Risk to human health: The initial focus of the re-evaluation of a pest control product in Program 3 is the risk to human health. As indicated in DIR2001-03, the reassessment in Program 3 pays particular attention to:

- pest control products with a common mechanism of toxicity,
- aggregate exposure to a pesticide arising from its residues in food and in drinking water, and from non-occupational exposure, such as from treatments in and around homes, and
- susceptibility and exposure of infants and children that may be different from that of adults during critical developmental stages.

The re-evaluation of risks to human health also includes a re-examination of the acceptability of risks resulting from occupational exposure. Once the reassessments of all the individual organophosphates have been completed, a cumulative assessment of all the remaining uses of organophosphates will be conducted.

Risk to the environment: The environmental assessments will be tiered, with refined environmental risk assessments taking place only on those actives, products or uses that pass the cumulative health risk assessment or, for unique mechanisms of toxicity, that are acceptable from a human health perspective. At the first tier, based on an identification of hazards to non-target organisms, measures to reduce environmental exposures will be implemented where warranted. These measures may include removing uses that are obsolete, reducing the number of applications, requiring buffer zones to protect sensitive habitats and taking regulatory action against uses that have been determined to be an extremely high risk to organisms in the environment. In general, uses that remain after the first tier assessment will be revisited when the results of refined environmental assessments are available.

A tiered approach is necessary for several reasons. For some products, initial environmental assessments indicate a high hazard. However, there is considerable uncertainty with regard to the frequency and magnitude of exposure and effects. For some products, there is also little data on field concentrations and (or) adverse effects. A tiered approach to environmental risk assessment would allow time for the development and implementation of refined ecological risk assessment methods, for additional data to be provided to refine the environmental exposure assessments and for consideration of the preferability of existing alternatives and the development of new ones. In addition, a tiered approach would make the most efficient use of assessment resources.

Value: The PMRA seeks to understand, as early as possible in the re-evaluation process, the current uses of products under review and their importance for pest management in agriculture, the nursery trades, forestry and public health. The PMRA relies to a great extent on provincial and territorial government input. Registrants and users are also an important source of information. Environment Canada, the Department of Foreign Affairs and International Trade, the Canadian Food Inspection Agency (CFIA) and Agriculture and Agri-Food Canada are also contacted, as needed, in the re-evaluation process for information specific to their areas of expertise.

The outcome of the re-evaluation of each pesticide, including proposed risk mitigation measures, will be published in a consultation document at the end of the aggregate human health risk assessment and the first tier environmental assessment. In some cases, the PMRA will implement changes in regulatory status of products prior to public consultation, especially where the PMRA considers risk mitigation ineffective or impractical, or where registrants have opted for voluntary discontinuation of the sale of products.

3.0 Re-evaluation of bensulide

Bensulide is one of the 27 organophosphate pesticides subject to re-evaluation in Canada. The re-evaluation of bensulide was announced in Re-evaluation Document REV99-01, *Re-evaluation of organophosphate pesticides*. Bensulide is a selective pre-emergence herbicide, effective in the control of grassy weeds of the family Graminaceae. It is adsorbed on the root surfaces, but not translocated to the leaves. It acts by inhibiting the growth of lateral roots on grass weeds by inhibiting lipid synthesis. In animals, bensulide inhibits acetylcholinesterase enzyme, interrupting the transmission of nerve impulses. First registered in 1964, bensulide has been used in Canada for the control of Graminaceae on cucumber and turf. The registered products containing bensulide are listed in Appendix I.

Much of the scientific information used by the PMRA in its assessment of bensulide came from reviews conducted by the United States Environmental Protection Agency (EPA). The EPA reviews of bensulide can be referenced for further details regarding the scientific studies used by the PMRA. These reviews, as well as other information on the regulatory status of bensulide in the United States, can be found at the Web site of the Environmental Protection Agency, http://www.epa.gov/pesticides/op/status.htm.

3.1 Chemical identification

Chemical name:

International Union of Pure and Applied Chemistry:

S-2-benzenesulfonamidoethyl *O*,*O*-di-isopropyl phosphorodithioate

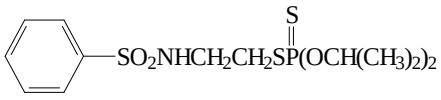
or

O,*O*-di-isopropyl *S*-2-phenylsulphonylaminoethyl phosphorodithioate

Chemical Abstracts Service:

O,*O*-bis(1-methylethyl) *S*-[2-[(phenylsulphonyl)amino]ethyl] phosphorodithioate

Structural formula:



3.2 Description of current registered uses

3.2.1 Terrestrial food crops (Use–Site Category (USC) 14)

The only food use of bensulide registered in Canada is in the production of cucumbers (flat planted or bedded). Of the Commercial Class EPs, only one, Prefar 4.8 E Emulsifiable Liquid Selective Herbicide (PCPA Registration Number 14113), is registered for this purpose. The product may be used as a preplant broadcast application that is incorporated into the soil at a rate of 5.76–6.72 kg active ingredient (a.i.)/ha. This application rate is often reduced by applying the product as a band treatment only over the crop row. The product is to be applied once per season. The actual use of bensulide is not very common in cucumbers, but it is used as a weed resistance management tool due to its unique mode of action.

For broad spectrum weed control, bensulide (4.5–6.7 kg a.i./ha) may also be tank-mixed with naptalam (2.2–4.5 kg a.i./ha) in 100–400 L/ha of spray solution and applied preplant, incorporated into mineral soils.

3.2.2 Non-food (turf) uses (USC 30)

There are three Commercial Class and one Domestic Class bensulide products (Appendix I) currently registered for use in clover and perennial grass lawns on golf courses, in parks and around homes. Bensulide is listed in the "Compendium of Fertilizer Use Pesticides" published by the CFIA, which means that it is registered by the CFIA as a fertilizer and pesticide combination product for use on the sites listed above.

Bensulide is applied to lawns at the rate of 11.0–15.6 kg a.i./ha for the control of crabgrass (*Digitaria sanguinalis* L.). This treatment is carried out prior to weed emergence, any time from fall (September to October) through early spring for spring and summer control. For the control of annual bluegrass (*Poa annua* L.) and other annual weeds, bensulide is also applied before weed emergence. It may be applied as a foliar spray (emulsifiable concentrate formulation) or in dry form (granular formulation).

The use of the Commercial Class products is uncommon due to their high cost and the fact that they must be used before the weed problem is evident. For this reason, they are rarely used on residential lawns. Use of the Domestic Class product appears also to be limited. The principle use of Commercial Class bensulide products is on golf greens (fine putting turf) to control crabgrass before it has a chance to grow.

4.0 Effects having relevance to human health

4.1 Toxicology summary

Based on the submitted data in laboratory animals, bensulide was found to be highly acutely toxic following acute oral exposures and of low acute toxicity by the dermal and inhalation route of exposure. Following both single and repeated dosing, one of the most sensitive indicators of toxicity was the inhibition of acetylcholinesterase, an enzyme necessary for the proper functioning of the nervous system or clinical signs of cholinergic toxicity. Bensulide did not cause delayed neurotoxicity and there was no evidence of histopathological effects on the central nervous system in any of the available studies. On the basis of the available toxicity studies, bensulide is anticipated to have a low dermal absorption potential. Bensulide was not found to be genotoxic nor was it carcinogenic to either rats or mice. Liver was also a target organ in mice, rats and dogs. The sensitivity of dogs to both cholinergic effects as well as liver toxicity appeared to increase with prolonged dosing. Bensulide did not cause fetal malformations in either rats or rabbits, nor did it cause reproductive toxicity in rats. The developmental and reproductive toxicity studies did not demonstrate any sensitivity of young animals relative to adult animals although the lack of cholinesterase measurements in these studies precluded a definitive assessment of this issue. However, reduced viability of the young was observed at maternally toxic doses in the reproductive toxicity study and an increase in late resorptions and abortions was noted in the oral rabbit developmental study at a dose that was maternally toxic. Due to the serious nature of these end points, these studies were considered during risk assessment to ensure an adequate margin of safety (MOS).

Reference doses have been set based on no observed adverse effect levels (NOAELs) for the most relevant end points, namely cholinergic toxicity and hepatic toxicity. These reference doses incorporate various uncertainty factors (UFs) to account for extrapolating between rats and humans, for variability within human populations and for data gaps. Additional safety factors (SFs) have also been employed, where warranted, to protect pregnant females and their unborn children as well as nursing children from identified end points of concern. The resorptions and abortions in the developmental study were considered relevant to risk assessments of all durations with the exception of the acute reference dose (ARfD), as the effects could not be ascribed to a single dose due to the late occurrence of the observations. The reduced viability of the young in the reproductive toxicity study was only considered for risk assessments of intermediate or chronic duration, as the effects were seen in the second generation only following prolonged repeated dosing.

The toxicology end points used in the risk assessment of bensulide are summarized in Appendix II.

4.2 Occupational risk assessment

Occupational risk is estimated by comparing the potential exposure (in mg a.i./kg bw/d) of persons mixing, loading and applying pesticides with the most relevant end points from toxicology studies to generate a margin of exposure (MOE). The risk exceeds the PMRA's level of concern if the obtained MOE is less than the desired or target MOE.

For short-term dermal risk assessment reflecting the current use pattern (exposures < 1 week duration), the most relevant toxicology study was a 21-day dermal toxicity study in rats with a NOAEL of 50 mg/kg bw/d (lowest observed adverse effect level (LOAEL) of 500 mg/kg bw/d based on brain cholinesterase depression). The low dermal absorption demonstrated by bensulide in this study supported the selection of this study for risk assessment even though this study did not address an end point of concern for short-term exposure, that being developmental toxicity (increased late abortions and resorptions noted in the oral rabbit developmental study in the presence of maternal toxicity). However, to ensure protection of the pregnant worker and her unborn child, an additional SF of 3× was required along with the 10× UF to account for the extrapolation between test animals and humans and 10× UF to account for the variability within the human population for a total MOE of 300×.

For short-term inhalation risk assessment reflecting the current use pattern (exposures < 1 week), no short-term inhalation toxicity study was available. Thus, an oral study was considered relevant assuming equal systemic absorption from either the oral or inhalation route. The repeat-dose study of shortest duration with the lowest LOAEL (15 mg/kg bw/d) for brain cholinesterase inhibition was the 13-week dietary toxicity study in rats. This study had a NOAEL of 5 mg/kg bw/d. The use of this NOAEL may be conservative, in that the study duration exceeded the time period of interest (up to 1 week) and thus may overestimate the hazard. Standard UFs (10× for interspecies extrapolation and 10× for intraspecies variation) were used to establish a target MOE of 100. This target MOE would provide an MOS of 400 to the developmental NOAEL of 20 mg/kg bw/d (increased late abortions and resorptions in the oral rabbit developmental study at 80 mg/kg bw/d) and thus was considered protective of the pregnant worker and her unborn child.

For intermediate-term dermal and inhalation risk assessment reflecting the current use pattern (exposures < 2 months), no dermal or inhalation studies of appropriate duration were available.

Thus, an oral study was considered and the 13-week dietary toxicity study in dogs was selected for risk assessment, since the database suggests the sensitivity of the dog increases with longer durations of exposure. The NOAEL of this study was 3 mg/kg bw/d (LOAEL of 10 mg/kg bw/d based on hepatic effects). A total MOE of 300× was required (10× to account for the extrapolation between test animals and humans, 10× to account for the variability within the human population, and an additional UF of 3× to account for the lack of a subchronic neurotoxicity study). The selection of this study and target MOE offers an intrinsic MOS of >2000 to the oral rabbit developmental NOAEL of 20 mg/kg bw/d and >1200 to the offspring NOAEL of 12.3 mg/kg bw/d from the reproductive toxicity study and is thus considered protective of the pregnant worker and her unborn child as well as a nursing child.

4.2.1 Mixer/loader/applicator exposure

For agricultural application and for residential and recreational turf, dermal and inhalation exposure estimates for mixer/loader/applicators are based on data from the Pesticide Handlers Exposure Database Version 1.1 (PHED) and several Outdoor Residential Exposure Task Force (ORETF) studies.

PHED is a compilation of generic mixer/loader applicator passive dosimetry data with associated software that facilitates the generation of scenario-specific exposure estimates. To estimate exposure for each use scenario, appropriate subsets were created from the mixer/loader and applicator database files of PHED. All data were normalized for the amount, in kilograms, of active ingredient handled. Exposure estimates are presented on the basis of the best-fit measure of central tendency, i.e., summing the measure of central tendency for each body part that is most appropriate to the distribution of data for that body part.

The ORETF recently generated several exposure studies that monitored exposure of workers and homeowners mixing/loading and applying pest control products to turf. These studies have been evaluated by the PMRA and are considered appropriate for use as surrogate data to estimate exposure of professional lawn care operators and homeowners treating turf with bensulide. Mixer/loader/applicator exposure was monitored using passive dosimetry, hand washes, face and neck wipes and personal air samplers. Exposure estimates are presented on the median measure of central tendency.

Exposure is calculated as the product of the unit exposure for a given scenario, the application rate and the area treated per day divided by the body weight. The average body weight of adult females was used because the severity of the toxic end points requires protection of the pregnant female and her unborn child. Occupational risk is estimated by comparing a calculated MOE with a target MOE incorporating SFs protective of the most sensitive subpopulation.

All inhalation MOEs are above the target value of 100 and therefore not of concern. All MOEs for occupational handlers in an agricultural setting are above the target of 300. The dermal MOEs for several golf course application scenarios are below the target MOE of 300. MOEs for handlers on golf courses wearing long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes are below the target when applying liquid formulation to tees and greens using a low pressure turf gun or when using a push-type spreader to apply a granular formulation to tees and greens. Additional personal protective equipment (PPE), i.e., coveralls over long sleeves and long pants, would reduce exposure from push-type granular spreader application to acceptable levels. MOEs for spot treatment using low pressure hand wand are above the target. Treating an entire golf course using a ground boom, without engineering controls or additional PPE, also results in an MOE below the target of 300. Refer to Section 7.0, Proposed regulatory actions relating to human health, for proposed mitigation measures to address the areas of concern.

For professional lawn care handlers, four scenarios are of concern: mixer/loader/applicator with a high pressure handwand, backpack, push-type granular spreader and low pressure turf gun. Additional PPE, i.e., coveralls over long sleeves and long pants, would reduce exposure from push-type granular spreader and low pressure turf gun scenarios to acceptable levels (refer to Section 7.0, Proposed regulatory actions relating to human health, for mitigation proposals).

4.2.2 Post-application exposure

Golf course workers who re-enter treated sites to conduct turf maintenance activities may be exposed to bensulide. Potential exposures for re-entry workers were estimated using a generic agricultural transfer coefficient for workers aerating, fertilizing or mowing treated turf. The dermal MOEs for golf course workers performing turf maintenance duties are above the target and are not of concern.

4.3 Residential risk assessment

The same short-term toxicology end points and MOEs as selected for the occupational risk assessment are relevant for adults in the residential risk assessment and are considered protective of pregnant females and their unborn children and nursing children.

For the short-term dermal risk assessment (exposures $\leq$ 1 week duration) in children, the 21-day dermal toxicity study in rats with a NOAEL of 50 mg/kg bw/d (LOAEL of 500 mg/kg bw/d based on the inhibition of brain stem cholinesterase activity) was selected. The duration and route of exposure in this study were considered appropriate. No additional SF was warranted for the directly exposed child, as the end point of concern (abortions and resorptions) noted in the rabbit developmental study was not considered relevant to this population. The target MOE selected when using the dermal study is 100; this accounts for standard UFs of 10 for interspecies extrapolation and 10 for intraspecies variability.

For the short-term inhalation risk assessment (exposures ≤ 1 week duration), no short term inhalation study was available in the bensulide database, thus an oral study was considered relevant assuming equivalent oral and inhalation absorption. The repeat-dose study of shortest duration with the lowest LOAEL (15 mg/kg bw/d) for brain cholinesterase inhibition was the 13-week dietary toxicity study in rats. This study had a NOAEL of 5 mg/kg bw/d. The use of this NOAEL may be conservative, in that the study duration exceeded the time period of interest (up to 1 week) and thus may overestimate the hazard. The target MOE selected when using this study for the directly exposed child is 100; this accounts for standard UFs of 10 for interspecies extrapolation and 10 for intraspecies variability.

For toddlers and the non-dietary (incidental) oral ingestion risk assessment, a scenario of short-term duration was considered (i.e., <14 days). Consequently, the same end point and target MOE as selected for the short-term inhalation assessment for children was used. For toddlers and the non-dietary single day (accidental) oral ingestion of granules, the acute neurotoxicity study in rats with a NOAEL of 50 mg/kg bw/d was selected for risk assessment (LOAEL of 150 mg/kg bw based on erythrocyte and brain cholinesterase inhibition and clinical signs of toxicity). The target MOE selected when using this study for the directly exposed child is 100; this accounts for standard UFs of 10 for interspecies extrapolation and 10 for intraspecies variability.

4.3.1 Mixer/loader/applicator exposure

Dermal and inhalation exposure estimates for homeowner application to residential turf are based on data from an ORETF study that has been evaluated by the PMRA and considered appropriate for use as surrogate data to estimate exposure of homeowners treating turf with bensulide. Exposure estimates are presented on the median measure of central tendency.

Exposure is calculated as the product of the unit exposure for a given scenario, the application rate and the area treated per day divided by the body weight. The average body weight of adult females was used because the severity of the toxic end points requires protection of the pregnant female and her unborn child. The risk is estimated by comparing a calculated MOE with a target MOE incorporating SFs protective of the most sensitive subpopulation.

The inhalation and dermal MOEs are above their respective target values of 100 and 300, and therefore, are not of concern.

4.3.2 Post-application exposure

Post-application exposure estimates were assessed for children, other residents and golfers. Post-application inhalation exposure is negligible. Post-application dermal exposure of children and adults to treated turf was estimated using generic transfer coefficients and bensulide-specific turf transferable residue (TTR) data. Transfer coefficients measure the relationship between exposure and TTRs for individuals engaged in a specific activity on treated turf. Toddlers are subject to orally ingesting residues on turf by mouthing grass, through hand-to-mouth activities and by ingesting soil. The oral exposure risk from ingestion of granules by children is not considered to be a typical exposure, but it is an acute, episodic exposure event of concern. However, post-application exposure risks are not of concern when bensulide is watered in after application. (Refer to Section 7.0, Proposed regulatory actions relating to human health, for mitigation proposals.)

4.4 Dietary risk assessment

In a dietary exposure assessment, the PMRA determines how much of a pesticide residue, including residues in milk and meat, may be ingested with the daily diet. These dietary assessments are age specific and incorporate the different eating habits of the population at various stages of life. For example, assessments take into account children's greater consumption of fruit, vegetables and juices for their body weight compared with adults.

Acute dietary risk is calculated considering food consumption and residue values in food. A probabilistic statistical analysis allows all possible combinations of consumption and residue levels to be combined to estimate a distribution of the amount of bensulide residue that might be eaten in a day. A value representing the high end (99.9^{th} percentile) of this distribution is compared with the ARfD, which is the dose to which an individual could be exposed on any given day and expect no adverse health effects. When the expected intake from residues is less than the ARfD, the expected intake is not considered to be of concern.

The chronic dietary risk is calculated by using the average consumption of different foods, and average residue values on those foods, over a 70-year lifetime. This expected intake of residues is compared with the acceptable daily intake (ADI), which is the dose to which an individual could be exposed over the course of a lifetime and expect no adverse health effects. When the expected intake from residues is less than the ADI, the expected intake is not considered to be of concern.

The acute (single day) dietary reference dose or ARfD for all populations is 0.5 mg/kg bw, based on a NOAEL of 50 mg/kg bw derived from an acute neurotoxicity study in rats (LOAEL of 150 mg/kg bw based on erythrocyte and brain cholinesterase inhibition and clinical signs of toxicity). A standard 100× UF is applicable, to account for interspecies extrapolation (10×) and intraspecies variability (10×).

The chronic (lifetime) dietary reference dose or ADI for all populations is 0.0017 mg/kg bw/d based on a NOAEL of 0.5 mg/kg bw/d from a 1-year toxicity study in dogs (LOAEL of 4 mg/kg bw/d based on brain cholinesterase inhibition in males and decreased weight gain in females). A total UF of 300× is applicable, to account for interspecies extrapolation (10×) and intraspecies variability (10×), as well as a 3× UF to account for the lack of a subchronic neurotoxicity study. The ADI provides an MOS of >10 000 to the rabbit oral developmental NOAEL of 20 mg/kg bw/d (LOAEL of 80 mg/kg bw/d based on increased late resorptions) and >7000 to the offspring NOAEL of 12.3 mg/kg bw/d from the oral rat multigeneration reproduction study (LOAEL of 86.5 mg/kg bw/d based on decreased viability). The ADI is thus considered protective of pregnant females and the young.

4.4.1 Dietary exposure

Acute and chronic dietary exposure and risk estimates were generated using the Dietary Exposure Evaluation Model™ software and updated consumption data from the Food and Drug Administration's Continuing Surveys of Food Intake of Individuals (1994–1998).

The acute dietary exposure was assessed in a Tier I analysis using the entire consumption distribution and using the default maximum residue limit (MRL) of 0.1 ppm for all commodities or crop groups on which bensulide is registered in the U.S. and in Canada. The acute PDI accounted for <2% (99.9th percentile) of the ARfD for all subpopulations.

The chronic dietary exposure was assessed using the default MRL of 0.1 ppm for all commodities or crop groups on which bensulide is registered in the U.S. and in Canada. The chronic PDI accounted for <40% of the ADI for all population subgroups, with children 1–6 years old being the most highly exposed subpopulation.

These chronic and acute dietary risk assessments demonstrated that there were no concerns for any population subgroup in Canada, including infants, children, teenagers, adults and seniors. In addition, no dietary concerns were evident for nursing or pregnant females or based on gender in general.

Although there is conservatism in the dietary risk assessments that use MRLs or U.S. tolerances as potential residues, there are data gaps in the field residue data to establish the MRLs to be used in compliance and enforcement activities. The data in the PMRA files do not meet the modern Residue Chemistry Guidelines and may not reflect current rates and methods of application. Monitoring has shown the residues of organophosphate pesticides on foods in trade seldom exceed (and are mostly well below) the current MRLs or the Canadian default level of 0.1 ppm. During the 4-year period (1994–1998), of the 44 379 shipments of fruits and vegetables tested by the CFIA, no domestic or imported samples had detectable levels of bensulide.

4.5 Aggregate risk assessment

4.5.1 Acute aggregate risk

Acute aggregate exposure to bensulide is comprised of dietary and drinking water exposures only.

Acute aggregate risk assessments do not incorporate residential exposure, as it is improbable that an individual would be exposed to high end dietary and residential exposure on the same day. A probabilistic model with supporting data would be required to include acute residential exposures.

The acute oral neurotoxicity study in rats with a NOAEL of 50 mg/kg bw (females) was selected for the acute aggregate risk assessment. A LOAEL of 150 mg/kg bw was established based on the inhibition of erythrocyte and brain cholinesterase and clinical signs. Standard UFs (10× for interspecies extrapolation and 10× for intraspecies variation) were used to establish a target MOE of 100.

The PMRA does not have sufficient reliable monitoring data to quantify the risk from drinking water. However, concentrations in drinking water were estimated using drinking water exposure models (see Section 5.3). A Canadian drinking water level of comparison (DWLOC) was derived from the overall allowable risk from residues permitted in the diet after considering the contribution by food. The DWLOC is the maximum concentration in drinking water that, when considered together with dietary exposure, does not exceed a level of concern based on the respective reference dose. For acute risk, the DWLOCs range from 4900 to 17400 µg/L. The estimated environmental concentration in drinking water, when only tees and greens of golf courses are treated with bensulide, is considerably less than the DWLOC. Thus, acute aggregate risk is not of concern.

4.5.2 Short-term aggregate risk

Short-term aggregate exposure to bensulide is comprised of contributions from food, residential exposure (dermal, inhalation and incidental oral components) and drinking water. The repeat-dose study of shortest duration with the lowest LOAEL (15 mg/kg bw/d) for brain cholinesterase inhibition was the 13-week dietary toxicity study in rats. This study had a NOAEL of 5 mg/kg bw/d, which was used for the short-term aggregate assessment. The use of the oral NOAEL to calculate an aggregate risk MOE may be conservative in that the study duration exceeds the time period of interest (up to 1 week) and thus may overestimate the hazard. Standard UFs (10× for interspecies extrapolation and 10× for intraspecies variation) were used to establish a target MOE of 100.

The chronic dietary exposure was considered representative of a typical exposure, since it represents the average daily exposure over an individual's lifetime. Ingestion of granules is not aggregated in the short-term oral scenario, as this is an episodic event rather than a typical exposure event. The dermal exposure was extrapolated to a systemic exposure by considering a 10% dermal absorption factor. Inhalation exposure and oral ingestion through dietary and non-dietary pathways are considered to be 100% absorbed. However, the contribution from inhalation exposure in post-application scenarios is considered to be negligible due to the low volatility of bensulide and the dilution effect of outdoor use patterns.

The calculated DWLOCs range from 60 to 1470 µg/L, with the most sensitive population subgroup being toddlers. The estimated environmental concentration in drinking water, when only tees and greens of golf courses are treated with bensulide, is below the lowest DWLOC calculated. Therefore, short-term aggregate exposure is not of concern when bensulide is watered in thoroughly.

4.5.3 Chronic aggregate risk

Chronic aggregate exposure to bensulide is comprised of dietary and drinking water exposures only. The limited use of bensulide on turf precludes the likelihood of chronic exposures. The one-year toxicity study in dogs with a NOAEL of 0.5 mg/kg bw was selected for the chronic aggregate risk assessment. A LOAEL of 4 mg/kg bw was established based on inhibition of brain cholinesterase in males and decreased weight gain in females. Standard UFs (10× for interspecies extrapolation and 10× for intraspecies variation) and a 3× UF to account for the lack of a subchronic neurotoxicity study were used to establish a total UF of 300.

The PMRA does not have sufficient reliable monitoring data to quantify the risk from drinking water. Concentrations in drinking water, however, were estimated by using drinking water exposure models (Section 5.3). A Canadian DWLOC was derived from the overall allowable risk from residues permitted in the diet after considering the contribution by food. For chronic risk, the calculated DWLOC ranged from 13 to 49 µg/L, the most sensitive population subgroup being non-nursing infants less than one year old. The estimated environmental concentration in drinking water, when only tees and greens of golf courses are treated with bensulide, is below the calculated DWLOCs. Thus, chronic aggregate risk is not of concern.

5.0 Environmental assessment

In characterizing the environmental risk of bensulide, the PMRA utilized a deterministic approach that characterizes the risk by the quotient method, in which, a risk quotient (RQ) is calculated as the ratio of the estimated environmental concentration (EEC) to the toxicity end point of concern. RQs less than 1 are considered as a low risk to non-target organisms, whereas RQs greater than 1 indicate some degree of risk.

In this assessment, EECs for aquatic and terrestrial ecosystems were based on maximum label rates (turf and cucumbers). Toxicity end points (acute or chronic) were chosen for the most sensitive species and used as surrogates for the range of species that can potentially be exposed following treatment with bensulide.

5.1 Environmental fate

Available data indicate that bensulide is persistent in the environment. On soil, the phototransformation of bensulide was negligible (half-life = 220 days). In soil, biotransformation was not an important route in the transformation of bensulide, as in aerobic soil, the dissipation time to 50% was 363 days and in anaerobic soil, 91% of the applied bensulide remained after 60 days. Although the transformation of bensulide was slow, the major transformation product in aerobic soil was bensulide oxon as observed in laboratory studies. This transformation product was detected in amounts of 13.8 and 10.1% at 270 and 360 days, respectively, which indicated it may be persistent in soil. In water, hydrolysis and phototransformation were not important routes in the transformation of bensulide as the reported half-lives were greater than 200 days.

Bensulide is non-volatile from moist soil and water as indicated by its Henry's Law Constant (1.7×10^{-8} atm·m^3/mole). It has the potential, however, to bioaccumulate as indicated by its octanol–water partition coefficient (log K_{ow} = 4.2). In fish, the bioconcentration factor (BCF) was 550–640 in different tissues. Under field conditions, bensulide is expected to be slightly mobile to immobile in soil; however, its major transformation product, bensulide oxon, is expected to have moderate to high mobility and thus has the potential to leach to groundwater and move off-target in surface runoff water.

5.2 Environmental toxicology

Laboratory studies demonstrated that bensulide was acutely toxic to some non-target organisms. In bees, bensulide was classified as highly toxic (contact lethal dose to 50% (LD_{50}) = 1.6 µg a.i./bee) and moderately toxic to highly toxic to aquatic invertebrates (lethal concentration to 50% (LC_{50}) = 62–3300 µg a.i./L) and fish (LC_{50} = 380–1100 µg a.i./L). In freshwater plants, the most sensitive species was *Lemna gibba* with an estimated no observed effect concentration (NOEC) of 13.6 µg a.i./L.

5.3 Drinking water assessment

Residues of bensulide in drinking water sources in Canada were estimated using Level 1 LEACHM and PRZM/EXAMS models. LEACHM was used to estimate the residues in groundwater, whereas the residues in reservoirs were estimated using PRZM/EXAMS. Residues in farm dugouts were not estimated as the use-pattern for bensulide does not include uses in the Canadian Prairies. In addition, bensulide use in cucumbers was not considered as a potential drinking water source as the total treated hectarage in Canada is very small (approximately 268 ha). For residues in groundwater, the concentration was

estimated to be 4.9 µg a.i./L for acute and chronic exposure. For residues in reservoirs, the acute and chronic exposure concentrations were estimated to be 364 and 97 µg a.i./L, respectively. These reservoir concentrations were based on one application per year at the highest label rate in turf (golf courses) and with the assumption that the entire watershed is treated with bensulide. Under operational conditions, however, only the tees and greens of golf courses are treated, thus, using this scenario, the acute and chronic concentrations of bensulide in reservoirs were estimated to be 14.6 and 3.9 µg a.i./L, respectively. These concentrations represent the maximum or upper bound exposure concentrations. An estimation of a minimum or lower bound exposure concentration is not possible for bensulide at this time as there is a lack of monitoring data both in Canada and the U.S. In addition, refined levels of the water models are currently not available.

5.4 Terrestrial assessment

The results of this screening level assessment identified various levels of risk to non-target terrestrial organisms exposed to bensulide.

Birds could be exposed to bensulide by ingestion of contaminated food (e.g., seeds, insects or grasses). Based on the acute oral toxicity of bensulide in birds (LD_{50} = 1386 mg a.i./kg; no observed effect level (NOEL) = 138.6 mg a.i./kg) and using standard PMRA exposure scenarios, it was determined that birds would have to consume contaminated food sources for 14 days for their population to be reduced by 50% (LD_{50}). For no observable effects on a population, birds can consume contaminated food for up to 1.4 days (NOEL). As the number of feeding days required for an adverse effect is greater than 1, there is a negligible risk to birds consuming contaminated food sources. It should also be noted that this assessment was based on the assumption that birds would be feeding exclusively on contaminated food. In addition, the assessment does not consider feeding preference or avoidance behaviour toward contaminated food as these data are not currently available.

Birds may also be exposed to bensulide through ingestion of formulated granules either intentionally for grit or unintentionally while foraging. By considering the number of granules to reach the acute NOEL (1663–2079 granules), however, it is not likely that birds would consume that many granules over a relatively short time period. Thus, low levels of risk are expected in birds ingesting formulated granules of bensulide.

Similarly, wild mammals could be exposed to bensulide by ingestion of contaminated food (e.g., grass, seeds and leafy plants). Based on the acute oral toxicity of bensulide in small mammals (LD_{50} = 312 mg a.i./kg; NOEL = 31.2 mg a.i./kg) and using standard PMRA exposure scenarios, it was determined that animals would have to consume contaminated food sources for 1.8 days for their population to be reduced by 50% (LD_{50}). For no observable effects on a population, animals can consume contaminated food for up to 0.18 days (NOEL). As the number of feeding days required for an adverse effect is less than 1, there is a risk to small mammals consuming contaminated food sources. It should be noted, however, that this assessment was based on the assumption that small mammals

would be feeding exclusively on contaminated food. In addition, the assessment does not consider feeding preference or avoidance behaviour toward contaminated food as these data are not currently available. Thus, more realistic exposure scenarios are required to refine the risk assessment for small mammals.

Mammals may also be exposed to bensulide by ingesting formulated granules unintentionally while foraging. By considering the number of granules to reach the acute NOEL (832–1040 granules), however, it is not likely that small mammals would consume that many granules over a relatively short time period. Thus, low levels of risk are expected in small mammals ingesting formulated granules of bensulide.

Bees and other beneficial insects may be exposed to bensulide through spray deposit. Based on the acute contact toxicity in bees (LD_{50} = 1.8 kg a.i./ha; NOEC = 0.18 kg a.i./ha), the RQs were calculated to be 37 and 83 for ground spraying in cucumbers and turf, respectively, and indicated that bensulide poses a high risk to terrestrial invertebrates according to the PMRA classification of risk.

Similarly, non-target terrestrial plant species may be exposed to bensulide through spray deposit. Based on the most sensitive crop species tested (soybean; effective concentration to 25% (EC_{25}) = 2.02 kg a.i./ha), the RQs were determined to be 3.3 (cucumbers) and 7.7 (turf), indicating that bensulide is a moderate risk to non-target terrestrial plant communities.

5.5 Aquatic assessment

The results of this screening level assessment identified various levels of risk to non-target aquatic organisms exposed to bensulide.

Aquatic organisms can be exposed to bensulide that enters aquatic systems through spray drift. In this assessment, the potential exposure was determined using a screening-level model to obtain EECs at three water depths (0.3, 1 and 3 m) for the maximum application rates in cucumbers and turf.

For laboratory-derived data, RQ values were based on estimates of the acute NOEC for the most sensitive species (i.e., 0.10 LC_{50}). In freshwater fish (NOEC = 38 µg a.i./L), the RQs were 6–59 (cucumbers) and 14–137 (turf), and indicated that bensulide would pose a moderate risk to very high risk. Similarly, in estuarine and marine fish (NOEC = 32 µg a.i./L), the RQs were 7–71 (cucumbers) and 16–161 (turf), which indicated a moderate to very high risk. In aquatic invertebrates (freshwater and estuarine and marine) and aquatic vascular plants, the RQs (17–833) indicated a high to very high risk.

5.6 Toxic Substances Management Policy

During the review of bensulide, the PMRA has taken into account the federal Toxic Substances Management Policy (TSMP)[2] and has followed its Regulatory Directive DIR99-03[3]. It has been determined that this active does not meet all the TSMP criteria for a Track-1 substance based on the following:

- Bensulide does not meet the criteria for bioaccumulation. The BCF in fish is 550–640 in various tissues (TSMP criterion >5000) and the octanol–water partition coefficient (log K_{ow}) is 4.2, which is below the TSMP Track-1 cut-off criterion of log $K_{ow} \geq 5.0$.

- Bensulide meets the criteria for persistence, as its half-life values in water (200–230 days) and soil (363 days) are above the TSMP Track-1 cut-off criteria for water (≥182 days) and soil (≥182 days).

- The toxicity of bensulide is addressed under Sections 4.0 and 5.2.

Technical bensulide contains no known microcontaminants or impurities identified as TSMP Track-1 substances.

5.7 Formulants in pest control products

Formulant issues are being addressed through PMRA formulant initiatives or the formulant policy under development, including:

- List 1 formulants are subject to removal from products as communicated to registrants of affected products in September 2001.

- Registrants of products containing nonylphenol ethoxylates are requested to replace nonylphenol ethoxylates with less harmful alternatives.

- Registrants of products containing aromatic petroleum distillates are required to identify the distillate on the label.

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[2] The federal Toxic Substances Management Policy is available through Environment Canada's Web site at: www.ec.gc.ca/toxics.

[3] *The PMRA's Strategy for Implementing the Toxic Substances Management Policy*, Dir99-03, is available through the Pest Management Information Service: Phone 1-800-267-6315 within Canada or 1-613-7363799 outside Canada (long distance charges apply); Fax (613) 736-3798; E-mail pminfoserv@hc-sc.gc.ca or through our Web site at www.hc-sc.gc.ca/pmra-arla.

- Other formulants, including List 2 formulants, formulation preservatives and allergens, will be subject to future regulatory action as outlined in the PMRA's proposed formulant policy, PRO2000-04 *Formulants Policy* (soon to be issued as a regulatory directive).

5.8 Environmental assessment conclusions

Bensulide poses the greatest risk to aquatic organisms. There is a moderate to very high risk (RQ = 6–161) in fish exposed to bensulide that enters aquatic systems through spray drift. In aquatic invertebrates and aquatic vascular plants, there is a high to very high risk (RQ = 17–833).

For terrestrial organisms, there are low levels of acute risk to birds ingesting bensulide-contaminated food or formulated bensulide granules. Similarly, there is a low level of acute risk to small mammals ingesting formulated bensulide granules. A risk was identified in small mammals ingesting bensulide-contaminated food; however, to determine the magnitude of this risk, development of more realistic exposure scenarios is required. A high risk (RQ = 37–83) was determined for bees and other beneficial insects exposed to bensulide through spray drift. A moderate risk (RQ = 3–8) was determined for non-target terrestrial plants exposed to spray drift.

5.9 Environmental risk mitigation

Mitigation of potential impacts on terrestrial ecosystems is difficult given that the non-target organisms frequent treated areas. In the case of bees, it may be possible to reduce the risk, as bees are not actively foraging when bensulide is applied (early spring or fall). A precautionary statement to alert applicators that bensulide, even though it is a herbicide, exhibits insecticidal properties should be included on the label (see Section 7.0, Proposed regulatory actions relating to environment, for proposed mitigation measures).

Bensulide can enter terrestrial and aquatic ecosystems through spray drift. The observance of buffer zones, however, can effectively mitigate the risk to off-site non-target organisms. Pesticide spray drift from ground application to habitats of concern was predicted using the data of Nordby and Skuterud (1975).[4] Based on the spray drift predictions and the most sensitive toxicity end point, buffer zones were calculated for mitigating the entry of bensulide into terrestrial and aquatic habitats. The most sensitive toxicity end points used in calculating buffer zones are the NOEC of 6.9 µg a.i./L (*Daphnia magna*) for aquatic habitats and the EC_{25} of 2.02 kg a.i./ha (soybean) for terrestrial habitats.

[4] Nordby, A. and R. Skuterud. 1975. The effects of boom height, working pressure, and wind speed on spray drift. Weed Research, **14**: 385–395.

From the predictions of the spray drift model for ground application, it was determined that a buffer zone is not required for terrestrial habitats; however, buffer zones of 13–42 m are required for protection of aquatic habitats depending on the depth of the water body (see Table 1, Section 7.0, Proposed regulatory actions relating to environment).

Currently, the buffer zones estimated for ground applications are based on a standard set of assumptions for spray configuration and weather conditions, yet many variable conditions exist at any spray site. To allow for increased flexibility, the PMRA is developing, together with the provinces, a proposal that would allow the applicator to consider the actual values for spray characteristics, wind speed and, to some extent, the sensitivity of the habitat to be protected. There would also be the possibility of factoring in advances in spray technology that can reduce drift (e.g., low drift nozzles, shrouds). Consequently, individual applicators could reduce the size of the spray buffer zone if they employ some of these measures to protect the habitat in question. With the use of shrouds and cones on spray booms, it has been estimated that the buffer zones can be reduced by 70 and 30%, respectively. Thus the recommended buffer zones of 13–42 m could be reduced to 4–13 m or 9–29 m with the use of shrouds or cones, respectively, depending on the water depth of the aquatic system to be protected (see Tables 2 and 3, Section 7.0, Proposed regulatory actions relating to environment).

6.0 Value

The total amount of bensulide used in Canada on an annual basis (average of 1986, 1988, 1990 and 1994 data) was 8 tonnes a.i. per year, although usage declined to 2.3 tonnes a.i. in 1994. The total for the U.S. has been 250 tonnes a.i. per year.

Information regarding actual field use of organophosphates on food crops in Canada was obtained from a survey conducted by the PMRA in 1998 with the cooperation of the provincial governments, and from consultation with crop production specialists. There was no reported bensulide use in this survey.

Further consultations with provincial research and extension personnel showed that use of bensulide is not very common in cucumbers. Cucumber producers rely mainly on the modern graminicides such as sethoxydim and fluazifop-*p*-butyl to control grass weeds. However, when the Ontario Vegetable Growers Marketing Board (OVGMB) was contacted, a strong need for maintaining bensulide as a weed management tool in cucumbers was expressed. Bensulide is on the recommended list for the growers' associations, OVGMB and the Fédération Québécoise des Producteurs de Fruits et Légumes de Transformation. The mode of action of bensulide is unique in weed resistance management in field-grown cucumbers in eastern Canada. Bensulide is the only pre-emergent herbicide registered for use on cucumber crops in Canada. It is used as

a preplant treatment; therefore, weeds are controlled before any competition takes place. On the other hand, sethoxydim and fluazifop-*p*-butyl are post-emergence herbicides; thus, the cucumber crop may be stressed by weed competition before these herbicides could be applied.

Informal consultations with provincial research and extension personnel showed that use of bensulide is not very common in turf. In turf management, although two modern alternatives, dithiopyr and fenoxaprop-*p*-ethyl, are available for crabgrass control, the continuing registration of bensulide offers another mode of action for weed resistance management.

The use of Commercial Class bensulide on turf is uncommon due to its high cost and the fact it must be used before the grass weed problem is evident. Well maintained ornamental grasses can out-compete weeds. For these reasons, Commercial Class bensulide is rarely used on residential lawns. The principal use of bensulide on turf is on golf greens (where uniform playing surfaces are important aesthetically and for putting), to control crabgrass before it has a chance to grow. Other herbicides that control crabgrass do so after the crabgrass has emerged, thus leaving unsightly brown patches in the tees and greens. Bensulide is generally not applied to fairways due to its prohibitive cost. There is limited use of Commercial Class bensulide on commercial sod farms.

The PMRA has limited information on the extent of use of the one Domestic Class bensulide product, but it is assumed to be small for the reasons discussed above for Commercial Class bensulide.

7.0 Proposed regulatory action

The PMRA has determined that the aggregate risks for bensulide are acceptable provided that the mitigation measures proposed below are adopted. As indicated earlier in the document, these proposed actions represent an interim decision until a full reassessment of the cumulative risk from all organophosphate pesticides is completed. The acceptable uses for bensulide products, together with proposed mitigation measures and use limitations, are presented in Appendices III and IV.

7.1 Proposed regulatory actions relating to human health

1. Labels of pesticide products carry statements regarding symptoms of poisoning and treatment, which are especially important for those who may be overexposed when working with the product in a commercial or industrial setting, e.g., mixers/loaders who handle the more concentrated forms. Based on the toxicological assessments, the label text of the bensulide containing products should be expanded and (or) standardized, as follows:

   "Toxicological information:

   Bensulide is a cholinesterase inhibitor. Typical symptoms of overexposure to cholinesterase inhibitors include headache, nausea, dizziness, sweating, salivation, runny nose and eyes. This may progress to muscle twitching, weakness, tremor, in coordination, vomiting, abdominal cramps and diarrhea in more serious poisonings. A life-threatening poisoning is signified by loss of consciousness, incontinence, convulsions and respiratory depression with a secondary cardiovascular component. Treat symptomatically. If exposed, plasma and red blood cell cholinesterase tests may indicate degree of exposure (baseline data are useful). Atropine, only by injection, is the preferable antidote. Oximes, such as Pralidoxime Chloride, may be therapeutic if used early; however, use only in conjunction with atropine. In cases of severe acute poisoning, use antidotes immediately after establishing an open airway and respiration. With oral exposure, the decision of whether to induce vomiting or not should be made by an attending physician."

2. For those products that contain greater than 10% petroleum distillates, the following text should also be added to the Toxicological Information section (placed at the end of the paragraph presented above), as an additional aid to the attending physician:

   "**NOTE:** Product contains a petroleum distillate solvent."

3. Mitigation measures:

   a. Measures to mitigate worker risks from turf use (golf course and residential turf):

      - Bensulide should not be applied by backpack sprayer.

      - Prohibit treatment of large turf areas, such as parks, with the exception of golf courses (see restrictions below for golf courses).

- Golf course use should be limited to tees and greens, but not applied by low pressure turf gun.

- Coveralls must be worn when applying bensulide-containing products.

b. Measures to mitigate residential risks:

- All bensulide formulations must be watered in.

c. Labelling pertaining to agricultural use (cucumbers):

- Use should be restricted to field cucumbers only.

- There should be a plantback interval of 120 days, and the soil must be tilled to a depth of 10 cm prior to replanting.

7.2 Proposed regulatory actions relating to dietary risk

Currently, there are no specific maximum residue limits (MRLs) for bensulide in food. Consequently, any residues on imported or domestic commodities must not exceed 0.1 ppm, a default value specified by the Food and Drug Regulations subsection B.15.002(1).

In general, when the re-evaluation of a pesticide has been completed, the PMRA intends to prevent unauthorized use of the pesticide by recommending new MRLs at the limit of quantification for any agricultural commodities not approved for continued treatment in Canada. Additional MRLs for import purposes will be considered if sufficient data are provided by interested parties to allow a reassessment of those residues. The U.S. EPA undertakes similar action in such circumstances. Proposed amendments to the Food and Drug Regulations reflecting these MRLs will be published in the Canada Gazette.

In the case of bensulide, continuing registration is proposed only for products used to treat field cucumbers. Based on the available information, the PMRA will recommend the following:

- that the residue of concern for bensulide be defined as bensulide (O,O-di-isopropyl S-2-phenylsulfonylaminoethyl phosphorodithioate) and bensulide oxygen analog (O,O-di-isopropyl S-2-phenylsulfonylaminoethyl phosphorothioate)

- that an MRL for bensulide in cucumbers be established at 0.1 ppm; and

- that an MRL be established at the limit of quantification of bensulide residues for all other agricultural commodities (i.e., 0.05 ppm), unless additional data are provided to support additional import MRLs.

Parties interested in supporting an MRL to allow imports of other commodities treated with bensulide should contact the PMRA during the consultation period to discuss the submission of appropriate data.

7.3 Proposed regulatory actions relating to the environment

1. The following precautionary statements should be included on all bensulide product labels to mitigate the risk to bees:

   > "Bensulide is toxic to bees exposed to direct treatment. Do not apply when bees are present in the area to be treated."

2. The labels for all liquid bensulide formulations should include the following statements to reduce the entry of bensulide into aquatic systems:

   > "Ground Boom Application:
   >
   > Avoid overspray or drift to sensitive aquatic habitats. An appropriate buffer zone from Table 1 is required between the downwind point of direct application and the closest edge of sensitive aquatic habitats including sloughs, coulees, ponds, prairie potholes, lakes, rivers, streams, reservoirs and wetlands that are situated on the periphery of the treated area. Also included are natural bodies of water that flow through and exit treated areas (e.g., golf courses). Do not contaminate any of these habitats when cleaning and rinsing spray equipment or containers. Any self-contained bodies of water within the golf course property do not require buffer zones.
   >
   > Do not apply during periods of dead calm or when winds are gusty.
   >
   > Buffer zones for ground applications are dependent on the application rate specific to the crop and the depth of the aquatic ecosystem to be protected. It is the applicator's responsibility to determine the maximum depth of the aquatic ecosystem."

Table 1 **Buffer zones (in metres) for protection of aquatic habitats of various water depths for ground application of bensulide in different crops without the use of shrouds or cones**

Crop	Ground buffer zone (m)		
	Water depth <1 m	Water depth 1–3 m	Water depth >3 m
Cucumbers	34	23	13
Turf	42	31	21

Table 2 **Buffer zones (in metres) for protection of aquatic habitats of various water depths for ground application of bensulide in different crops with the use of shrouds.**

Crop	Ground buffer zone (m)		
	Water depth <1 m	Water depth 1–3 m	Water depth >3 m
Cucumbers	10	7	4
Turf	13	9	6

Table 3. **Buffer zones (in metres) for protection of aquatic habitats of various water depths for ground application of bensulide in different crops with the use of cones.**

Crop	Ground buffer zone (m)		
	Water depth <1 m	Water depth 1–3 m	Wter depth >3 m
Cucumbers	24	16	9
Turf	29	22	15

7.4 Proposed regulatory action relating to value

The labels for all bensulide products should reflect the following:

- All bensulide formulations must be watered in to be efficacious.

8.0 Additional data requirements

As also indicated in Section 7.2, residue data are needed to determine appropriate import MRLs for any commodity other than cucumber.

The following confirmatory data would be required. Scientifically based rationales for data waivers may also be acceptable for some of the following data requirements.

8.1 Data requirements related to chemistry

- A Statement of Product Specification Form is required in accordance with Table 1 in Section 2.12 of DIR98-04, *Chemistry requirements for the registration of a technical grade of active ingredient or an integrated system product* (DACO 2.12.2).

- Data from five recent batches of the TGAI analysed to 0.1%, as per Section 2.13.3 of DIR98-04, are required in support of the specifications (DACO 2.13.3).

8.2 Data requirements related to toxicology

The following confirmatory data would be required to support the continued registration of bensulide and to support any expansion of bensulide use:

- a short-term neurotoxicity study (DACO 4.5.11)
- a developmental neurotoxicity study (DACO 4.5.12)

Although not critical to the current bensulide re-evaluation, the following data may be required to support any expansion of bensulide use:

- improved identification of biotransformation products (DACO 4.5.9)
- a short-term inhalation study (DACO 4.3.6 or 4.3.7)

8.3 Data requirements related to exposure

- Plant metabolism studies are required to confirm whether or not the bensulide oxygen analog need be included in the definition of the residue of concern (DACO 6.3).

- Storage stability studies are required to evaluate the stability of residues in stored frozen samples, especially for cucumbers (DACO 7.3).

- A validated analytical method is required for the analysis of bensulide and bensulide oxygen analog in agricultural commodities (DACO 7.2.2).

- Data in support of import MRLs would be required for all imported commodities on which bensulide is used (DACO 7.4.1).

8.4 Data requirements related to environmental risk

Although not critical to the current bensulide re-evaluation, the following data may be required to support any expansion of bensulide use:

- Terrestrial field studies of dissipation/accumulation in an area representative of use in Canada (DACO 8.3).

9.0 Proposed re-evaluation decision

The PMRA has carried out an assessment of available information and has concluded that the use of bensulide and its end-use products on cucumber and turf does not entail an unacceptable risk to human health and the environment pursuant to Section 20 of the PCP Regulations, provided that the proposed mitigation measures described in this document are implemented. Further measures may be necessary or proposed pending the outcome of the cumulative risk assessment for the organophosphates, which share a common mechanism of toxicity, and pending refinements to environmental risk assessment methodologies.

It is proposed that the Food and Drug Regulations be amended so that, with the exception of cucumber, food with quantifiable residues of bensulide cannot be sold in Canada once Canadian use has been phased out, unless additional data to support bensulide residues in imported food are provided.

The PMRA will accept written comments of this proposal up to 60 days from the date of publication of this document to allow interested parties an opportunity to provide input into the proposed re-evaluation decision for these products.

List of abbreviations

ADI	acceptable daily intake
a.i.	active ingredient
ARfD	acute reference dose
atm	atmospheres
BCF	bioconcentration factor
bw	body weight
CFIA	Canadian Food Inspection Agency
d	day
DACO	data code
DWLOC	drinking water level of comparison
EC	emulsifiable concentrate
EC_{25}	effective concentration to 25%
EEC	expected environmental concentration
EP	end-use product
GR	granular
ha	hectare
kg	kilogram
K_{ow}	octanol–water partition coefficient
LC_{50}	lethal concentration to 50%
LD_{50}	lethal dose to 50%
L	litre
LOAEL	lowest observable adverse effect level
m	metre
mg	milligram
MOE	margin of exposure
MOS	margin of safety
MRL	maximum residue limit
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
ORETF	Outdoor Residential Exposure Task Force
OVGMB	Ontario Vegetable Growers Marketing Board
PCP	Pest Control Products
PCPA	*Pest Control Products Act*
PDI	potential daily intake
PHED	Pesticide Handlers' Exposure Database
PMRA	Pest Management Regulatory Agency
PPE	personal protective equipment
ppm	parts per million
RQ	risk quotient
SF	safety factor

TGAI	technical grade active ingredient
TSMP	Toxic Substances Management Policy
TTR	turf transferable residue
µg	microgram

Appendix I Bensulide products currently registered

Registrant	Registration number	Guarantee	Product name	Class
Gowan	20206	92%	Betasan Technical Selective Herbicide	Technical
Gowan	21346	690 g/L	Betasan Manufacturing Concentrate	Manufacturing concentrate
Gowan	9057	EC 480 g/L	Betasan 4.8-E Emulsifiable Liquid Selective Herbicide	Commercial
Gowan	10806	GR 12.5%	Betasan 12.5-G Granules Selective Herbicide	Commercial
Gowan	14113	EC 480 g/L	Prefar 4.8-E Emulsifiable Liquid (Selective Herbicide)	Commercial
Scott	14561	GR 8.5%	Scotts Proturf Granular Weedgrass Preventer	Commercial
Gowan	21184	EC 145 g/L	Betasan Crabgrass Preventer	Domestic

Appendix II Toxicology end points for health risk assessment for bensulide

Exposure scenario	Dose (mg/kg bw/d)	End point	Study	UF/SF or MOE[e]
Acute dietary	NOAEL = 50	Clinical signs, erythrocyte and brain cholinesterase inhibition	Acute neurotoxicity: rat	100
	ARfD = 0.5 mg/kg bw			
Chronic dietary	NOAEL = 0.5	Decreased weight gain and brain cholinesterase inhibition	1-year oral toxicity: dog	300
	ADI = 0.0017 mg/kg bw/d			
Short-term[a] incidental oral	Oral NOAEL = 5	Brain cholinesterase inhibition	13-week oral toxicity: rat	100
Short-term[a] dermal	Dermal NOAEL = 50	Brain cholinesterase inhibition	21-day dermal toxicity: rat	100 for children, 300 for adults
Intermediate-term[b] dermal[c]	Oral NOAEL = 3	Hepatic effects	13-week oral toxicity: dog	300
Short-term[a] inhalation[d]	Oral NOAEL = 5	Brain cholinesterase inhibition	13-week oral toxicity: rat	100
Intermediate-term[b] inhalation[d]	Oral NOAEL = 3	Hepatic effects	13-week oral toxicity: dog	300
Aggregate[a]	Oral NOAEL = 5	Brain cholinesterase inhibition	13-week oral toxicity: rat	100

[a] Duration of exposure is 1–7 days.

[b] Duration of exposure is 8 days to 2 months.

[c] Since an oral NOAEL was selected, a dermal absorption factor of 10% should be used in route-to-route extrapolation.

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

[e] UF and SF refer to total of UFs and SFs for dietary assessments; MOE refers to desired MOE for occupational or residential assessments.

Appendix III Use standard for commercial class products containing bensulide

(**NOTE:** The information in this appendix summarizes the acceptable uses, limitations and precautions for commercial class products containing bensulide, but does not identify all label requirements for such products. Registrants are referred to the PMRA Registration Handbook for further guidance on label requirements for pest control products.)

COMMON NAME: bensulide

CHEMICAL NAME: *O,O*-di-isopropyl *S*-2-phenylsulphonylamidoethyl phosphorodithioate

FORMULATION TYPE:

EC	emulsifiable concentrate
GR	granular

SITE CATEGORIES:

Terrestrial Food Crops	14
Turf	30

GENERAL LIMITATIONS:

The product should be used only for recommended purposes and at recommended rates. Do not exceed label rates.
Do not store near seeds or fertilizer.
Use on mineral soils only.
Do not apply by aircraft.
Do not contaminate irrigation water or water used for domestic purposes.
Do not pour near heat or open flames.
Uses on turfgrass are restricted to residential lawns and tees and greens of golf courses only.

TOXICOLOGICAL INFORMATION:

Bensulide is a cholinesterase inhibitor. Typical symptoms of overexposure to cholinesterase inhibitors include headache, nausea, dizziness, sweating, salivation and runny nose and eyes. This may progress to muscle twitching, weakness, tremor, in coordination, vomiting, abdominal cramps and diarrhea in more serious poisonings. A life-threatening poisoning is signified by loss of consciousness, incontinence, convulsions and respiratory depression with a secondary cardiovascular component. Treat symptomatically. If exposed, plasma and red blood cell cholinesterase tests may indicate degree of exposure (baseline data are useful). Atropine, only by injection, is the preferable antidote. Oximes, such as Pralidoxime Chloride, may be therapeutic if used early; however, use only in conjunction with atropine. In cases of severe acute poisoning, use antidotes immediately after establishing an open airway and respiration. With oral exposure, the decision of whether to induce vomiting or not should be made by an attending physician.

[For those products that contain greater than 10% petroleum distillates, the following text should also be added to the TOXICOLOGICAL INFORMATION section (placed at the end of the paragraph presented above) as an additional aid to the attending physician:

NOTE: Product contains a petroleum distillate solvent.]

PROTECTIVE CLOTHING AND EQUIPMENT:
For all persons handling GR and EC formulations: Persons handling this product must wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes. Rinse gloves before removal.

Coveralls over long sleeves and long pants should also be worn when mixing, loading and applying to turf (residential lawns or golf courses).

ENVIRONMENTAL HAZARDS:
Bensulide is toxic to bees exposed to direct treatment. Do not apply when bees are present in the area to be treated.

Toxic to fish and other aquatic organisms. Do not contaminate any body of water by direct application, cleaning of equipment or disposal of wastes and containers.

BUFFER ZONE INFORMATION (FOR EC FORMULATIONS ONLY):

Ground Boom Application:

Avoid overspray or drift to sensitive aquatic habitats. An appropriate buffer zone from Table 1 is required between the downwind point of direct application and the closest edge of sensitive aquatic habitats including sloughs, coulees, ponds, prairie potholes, lakes, rivers, streams, reservoirs and wetlands that are situated on the periphery of the treated area. Also included are natural bodies of water that flow through and exit treated areas (e.g., golf courses). Do not contaminate any of these habitats when cleaning and rinsing spray equipment or containers. Any self-contained bodies of water within the golf course property do not require buffer zones.

Do not apply during periods of dead calm or when winds are gusty.

Buffer zones for ground applications are dependent on the application rate specific to the crop and the depth of the aquatic ecosystem to be protected. It is the applicator’s responsibility to determine the maximum depth of the aquatic ecosystem.

Table 1. Buffer zones (in metres) for the protection of aquatic habitats of various water depths for ground application of bensulide in different crops without the use of shrouds or cones

Crop	Ground buffer zone (m)		
	Water depth <1 m	Water depth 1–3 m	Water depth >3 m
Cucumbers	34	23	13
Turf	42	31	21

Table 2. Buffer zones (in metres) for the protection of aquatic habitats of various water depths for ground application of bensulide in different crops with the use of shrouds

Crop	Ground buffer zone (m)		
	Water depth <1 m	Water depth 1–3 m	Water depth >3 m
Cucumbers	10	7	4
Turf	13	9	6

Table 3. Buffer zones (in metres) for the protection of aquatic habitats of various water depths for ground application of bensulide in different crops with the use of cones

Crop	Ground buffer zone (m)		
	Water depth <1 m	Water depth 1–3 m	Water depth >3 m
Cucumbers	24	16	9
Turf	29	22	15

ACCEPTABLE USES FOR BENSULIDE:

Section 1. Field crops
Section 2. Turf

SITES AND PESTS	RATES (AS ACTIVE) AND DIRECTIONS
1. FIELD CROPS	
CUCUMBER (field)	EC formulation: Do not apply in combination with fluid fertilizers. Use on mineral soils only. Do not apply more often than once every 12 months. A plantback interval of 120 days must be observed between application and planting of rotational crops. Soil must be tilled to a depth of 10 cm prior to replanting to rotational crops. To avoid crop injury, rotate only to other cucurbits, peppers, cole crops, carrots, lettuce or tomatoes.
Barnyard grass, crabgrass, foxtail	EC formulation: 5760–6720 g a.i. in 100–500 L/ha Apply as a preplant application. Apply to well worked soil that is dry enough to permit thorough incorporation. Incorporate to the depth of 2.5–5 cm before planting. Rates of application are presented on a broadcast basis; reduce rate proportionally for band treatment.
Tank-mix with Alanap (naptalam) for the control of: barnyard grass, crabgrass, foxtail, chickweed, lamb's quarters, mustards, redroot pigweed, purslane, ragweed, shepherd's purse	EC formulation: Apply as a preplant application. Apply 4560–6720 g a.i./ha of bensulide as a tank-mix with 2280–4560 g a.i./ha of naptalam in sufficient water (100–400 L/ha) to provide sufficient coverage. Incorporate lightly (1–3 cm) into the soil prior to planting. Use the lower application rates in light (sandy) soil and higher rates in heavier (clay) soil. Rates of application are presented on a broadcast basis; reduce rate proportionally for band treatment. Follow all use directions and precautions that appear on the labels for the bensulide and naptalam tank-mix products. Where the labels for the two tank-mix partners have different precautions or limitations, the most restrictive precautions and limitations must be followed.

SITES AND PESTS	RATES (AS ACTIVE) AND DIRECTIONS
2. TURF	
GOLF COURSES (tees and greens)	For use only on tees and greens of golf courses. Do not use on putting greens composed of 50% or more annual bluegrass. Apply only to well established turfgrass. On newly planted areas, wait until the grass has been mowed at least twice and has achieved good coverage. After application, avoid any severe aerating or raking that might disturb the surface and break the chemical barrier. Delay seeding, sprigging or sodding for 1 year after application. Application must precede emergence of weeds from the soil. This product does not control established weeds. Remove leaves, dead tall grass and other debris before applying. Do not apply more than once yearly. This product will not be effective unless it is watered in for 10–15 min after application. For safety reasons, water this product in as soon as possible following application and do not allow children or pets on treated areas until dry following the watering. EC formulation: This product may only be broadcast applied by ground boom sprayer. Apply by low pressure handwand for spot treatment only. Do not apply with a low pressure turf gun or backpack sprayer. GR formulation: This product may only be broadcast applied by tractor-drawn spreader. Apply by push-type spreader for spot treatment only.
Annual bluegrass	Apply in late summer or early fall, before germination. EC formulation: 144 g a.i. in 25–50 L/100 m^2 GR formulation: 140–156 g a.i./100 m^2
Crabgrass (hairy, smooth)	Apply any time from fall (September or October) through early spring, prior to crabgrass emergence. EC formulation: 110 g a.i. in 25–50 L/100 m^2 GR formulation: 156 g a.i./100 m^2
Barnyard grass, foxtail (green, yellow)	Apply in fall, winter or spring before germination. GR formulation: 140 g a.i./100 m^2

SITES AND PESTS	RATES (AS ACTIVE) AND DIRECTIONS
RESIDENTIAL LAWNS	For use only on residential lawns. Do not use on turfgrass in parks, recreational areas or other public sites [with exception of golf courses, see above]. Apply only to well established turfgrass. On newly planted areas, wait until the grass has been mowed at least twice and has achieved good coverage. After application, avoid any severe aerating or raking that might disturb the surface and break the chemical barrier. Delay seeding, sprigging or sodding for 1 year after application. Application must precede emergence of weeds from the soil. This product does not control established weeds. Remove leaves, dead tall grass and other debris before applying. Do not apply more than once yearly. This product will not be effective unless it is watered in for 10–15 min after application. For safety reasons, water this product in as soon as possible following application and do not allow children or pets on treated areas until dry following the watering. EC formulation: This product may be applied by ground boom, low pressure turfgun or handwand. Do not apply with a backpack sprayer. GR formulation: This product may be applied by tractor-drawn or push-type spreader.
Annual bluegrass	Apply in late summer or early fall, before germination. EC formulation: 144 g a.i. in 25–50 L/100 m^2 GR formulation: 140–156 g a.i./100 m^2
Crabgrass (hairy, smooth)	Apply any time from fall (September or October) through early spring, prior to crabgrass emergence. EC formulation: 110 g a.i. in 25–50 L/100 m^2 GR formulation: 156 g a.i./100 m^2
Barnyard grass, foxtail (green, yellow)	Apply in fall, winter or spring before germination. GR formulation: 140 g a.i./100 m^2

Appendix IV Use standard for domestic class products containing bensulide

(**NOTE:** The information in this appendix summarizes the acceptable uses, limitations and precautions for domestic class products containing bensulide, but does not identify all label requirements for such products. Registrants are referred to the PMRA Registration Handbook for further guidance on label requirements for pest control products.)

COMMON NAME: bensulide

CHEMICAL NAME: *O,O*-di-isopropyl *S*-2-phenylsulphonylamidoethyl phosphorodithioate

FORMULATION TYPE: EC emulsifiable concentrate

SITE CATEGORIES: Turf 30

GENERAL LIMITATIONS:
Do not allow spray to drift onto desirable trees and shrubs, vegetable gardens or flower beds.
Use on mineral soils only.
Do not contaminate irrigation water or water used for domestic purposes.

ENVIRONMENTAL HAZARDS:
Toxic to fish. Do not contaminate any body of water by direct application, cleaning of equipment or disposal of wastes and containers. Leave a buffer zone of untreated ground in areas draining into bodies of water.

TOXICOLOGICAL INFORMATION:
Bensulide is a cholinesterase inhibitor. Typical symptoms of overexposure to cholinesterase inhibitors include headache, nausea, dizziness, sweating, salivation and runny nose and eyes. This may progress to muscle twitching, weakness, tremor, in coordination, vomiting, abdominal cramps and diarrhea in more serious poisonings. A life-threatening poisoning is signified by loss of consciousness, incontinence, convulsions and respiratory depression with a secondary cardiovascular component. Treat symptomatically. If exposed, plasma and red blood cell cholinesterase tests may indicate degree of exposure (baseline data are useful). Atropine, only by injection, is the preferable antidote. Oximes, such as Pralidoxime Chloride, may be therapeutic if used early; however, use only in conjunction with atropine. In cases of severe acute poisoning, use antidotes immediately after establishing an open airway and respiration. With oral exposure, the decision of whether to induce vomiting or not should be made by an attending physician.

[For those products that contain greater than 10% petroleum distillates, the following text should also be added to the TOXICOLOGICAL INFORMATION section (placed at the end of the paragraph presented above) as an additional aid to the attending physician:

NOTE: Product contains a petroleum distillate solvent.]

PROTECTIVE CLOTHING AND EQUIPMENT:
For good hygiene practice, persons applying this product should wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes. Rinse gloves before removal.

DIRECTIONS FOR USE:

SITES AND PESTS	RATES (AS ACTIVE) AND DIRECTIONS
RESIDENTIAL LAWN	EC formulation: For use only on residential lawns. Do not use on turfgrass in parks, recreational areas or other public sites. Apply only to well established turfgrass. Do not apply to grass less than 3 months old. Application must precede the emergence of weeds from the soil. This product does not control established weeds. Remove leaves, dead tall grass and other debris before applying. After application, avoid any severe aerating or raking that might disturb the surface and break the chemical barrier. Delay seeding, sprigging or sodding for 1 year after application. Do not apply more than once yearly. This product will not be effective unless it is watered in for 10–15 min after application. For safety reasons, water this product in as soon as possible following application and do not allow children or pets on treated areas until dry following the watering.
Crabgrass	EC formulation: 145 g a.i./100 m^2 Apply in late fall or early spring before crabgrass seed germinates. Application equipment: Apply by hose-end applicator. Apply spray solution evenly over the surface of the lawn.