



The PMRA Initiative for Reduced-Risk Pesticides

The purpose of this regulatory directive is to inform applicants, provinces and territories, user groups, and other interested parties that the North American Free Trade Agreement (NAFTA) Joint Review Programs for Reduced-Risk Pesticides will be extended by the Pest Management Regulatory Agency (PMRA) to include submissions made to the PMRA only. The program is designed to encourage pesticide manufacturers to apply for Canadian registration of reduced-risk products that are currently available in the United States (U.S.) Canada will use the same criteria as the U.S. Environmental Protection Agency (EPA) to determine eligibility of chemicals for the reduced-risk program and recognize the U.S. EPA's biopesticide designation, thus further harmonizing the approaches between the two countries. Through this program, the PMRA will also commit to shorter review timelines for products that have been shown to qualify as a reduced-risk chemical or biopesticide.

The reduced-risk or biopesticide designation does not mean reduced from normal data requirements or no data requirements. In addition, any product submission with a reduced-risk or biopesticide designation will undergo a thorough evaluation and risk assessment. The expedited review times given to reduced-risk products will not compromise Canadian safety standards in any way. As with all pesticides, registration will only be considered if the proposed product meets current health and environmental safety standards..

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Foreword

It is the goal of the Pest Management Regulatory Agency (PMRA) to reduce the risk to Canadians, particularly children, from pesticides. This will be achieved by: using the newest approaches in risk assessment, which include additional safety factors applied when assessing the risks to children, aggregating exposure from food, water and residential sources, and doing cumulative risk assessments on pesticides that have a common mechanism of toxicity; reducing the use of the highest-risk pesticides; making lower-risk pesticides available; and fostering the use of alternative approaches to pest control.

The purpose of this regulatory directive is to inform applicants, provinces and territories, user groups, and other interested parties that the North American Free Trade Agreement (NAFTA) Joint Review Programs for Reduced-Risk Pesticides will be extended by the PMRA to include submissions made to the PMRA only. The same criteria that are already in place in the joint review programs will be used and are included in this directive for the convenience of applicants. Canadian submissions for products with uses that are identical to those determined by the United States Environmental Protection Agency (U.S. EPA) to be reduced-risk will receive the same designation in Canada upon receipt of the U.S. EPA decision and the information upon which it was based.

The program is designed to encourage pesticide manufacturers to apply for Canadian registration of reduced-risk products that are currently available in the U.S. Canada will use the same criteria as the U.S. EPA to determine eligibility of chemicals for the reduced-risk program and recognize the U.S. EPA's biopesticide designation, thus further harmonizing the approaches between the two countries. Through this program, the PMRA will also commit to shorter review timelines for products that have been shown to qualify as a reduced-risk chemical or biopesticide.

The reduced-risk or biopesticide designation does not mean reduced from normal data requirements or no data requirements, and an adequate data package with any submission is required. In addition, any product submission with a reduced-risk or biopesticide designation will undergo a thorough evaluation and risk assessment. The expedited review times given to reduced-risk products will not compromise Canadian safety standards in any way. As with all pesticides, registration will only be considered if the proposed product meets current health and environmental safety standards.

In addition, the PMRA recognizes that the expansion of these reduced-risk pesticides into minor uses is important to many Canadian growers, and the PMRA will continue to work with the U.S. EPA to harmonize registration of these minor uses. The number of minor-use registrations will be very dependent upon the generation of the limited but necessary data to support them, and growers are encouraged to continue to work through the U.S. Interregional Research Project No. 4 (IR4) to obtain these data. The PMRA will work closely with Agriculture and Agri-Food Canada (AAFC), the IR4 program and growers to encourage the submission of reduced-risk minor-use products, and with the U.S. EPA to expedite registration.

It is expected that this program will result in the registration of an increased number of reduced-risk products for use in horticulture, which is traditionally considered to be a minor use market, and in the urban use area.

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1.0 The NAFTA joint review programs for reduced-risk pesticides

The PMRA recognized the need to encourage registration of new reduced-risk pesticides and acted upon a government commitment to pursue harmonization as one of the key means of achieving efficiencies and facilitating access to new lower-risk technology. It also understood the need for Canadian growers to have access to the new technologies at the same time as their U.S. counterparts. These were the primary reasons that Canada, the U.S., and Mexico focussed first on implementing programs for reduced-risk products through the NAFTA Technical Working Group (TWG). Significant progress has been made in harmonizing the registration activities, and the following programs (Appendix I) relevant to reduced-risk pesticides have been introduced:

- **Joint Review Program for Reduced-Risk Chemicals, 1996**
Details on how registrants can apply to use this program are outlined in Appendix I. The benefit of having joint reviews is that the product is available to growers on both sides of the border at the same time. To encourage registrants to use this program, the PMRA reduced its review time from 18 months to 12 months for reduced-risk chemicals with one active ingredient and one or two end-use products.
- **Joint Review Program for Pheromones and Microbials, 1997**
Details on how registrants can apply to use this program are outlined in Appendix I. To encourage registrants to use this program, the PMRA reduced its review time from 18 months to 12 months.
- **Joint Review Program for Minor-Use (MU) Pesticides**
A pilot MU joint review has recently been completed and resulted in the simultaneous registration in the U.S. and Canada of fenhexamid on crop Group 13 A (caneberries). Procedures on how to use this program are now being finalized under the auspices of the NAFTA TWG. In the meantime the U.S. EPA and the PMRA are ready to entertain requests for other pilot MU joint reviews. This program will be an important way to expedite registration of reduced-risk pesticides.
- **PMRA User-Requested Minor-Use Program (URMUR)**
This program is for registration (Category A) of new chemical and biopesticide active ingredients and products that are recently registered in another Organisation for Economic Co-operation and Development (OECD) member country and that have small uses in Canada. Again, to encourage registrants to use this program, the PMRA reduced its review time from 18 months to 12 months. This program can be used for reduced-risk pesticides.

Since these programs were introduced, more than 50 percent of new products submitted to Canada are reviewed jointly or through workshare with the U.S. Forty (40) percent are reduced-risk chemical pesticides according to the U.S. EPA criteria.

Since 1997, the PMRA has registered 13 conventional pesticide active ingredients (plus 15 end-use products) and six biopesticide active ingredients (plus seven end-use products) through these programs.

The following is a list of the registered pesticides by accepted common names (if available) and their trade name (in parenthesis):

Joint Review Reduced-Risk Chemicals:

cyprodinil (Vanguard) - pome fruit, stone fruit, grapes
diflufenzopyr (Distinct) - corn
fenhexamid (Elevate) - ornamentals, grapes, strawberries
zoxamide (Zoxium, Gavel) - grapes (non-reduced risk for potatoes)

Joint Review Minor Uses:

fenhexamid (ELEVATE 50 WDG) - Crop Group 13 A (caneberries)

Joint Review Biopesticides (pheromones and microbials):

9-dodecenyl acetate (3M MEC pheromone) - forestry
cydia pomonella Granulosis Virus (Virosoft) - apples

Work Share Chemicals:

flucarbazone-sodium (Everest Solupak, Everest DF) - wheat
iprovalicarb (import MRL) - grapes, raisins, wine
sulfosulfuron (Sundance) - wheat
thiamethoxam (Helix, Helix Xtra) - canola/mustard seed treatment

User-Requested Minor-Use Registrations:

Chemicals

isoxaben (Gallery) - forestry
triflurosulfuron methyl (Upbeet) - sugar beets
aminoethoxyvinylglycine (Retain) - apples
methyl anthranilate (Avigon) - turf
trinexapac-ethyl (Primo Maxx) - turf grasses on commercial sod farms and golf courses

Biopesticides

Streptomyces griseoviridis strain K61 (Mycosstop) - cucumbers, ornamentals, tomatoes
cis-11-Tetradecenyl acetate (3M MEC pheromone) - cranberries
Trichoderma harzianum Rifai str. KRL-AG2 (FTR) (Rootshield Drench, Rootshield Granules) - greenhouse crops
Isomate-P Pheromone, containing (Z,Z)-3,13-Octadecadien-1-yl acetate and (E,Z)-3,13-Octadecadien-1-yl acetate - peach tree borer

2.0 The PMRA Initiative for reduced-risk pesticides

Since a number of reduced-risk products were submitted to the U.S. EPA before the 1996 Joint Review Program was implemented, there are reduced-risk products available in the U.S. that the registrants have not yet submitted for registration in Canada. To encourage these registrants to submit their products in Canada, the PMRA will give priority to products that meet the reduced-risk criteria that are used by EPA in their Reduced-Risk Initiative. Both the PMRA and the U.S. EPA continue to urge applicants to use the Joint Review Programs for Reduced-Risk Pesticides since they bring products to both Canada and the U.S. at the same time.

This directive applies to all applications for registration of new active ingredients and major new uses (Category A submissions) and registration of subsequent entry (Category B submissions and URMULEs) for pesticides that are not submitted as part of a program mentioned in Section 1.0 of this regulatory directive. The details are provided in Sections 4.0 to 6.0 for chemicals, in Section 7.0 for biopesticides. The term “chemical pesticides” as used in this directive includes all pesticides other than biopesticides, and includes conventional chemicals used in agricultural, antimicrobials, as well as pesticides used in an urban setting.

3.0 Effective date

This Regulatory Directive is effective as of the date of this document and will apply to submissions received after that date.

4.0 Characteristics of acceptable and unacceptable submissions for the reduced-risk initiative

The PMRA will review rationales submitted for reduced-risk submissions in order to determine those chemical pesticides that qualify as reduced-risk products. Since this is an extension of the existing joint review programs, the PMRA will use the same factors and will accept the same format for the reduced-risk rationale provided by the applicant as were developed by the U.S. EPA and are currently used in the joint review programs. If the active ingredient, the end products and uses determined to be reduced-risk by the U.S. EPA are identical to those being submitted to Canada, the PMRA will give the same designation based on receipt of the rationale and review done by the U.S. EPA.

The factors that are used and are likely to contribute significantly to the granting of reduced-risk status are summarized below in descending order:

- human health effects
 - very low mammalian toxicity
 - toxicity generally lower than alternatives (10–100×)

- displaces chemicals that pose potential human health concerns [e.g., organophosphates (OPs), probable carcinogens (B2s)]
- reduces exposure to mixers, loaders, applicators, and re-entry workers
- non-target organism effects (birds)
 - very low toxicity to birds
 - very low toxicity to honeybees
 - significantly less toxicity/risk to birds than alternatives—not harmful to beneficial insects, highly selective pest impacts
- non-target organism effects (fish)
 - very low toxicity to fish
 - less toxicity/risk to fish than alternatives
 - potential toxicity/risk to fish mitigable
 - similar toxicity to fish as alternatives but significantly less exposure
- groundwater
 - low potential for groundwater contamination
 - low drift, runoff potential
 - runoff mitigable
- lower use rates than alternatives, fewer applications
- low pest resistance potential (i.e., new mode of action)
- highly compatible with integrated pest management (IPM)
- efficacy.

Also based on the U.S. EPA experience, those factors that significantly contributed to an unacceptable decision (not reduced risk) are summarized below in descending order:

- human health effects
 - inadequate/inappropriate comparisons with alternatives
 - inadequate documentation of effects
 - human health risk-reduction case weak
 - risk-reduction case inadequate when compared to alternatives
- non-target organism effects (birds and fish)
 - toxic to birds
 - toxic to fish
 - risk-reduction case inadequate when compared to alternatives
- potential groundwater problems

- unlikely to displace higher-risk alternatives
- lack of efficacy data
- phytotoxicity.

This U.S. experience of past decisions should assist future applicants to Canada in preparing their submissions. A discussion of how the document describing these factors should be developed is given in Appendix II. Additional information on how to prepare a submission for the PMRA is given in Appendix III and what must be included in the Reduced-Risk rationale is in Appendix IV.

5.0 Expedited reviews of reduced-risk chemical pesticides

5.1 Performance standards

Under this new PMRA Initiative for Reduced-Risk Pesticides, the PMRA will reduce its existing performance standards for review of an acceptable Category A submission to 15 months, for review of an acceptable Category B submission to 10 months and for review of an acceptable minor-use submission (URMULE) to 5 months for chemical pesticides that “may reasonably be expected to accomplish one or more of the following:

- (i) Reduce the risks of pesticides to human health.
- (ii) Reduce the risks of pesticides to non-target organisms.
- (iii) Reduce the potential for contamination of groundwater, surface water or other valued environmental resources.
- (iv) Broaden the adoption of integrated pest management strategies, or make such strategies more available or more effective.”

Further reduction of the performance standards may be considered, on a case-by-case basis, for applications that contain reduced-risk products registered by the U.S. EPA since 1996 and that have all the U.S. EPA reviews.

5.2 Application for expedited review and designation of reduced-risk status for chemical pesticides

Step 1—Application

To initiate the process, the applicant must submit an application for expedited review:

- demonstrating how the use of the pesticide may reasonably be expected to accomplish one or more of the criteria listed in section 5.1 above
- containing a reduced-risk rationale (appendices II and IV)

Chemicals that have been assessed for reduced risk and accepted by the U.S. EPA's Office of Pesticide Programs, will be accepted by the PMRA as reduced-risk pesticides as long as the reduced-risk rationale and the U.S. EPA assessment of it are provided and the uses being sought in Canada are the same.

In this PMRA initiative, an application for expedited review as a reduced-risk chemical may be submitted for the following types of actions only:

(a) an application to register a chemical pesticide that contains an active ingredient not contained in any currently registered pesticide and not currently being submitted through the programs outlined in Section 1.0 of this regulatory directive (See appendices II and IV for reduced-risk rationale guidelines.);

or

(b) an application to register additional uses of or amend a currently registered chemical pesticide for an additional new use or formulation change, provided the pesticide is not currently being submitted through the programs outlined in section 1.0 of the Regulatory Directive (See appendices II and IV for reduced-risk rationale guidelines).

Step 2—Reduced-Risk Determination

If an application for expedited review qualifies under Step 1, the PMRA will review the detailed reduced-risk rationale presented by the applicant to determine whether the pesticide qualifies under the reduced-risk criteria described below. The PMRA will review the reduced-risk rationale and screen the submission for acceptable format and content to ensure the submission is also reviewable (Appendix III) at the same time.

If a pesticide qualifies for reduced-risk status and the submission is reviewable, the PMRA will grant an expedited review of the application.

If the PMRA denies a submission reduced-risk status, the applicant will be given only one opportunity to rebut this decision and will have four weeks to submit its rebuttal. Because of limited program resources, the PMRA can only allow one opportunity to rebut a decision. Pesticides that the PMRA determines do not qualify for reduced-risk status during Step 2 will be processed in accordance with existing PMRA procedures for non-reduced-risk pesticides.

If the reduced-risk status is lost during the review process, the submission will be reviewed according to standard time lines.

5.3 Guidelines for writing reduced-risk rationales for chemical pesticides

While participation in the reduced-risk pesticides program is voluntary, those who elect to participate must fully address all of the following areas in their written rationale:

(a) executive summary; (b) human health effects; (c) environmental fate and effects; (d) other hazards; (e) risk discussion; (f) pest resistance and management (e.g., IPM); (g) comparative performance; (h) other information and how the application complies with issues outlined in Appendix II. The PMRA will consider all of these areas in determining the acceptability of these applications; however, these may not be the exclusive factors in all cases. If an applicant identifies additional criteria that substantiate the argument that its product is indeed a reduced-risk pesticide, then the PMRA invites the applicant to submit a rationale with any supporting data to verify such a claim. The PMRA will consider this additional information.

An applicant's documentation must contain both a discussion of the inherent reduced-risk properties of its product, as well as a comparison of those properties with the properties of the commonly used alternatives where appropriate. Comparisons must be made to conventional chemical pesticides, antimicrobial pesticides, biopesticides, and cultural practices currently being used for pest control at the same use site(s) and for the same pest(s).

Please note that the PMRA does not expect the applicant to perform any additional testing to derive the data necessary to develop rationales for the Reduced-Risk Program. The applicant must summarize all data in the applicant's possession or control or available through the open literature for the product being submitted to the PMRA. If data addressing one of the stated factors have been developed but are not required for registration of the pesticide in Canada, the applicant must provide a summary of these data as part of the Reduced-Risk Rationale. If any of the required information is not known, that fact must be noted in the rationale.

If the rationale does not include a discussion of each of these factors or provide reasoning as to why the factor should not be considered in the PMRA's decision, the PMRA will consider the rationale to be incomplete and not responsive to this regulatory directive. However, if the applicant believes that the factor does not apply to the new pesticide, it must provide a short rationale for this reasoning.

In situations where the PMRA has already reviewed data on the active ingredient, the applicant should use the PMRA's review to address the relevant factor(s). Applicants must identify each study, where appropriate.

Details on what should be included in the Rationale are provided in Appendices II and IV.

5.4 Guidelines for writing rationales explaining compliance with enhanced risk assessment requirements for reduced-risk chemical pesticides

Reduced-risk submissions must also provide a rationale that explains how this registration action complies with the enhanced risk assessment requirements of the PMRA. The rationale should follow the guidance provided in Appendices II and IV and should address (at a minimum) aggregate risk, special sensitivities, endocrine effects, and potential common mechanisms of toxicity with other registered pesticides.

5.5 Submitting an application for a reduced-risk chemical registration

The reduced-risk rationale must accompany the registration application and supporting data packages. This regulatory directive does not supersede established submittal procedures as addressed in Appendix III; rather, this regulatory directive provides additional guidance for submitting the reduced-risk rationale. When preparing your submission to mail or deliver to the PMRA, direct your submission to Pest Management Regulatory Agency, 2720 Riverside Drive, Ottawa ON K1A 0K9, including the distribution code: **REDUCED-RISK/CHEMICAL APPL.**

6.0 Expedited review of new formulations for currently registered conventional pesticides

Some new formulations and amendments to currently registered chemical pesticide products could result in reduced risk. To qualify, an application for expedited review under this section must first demonstrate that it meets one or more of the Step 1 criteria listed in section 5.1 of this directive. Secondly, the registrant must demonstrate that the new formulation, when compared with all of the existing formulation(s) for the active ingredient, results in significant risk reduction. Examples of risk reduction that would most likely qualify for expedited review include new formulations that result in (a) at least a 35% reduction in the amount of active ingredient applied, (b) at least a tenfold reduction in risks to mixers, loaders, and applicators, (c) at least a 50% reduction in the product's potential to leach into groundwater or run off into surface water, or (d) a significant reduction in risk to non-target species. Actions that are accepted will qualify for expedited review but will not be classified as reduced-risk.

The process for submission of a new formulation or new end-use product does not differ from the new active ingredient/new uses procedures. Finally, if the applicant holds the registrations for the old formulations that this new formulation will replace, a request for discontinuation of the old formulations is also required. This request will not be processed until a registration is issued on the new formulation.

7.0 Expedited reviews of biopesticides

7.1 Performance standards

Under this new PMRA Initiative for Reduced-Risk Pesticides, the PMRA will reduce its existing performance standards for review of an acceptable Category A submission to 12 months (6 months for straight chain lepidopteran pheromones), for an acceptable Category B submission to 6 months, and for an acceptable minor use application (URMULE) to 5 months for microbial and straight chain lepidopteran pheromones (SCLP) pesticides that are not submitted as part of the programs mentioned in Section 1.0 of this regulatory directive. For other biopesticides (see section 7.2) including non-SCLP pheromones and biochemicals that are considered biopesticides, the PMRA will reduce its existing performance standards for review of an acceptable Category A submission to 15 months, for an acceptable Category B submission to 10 months and for an acceptable minor use application (URMULE) to 5 months for applications not submitted as part of a program mentioned in section 1.0 of this regulatory directive.

Further reduction of the performance standards may be considered, on a case-by-case basis, for applications that contain biopesticide products registered by the U.S. EPA since 1996 and that have all the U.S. EPA reviews.

7.2 Types of biopesticides

The types of biopesticides accepted for this initiative include:

- naturally occurring or genetically altered microorganisms (microbials);
- straight chain lepidopteran pheromones (SCLP);
- other pheromones (non-SCLP);
- pesticides, including biochemicals, that have been accepted and registered as biopesticides by the U.S. EPA, Office of Pesticide Programs, Biopesticides and Pollution Prevention Division.

7.3 Characteristics of biopesticides

7.3.1 Microbial Pesticides

Microbial pesticides contain a bacterium, fungus, virus, protozoan, or alga as the active ingredient. Approximately 13 microbial pesticide active ingredients and 34 end-use products are registered by the PMRA. The most widely known of these are varieties of the bacterium, *Bacillus thuringiensis* or Bt, which can control certain moths, beetles, and mosquitos. Data requirements for microbial pesticides are found in Regulatory Directive DIR2001-02, *Guidelines for the Registration of Microbial Pest Control Agents and Products*, <http://www.hc-sc.gc.ca/pmra-arla/english/pdf/dir/dir2001-02-e.pdf>. The PMRA encourages potential registrants to contact the PMRA for a presubmission consultation meeting to discuss these data requirements and the scientific rationales for study waivers.

7.3.2 Pheromone and other semiochemical pesticides

Approximately 12 pheromone and other semiochemical pesticide active ingredients and 9 end-use products are registered by the PMRA. Pheromone and other semiochemical pesticides are distinguished from conventional chemical pesticides by their non-toxic mode of action toward target organisms (usually species specific), e.g., growth regulation or mating disruption, and by the natural occurrence of the pesticidal substance. In contrast, conventional pesticides generally are toxic and may affect a wider range of target species. In many instances, these pesticides may be synthesized rather than isolated from nature. In order for synthesized pesticides to be considered as pheromone or other semiochemical pesticides, they must be demonstrated to be structurally similar and functionally identical to a naturally occurring pheromone or semiochemical.

Most semiochemical pesticides are applied at very low rates, are highly volatile, or are applied in bait, trap, or “encapsulated” formulations, thus resulting in less exposure (and less likelihood of adverse effects to humans and the environment than from use of most conventional pesticides). In keeping with their unique properties, these pesticides have been assigned a set of data requirements which are organized in a tiered testing scheme to ensure, to the greatest extent possible, that only the minimum data sufficient to make scientifically sound regulatory decisions will be required. The data requirements are outlined in Regulatory Directive DIR97-02, *Guidelines for the Research and Registration of Pest Control Products Containing Pheromones and Other Semiochemicals*, <http://www.hc-sc.gc.ca/pmra-arla/english/pdf/dir/dir9702-e.pdf>. Note that the PMRA is in the process of developing a regulatory proposal for pheromones which will incorporate work that has been completed with OECD countries. The PMRA encourages potential registrants to contact the PMRA for a presubmission consultation meeting to discuss these data requirements, and the scientific rationales for study waivers.

7.3.3 Other Biopesticides

Other biopesticides, including biochemicals that have been accepted and registered as biopesticides by the U.S. EPA, Office of Pesticide Programs, Biopesticides and Pollution Prevention Division will be accepted under this initiative.

7.4 Submitting an application for a biopesticide registration under the Reduced-Risk Initiative

A statement indicating which type of biopesticide (see 7.2) must accompany the registration application and supporting data packages For other biopesticides (see Section 7.2 and 7.3.3), information demonstrating that they have been accepted and registered as biopesticides by the U.S. EPA, Office of Pesticide Programs, Biopesticides and Pollution Prevention Division, must accompany the registration application and supporting data packages. If the active ingredient, and the end-use products determined to be biopesticides by the U.S. EPA are identical to those being submitted to Canada, the

PMRA will give the same designation based on receipt of the rationale and review done by the U.S. EPA.

This regulatory directive does not supersede established submittal procedures as addressed in Appendix III; rather, this regulatory directive provides additional guidance. When preparing your submission to mail or deliver to the PMRA, direct your submission to Pest Management Regulatory Agency, 2720 Riverside Drive, Ottawa ON K1A 0K9, including the distribution code: **REDUCED RISK/BIOPESTICIDE**.

Appendix I Existing programs

1.0 NAFTA joint review programs for reduced-risk pesticides

The PMRA and the EPA have established a process for the joint reviews of pest control products. One is for submissions in which the new active ingredient is a reduced-risk chemical that meets the U.S. EPA Pesticide Registration Notice PR 97-3, Guidelines for Expedited Review of Conventional Pesticides under the Reduced-Risk Initiative and for Biological Pesticides. The other is for biological products. The PMRA and the U.S. EPA are committed to joint reviews of submissions and work sharing of pesticide evaluations on a regular basis. Joint reviews will increase the efficiency of the registration process, facilitate simultaneous registration in Canada and the U.S., and increase access to new pest management tools in both countries. Efficient work sharing requires a shared understanding of the responsibilities of each agency, as well as common procedures and time frames.

These reduced-risk programs encourage the development, registration, and use of lower-risk pesticide products which would result in reduced risk to human health and the environment when compared to the existing pesticide alternatives.

A pest control product must meet the following general prerequisites to be considered for a joint review of data submitted in support of registration:

- a complete database is available;
- label, proposed use pattern, rates, and formulation type are the same for both countries; and
- the active ingredient is unregistered in both countries, at time of application.

1.1 Joint Review Program for Reduced-Risk Chemicals

In order to be considered a Group 1 Joint Review, the proposed new active ingredient and the uses of the proposed formulated product must meet the U.S. EPA's criteria for a reduced-risk pesticide.

Group 1A Joint Reviews

In order for submissions to be considered for a joint review, they must first have been accepted as reduced-risk chemicals by the U.S. EPA. This group accommodates submissions that contain one active ingredient and one or two end-use products, and a complete data package. They follow a 12-month timeline for evaluation and decision after passing the PMRA and U.S. EPA screens.

Group 1B Joint Reviews

In order for submissions to be considered for a joint review in this category, they must first have been accepted as reduced-risk chemicals by the U.S. EPA. This group accommodates larger reduced-risk submissions that may contain more than one active ingredient, more than one or two end-use products, and a complete data package. They follow an 18–24-month timeline for evaluation and decision after passing the PMRA and the U.S. EPA screens.

(Procedures for Joint Review Applications for Chemical Pesticides,
http://www.hc-sc.gc.ca/pmra-arla/english/pdf/nafta/naftajr/nafta-jr_pest-e.pdf)

1.2 NAFTA Joint Review Program for Microbial and Pheromone Pesticides

Microbial Joint Review

In order to be considered for a joint review, a product must be a microbial, the active ingredient must be unregistered in both countries at time of application, and it must have a complete database. They follow a 12-month timeline for evaluation and decision after passing the PMRA and the U.S. EPA screens.

Pheromone Joint Review

In order to be considered for a joint review, a product must be a pheromone or other semiochemical, the active ingredient must be unregistered in both countries at time of application, and it must have a complete database. They follow a 12-month timeline for evaluation and decision after passing the PMRA and EPA screens.

(Procedures for Joint Review of Microbials and Semiochemicals,
http://www.hc-sc.gc.ca/pmra-arla/english/pdf/nafta/naftajr/nafta-jr_micro-e.pdf)

2.0 User Requested Minor Use Registration (URMUR)

A User Requested Minor Use Registration of a pesticide is for a use (for example, in agriculture, forestry, aquaculture) in which the potential market volume of the product for that use is not sufficient to persuade the registrant to carry out the additional research required for registration.

All types of products, including traditional chemical products and biological pesticides (e.g., pheromones, microbials) may be eligible for the URMUR program, provided the following criteria are met:

1. The pest control product must be intended to meet an identified need, supported by a sponsor/user group.
2. The pest control product must comply with the URMUR definition.
3. The pest control product must contain an active ingredient that is registered in an OECD country but is not registered in Canada. (Canadian registered pesticides for

which minor uses are requested are eligible for the present User Requested Minor Use Label Expansion Program [URMULE]. Consult Regulatory Directive DIR2001-01, *User Requested Minor Use Label Expansion*.)

4. Registration of the pest control product in an OECD country must be less than five years old at the time of application in Canada, to ensure adequacy of the database and availability of foreign reviews.
5. The registration of the pest control product must not have been previously suspended, cancelled, or voluntarily withdrawn in Canada because of health or environmental concerns, or the pest control product must not have been previously assessed for registration and found to be unacceptable because of health or environmental concerns in Canada and other countries.
6. The registrant must submit the URMUR application to the PMRA and serves as the liaison point between the PMRA and the sponsor/user group for registration-related information. The sponsor/user group will work directly with the registrant.
7. The registrant must supply foreign reviews from OECD countries along with supporting data/studies.
8. The proposed area (i.e., hectarage) and volume of use must be identified.

(Regulatory Directive DIR99-05, *User Requested Minor Use Registration*,
<http://www.hc-sc.gc.ca/pmra-arla/english/pdf/dir/dir9905-e.pdf>)

Appendix II Points to consider when preparing submissions

It would be helpful if any submitted documentation were to contain a discussion of each of the following factors as it relates to the pesticide and proposed maximum residue limit (MRL). If information on any factor is not known, that fact, along with an explanation, should be noted in the rationale. It is important to note that the PMRA does not, at this time, expect the registrant or applicant to perform any additional testing to derive the data necessary to develop its rationales. However, if the registrant or applicant has in its possession data from preliminary reports of ongoing studies, articles from published literature, unpublished report information, previously unsubmitted studies, or supplemental data that are otherwise pertinent to the PMRA's concerns, it is encouraged to submit them. Likewise, if a registrant believes that a factor is not applicable to its product, a discussion as to why this view is held should also be included. The PMRA will consider all relevant factors in determining an application's completeness and in setting priorities for review.

The PMRA and the U.S. EPA have been working together for many years to harmonize the regulation of pesticides between Canada and the U.S. This work includes risk-assessment approaches and methods. In light of the new safety standard established by the U.S. *Food Quality Protection Act* (FQPA), the PMRA has been working closely with the U.S. EPA to ensure that Canada has a full understanding of, and input where appropriate to, the scientific issues raised by the implementation of the FQPA. The PMRA supports the new standard and has incorporated these new approaches into its review processes and methodologies.

Based on the new safety standard, as in the U.S., the PMRA will need the following additional information in order to make appropriate regulatory decisions. For details on each factor, please refer to the explanations below in Parts A and B.

1. An informative summary of the application, including a summary of the supporting data, information, accompanying rationales, and a statement providing permission to publish such summary, and
2. Information and discussion pertaining to a specific safety determination for infants and children including their special susceptibilities and exposure patterns to the particular pesticide.

Part A Food Use Pesticides: Registration and Re-evaluation Actions, Research Permits, Maximum residue limits

In the format described in Appendix I of this Regulatory Directive, address each of the following with respect to the pesticide and its use(s):

Special Sensitivities

a) Chronic Endpoints

For a chemical pesticide: Discuss and/or provide evidence as to whether or not the current reference dose (RfD) is sufficient to adequately protect infants and children. Discuss and/or provide evidence as to whether infants and children are more susceptible to the chemical. If you believe that an additional safety factor of 10×, to take into account potential pre- and post-natal toxicity to infants and children, is not necessary, provide evidence to support the additional safety factor, if any, that you believe to be more appropriate. Please bear in mind that the PMRA may accept a different margin of safety only if it concludes (based on reliable data) that the margin will be safe for infants and children.

For a pheromone pesticide: A pheromone is a naturally occurring compound, or substantially similar to a naturally occurring compound, with a non-toxic mode of action to the target pest. Does the toxicity testing indicate that the establishment of an RfD is warranted? If so, then discuss whether or not the RfD is sufficient to adequately protect infants and children. Discuss and/or provide evidence as to whether or not infants and children are more susceptible to the pheromone pesticide.

For a microbial pesticide: Certain subpopulations are more susceptible to certain disease-causing microorganisms; however, these are not the types of microorganisms that are considered for registration or use as microbial pesticides. The PMRA has not registered, and does not expect to register a microbial active ingredient that is known to be a common human pathogen. To address the potential risk from microbial pesticides, the PMRA requires a battery of acute toxicity/pathogenicity studies in order to perform a risk assessment. If results of the acute exposure studies indicate a toxicity concern, then subchronic or chronic studies are required.

Discuss the potential for chronic dietary risks for infants and children. Discuss and/or provide evidence as to whether or not infants and children are more susceptible to the microbial pesticide than is the adult population.

b) Acute Endpoints

Discuss the potential for greater acute dietary risk for infants and children. If the chemical or biological pesticide demonstrates acute effects, then discuss the endpoint used to perform the assessment including relevance to infants and children and the details as to how the exposure assessment was conducted and whether the estimated risk is within the PMRA's levels of concern.

c) Carcinogenic Endpoints

If the chemical or biochemical has been determined to be a carcinogen and has a cancer potency factor (Q1*), discuss the aggregate excess lifetime cancer risk resulting from exposure to the chemical from residues in food and drinking water (ground and surface water) and from residential and other non-occupational source(s).

Aggregate Exposure

a) Water

For a chemical or biological pesticide: Discuss the potential for the transfer of residues (of both the parent pesticide and any degradates) to drinking water. The discussion should include, but not be limited to, information indicating whether the pesticide is persistent and/or mobile, relevant product chemistry, and any available modelling data.

Has the chemical, or any of its degradates, been detected in groundwater or surface water? Would this chemical or any of its degradates likely pass through primary or secondary drinking water treatment into finished water? Is anyone conducting water monitoring programs for this pesticide? If so, data collected and all relevant information should also be included.

For a microbial pesticide: Discuss the potential for the transfer of the microbial pesticide to drinking water. The discussion should include, but not be limited to, information pertaining to the biology of the microorganism, and indicating whether the pesticide is persistent and/or mobile or has the potential for transport in air (spray drift and volatility data). Is anyone conducting water monitoring programs for this strain? If so, data collected and all other relevant information should also be included.

b) Non-occupational Exposures

Discuss the potential for significant exposure of children to the pesticide by routes other than dietary. Are there any non-occupational, structural, or residential uses (e.g., pet, swimming pool, lawn and garden, topical insect repellent)? Is the pesticide used in or around schools, parks, or recreation facilities? Provide all available exposure data. If the pesticide demonstrates acute effects, then discuss the endpoint used to perform the assessment, including relevance to infants and children and the details of how the residential exposure assessment was conducted and whether the estimated risk is within the PMRA's levels of concern.

c) Multiple Pathway Assessment

Discuss the chronic and/or acute risk of aggregate exposure via multiple pathways for the general population, and for infants and children. This should include a discussion of all assumptions used and uncertainties. You should also identify, and include in the discussion, any non-pesticidal uses of the chemical (e.g., industrial, pharmaceutical, cosmetic, food additive).

Cumulative Effects

Discuss the mechanism and mode of action of this pesticide. Identify other chemicals that may fall into this category (both pesticide and non-pesticide chemicals). Provide information regarding common mechanisms and modes of action with other chemical substances based on structural similarity, same or similar endpoints, and other relevant criteria. Provide any data and/or evidence illustrating similarities at the cellular/molecular level.

Discuss the appropriateness of combining exposures in this particular case. Where data are not available, discuss appropriateness of using default assumptions and what defaults should be used.

Endocrine Effects

Discuss and provide any evidence relevant to the possibility that the pesticide may have endocrine disrupter effects individually or in combination with another chemical. Include the potential for synergistic effects of your chemical in combination with other chemicals.

Identify any instances of reported (proven or alleged) adverse reproductive or developmental effects to domestic animals or wildlife arising from exposure to your chemical, or that occurred in an area where the chemical is known to have been used. Provide all information regarding the circumstances, estimated level of exposure, and details of the effect.

Residue Chemistry

Information should include a discussion of compatibility with established Codex Alimentarius Commission MRLs, submission of a practical analytical method with an appropriate limit of detection, and a discussion of the potential need for tolerances for processed foods. A summary of all MRLs and proposed exemptions from MRLs should also be included.

Part B Non-Food Use Pesticides

In the format described in Appendix III of this Regulatory Directive, address each of the following with respect to the pesticide and its use(s):

Special Sensitivities

Discuss and/or provide evidence as to whether or not infants and children are more susceptible to the chemical than are adults.

Discuss the potential for greater acute and/or chronic risk for infants and children. If the pesticide demonstrates toxic effects, then discuss the endpoint used to perform the assessment including relevance to infants and children and the details as to how the exposure assessment was conducted and whether the estimated risk is within the PMRA's levels of concern.

Potential for Exposure to Children

Describe the use pattern of your chemical. If you believe that its use(s) would not potentially result in significant exposure to infants and children, provide a discussion and rationale for this view. For chemicals that appear not to result in a significant exposure to infants and children, no additional information is needed.

If you believe that the use of your chemical may result in significant children's exposure, the following factors may need to be addressed:

Aggregate Exposure

Discuss the potential for the transfer of residues of both the parent chemical and any degradates or of the microbial pesticide to drinking water. For chemical pesticides, the discussion should include, but not be limited to, information indicating whether the pesticide is persistent and/or mobile, the potential for transport in air (spray drift and volatility data), and any available modelling data. For microbial pesticides, the discussion should instead include information pertaining to the biology of the micro-organism and indicate whether the pesticide is persistent and/or mobile.

Has the chemical, or any of its degradates, been detected in groundwater or surface water? Would this chemical, or any of its degradates, likely pass through primary or secondary drinking water treatment into finished water? Are any U.S. states conducting water monitoring programs for this pesticide? If so, data collected by those states and all relevant information should also be included.

Discuss the potential for significant exposure of children to the chemical by non-dietary routes. Are there non-occupational, structural, or residential uses (e.g., pet, swimming pool, lawn and garden, topical insect repellents)? Is the pesticide used in or around schools, parks, or recreation facilities? Provide all available exposure data.

Discuss the chronic and/or acute risk of aggregate exposure via multiple pathways for the general population, infants and children, including a discussion of all assumptions used and uncertainties.

Identify other non-pesticidal uses of the chemical (e.g., industrial, pharmaceutical, cosmetic, food additive).

Cumulative Effects

Discuss the mechanism and mode of action of this pesticide. Identify other chemicals that may fall into this category (both pesticide and non-pesticide chemicals). Provide information regarding common mechanisms and modes of action with other chemical substances based on structural similarity, same or similar endpoints, and other relevant criteria. Provide any data and/or evidence illustrating similarities at the cellular/molecular level. Discuss the appropriateness of combining exposures in this particular case. Where data are not available, discuss appropriateness of using default assumptions and what defaults should be used.

Endocrine Effects

Discuss and provide any evidence relevant to the possibility that the chemical may have endocrine disrupter effects individually or in combination with another chemical. Include the potential for synergistic effects of your chemical in combination with other chemicals and whether or not your chemical could act as a catalyst for another hormone-disrupting chemical.

Identify any instances of reported (proven or otherwise) adverse reproductive or developmental effects to domestic animals or wildlife as a result of exposure to your chemical, or that occurred in an area where the chemical is known to have been used. Provide all information regarding the circumstances, estimated level of exposure, and details of the effect.

Appendix III **Guidance on preparation of submissions to the PMRA**

The PMRA has published various documents containing guidance for preparing submissions and outlining data requirements. To obtain these documents applicants should contact the PMRA's Pest Management Information Service, at 1-800-267-6315, or (613) 736-3799 from outside Canada. These guidelines are also available on the PMRA web site as downloadable documents at <http://www.hc-sc.gc.ca/pmra-arla/english/pubs/pubs-e.html>. Applicants are encouraged to consult with the PMRA prior to making submissions.

Submissions to the PMRA are subject to the applicable fees. The registrant, however, may apply for fee exemptions or reduced fees based on the nature of the products and the volume of sale. For example, cost recovery fees do not apply to microbials and pheromones, nor to URMULEs. Reduced fees are available for URMURs. Please refer to the PMRA's *Guidance Document on Pest Control Product Cost Recovery Fees*, available at <http://www.hc-sc.gc.ca/pmra-arla/english/pdf/cost/feeguide-e.pdf>.

As with other regular registrations involving a new active ingredient, submissions for the technical grade active ingredient and at least one end-use product are required.

Appendix IV **Details on the content and format of the reduced-risk rationale**

4.1 **Content**

Part A Executive Summary

Provide an executive summary that addresses the following considerations:

- chemical name
- Chemical Abstracts Service registry number
- chemical structure
- chemical class or family name of the active ingredient
- mode/mechanism of pesticidal action for the active ingredient (if known)
- proposed use pattern—including site(s) of application and pest(s) controlled, application methods, application rates, frequency of application, and product formulation percentages. Also indicate whether the new chemical will be used in combination with other registered pesticides.
- brief overview summary of the health, ecological and environmental fate effects
- statement as to which of the four enhanced risk-assessment criteria (special sensitivities, aggregate exposure, cumulative effects, endocrine effects) are being met by the application (see Appendix II)
- Reduced-Risk Statement, articulating the specific factors that led the applicant to the conclusion that the active ingredient offers the opportunity for risk reduction
- data matrix, providing tabular information on all data available for the active ingredient. The table should include the guideline reference number, the study title, outcome of the PMRA's evaluation (i.e., in review, acceptable, supplemental, data waived, etc.), and date of the PMRA's review (if applicable).

Part B Human Health

Clearly identify the portion of the rationale which addresses the potential effects of the active ingredient on human health. When specifying the dose levels used in the toxicity studies, present the no-observable-effects level (NOEL) and the lowest-observable-effects level (LOEL). Doses need to be specified in terms of mg/kg/day. Also, describe qualitatively and quantitatively the array of effects at all dose levels tested. In the format described in this Regulatory Directive, address each of the following aspects of the active ingredient and its use:

1. Acute Toxicity of the active ingredient and the formulations. Provide the toxicity category for each of the acute toxicity studies conducted on the active ingredient and the formulated products.
2. Reproductive, Developmental, Mutagenic and Neurotoxic Properties of the active ingredient
3. Oncogenic and Other Subchronic and Chronic Effects of the active ingredient
4. Toxicity of Mammalian and Plant Metabolites

Part C Environmental Fate and Effects

Clearly identify the portion of the rationale which addresses the potential ecological effects of the active ingredient and its environmental fate. The discussion should also address potential environmental degradates or metabolites of the active ingredient. Address each of the following aspects of the active ingredients and its use:

- mammalian acute toxicity
- avian acute and subacute toxicity
- avian reproductive toxicity
- fish acute and chronic toxicity
- aquatic invertebrate toxicity
- honeybee acute contact toxicity
- effects on terrestrial plant growth
- effects on aquatic plant growth
- potential exposure to non-target organisms
- environmental persistence (soil and water)
- mobility in soil and water
- transport in air (spray drift and volatility)
- bioaccumulation as indicated by the Octanol/Water Partition Coefficient

Part D Other Hazards

Clearly identify the portion of the rationale which addresses other potential human health and environmental hazards produced by the following:

1. Potential to Deplete Stratospheric Ozone thus increasing the ultraviolet radiation
2. Potential to Present a Hazard through Storage, Transportation, Mixing, Use, or Disposal based on its physical or chemical characteristics:
 - a. stability
 - b. flammability
 - c. corrosion characteristics
 - d. explodability
 - e. oxidizing or reducing action
 - f. storage stability
3. Potential to Affect Endangered and/or Threatened Plant and Animal Species

Part E Risk Discussion

Clearly identify the portion of the rationale which addresses the following items:

1. Discuss the information which supports the claims that the active ingredient presents reduced toxicity, reduced exposure to humans or non-target organisms, and/or reduced environmental burden.
2. Where alternative, registered pesticides or pest control practices exist, make a quantitative and/or qualitative comparison between the risks posed by the active

ingredient under consideration and all the other pesticides commonly used, and/or the other current pest control practices.

3. The comparisons with alternative technology should also include biological pesticides as well as cultural and mechanical pest management practices.

Part F Pest Resistance and Management

Clearly identify the portion of the rationale which addresses the following items:

1. Describe how the active ingredient addresses the development of pest resistance, either to the active ingredient itself or to existing pesticides registered for the same use.
2. Discuss the suitability of the active ingredient for use in, or encouraging the adoption of, IPM programs. This discussion should include information on the effects of the pesticide on natural predators, parasites and pathogens of each target pest, if such information is known. The degree of risk and/or usage reduction to be achieved by the IPM program must also be addressed.

Part G Comparative Performance Data (efficacy data)

These data are important to ensure that risk reduction has a reasonable opportunity to be accomplished by adoption of the new pesticide by growers.

1. It is desirable to have summaries of comparative performance data in which the performance of the candidate pesticide is compared to that of alternative control measures under actual-use or simulated actual-use conditions.
2. Summaries of the available efficacy data to be provided if comparative performance data are not available.

Summaries should include statistical analysis of significant differences between the new pesticide and the commonly used alternatives. Summaries should also include experimental methodologies such as application rates, application intervals, pest pressure, weather conditions, varieties of the crop used, etc. Unfavourable results must be included. Efficacy experiments performed under substantially different conditions should not be combined. (Examples include differences in pest pressure, geography, strain/race of pest, and weather.)

Part H Other Information

Submission of a copy of the proposed product label(s) will assist the PMRA in making its decision on the active ingredient.

The PMRA will consider all criteria using a weight-of-evidence approach.

4.2 Format

The reduced-risk rationale document must include the following elements in the order indicated:

1. Title Page
2. Statement or Supplemental Statement of Data Confidentiality Claims
3. Cover Sheet to Confidential Attachment and Confidential Business Information (CBI) Reduced-Risk Attachment
4. Any supporting data must comply with the formatting requirements of the PMRA (Data Code or OECD format). The Reduced-Risk Rationale must be bound as a separate entity and consecutively paginated beginning with the title page as page 1. The total number of pages must be represented on the title page. Do not include CBI on the title page. On the title page, include titles and author(s).

Appendix VI Acronyms and Abbreviations

AAFC	Agriculture and Agri-Food Canada
CBI	Confidential Business Information
IPM	Integrated Pest Management
IR4	United States Interregional Research Project No. 4
MU	minor use
NAFTA	North American Free Trade Agreement
OECD	Organisation for Economic Co-operation and Development
PMRA	Pest Management Regulatory Agency (Health Canada)
RfD	Reference Dose
SCLP	straight chain lepidopteran pheromones
TWG	Technical Working Group
URMULE	User Requested Minor Use Label Expansion
URMUR	User Requested Minor Use Registration
U.S. EPA	United States Environmental Protection Agency