Archived Content

NAFTA Technical Working Group on Pesticides

Updated Procedures for the Joint Review of Biopesticides (i.e., Microbials and Biochemicals)

Updated November 2010

Canada

Health Canada's Pest Management Regulatory Agency (PMRA) and the United States (U.S.) Environmental Protection Agency (EPA) have established a process for the joint review of pest control products in which the active ingredient is a biopesticide (i.e,. microbial or biochemical). The procedure entails a joint pre-submission consultation to establish specific data requirements for the product, provided that the proposed use pattern is common to both countries. This document describes processes for pre-submission consultation and the registration of products that applicants nominate for joint review. This document replaces all earlier documents on the Joint Review of microbials and semiochemicals.

The PMRA and the EPA are committed to the joint review of pesticide evaluations on a regular basis. Joint reviews 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 mutual understanding of the responsibilities of each agency, as well as common procedures and time frames.

Requests for joint pre-submission consultation for a biopesticide (i.e., microbial or biochemical pesticide) should be submitted at the same time to all participating regulatory authorities to the attention of the following contacts:

Health Canada – PMRA Contact

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Pest Management Regulatory Agency, Health Canada
Sir Charles Tupper Building
2720 Riverside Drive
Ottawa, Ontario, Canada
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(613) 736-3772
E-mail: martha.farkas@hc-sc.gc.ca

U.S. EPA Contact

Driss Benmhend
Biochemical Pesticides Branch
(703) 308-9525
E-mail: benmhend.driss@epa.gov

Mailing Address:
U.S. EPA-OPP
Biopesticides and Pollution Prevention Division Mailcode: 7511P
1200 Pennsylvania Avenue, NW
Washington DC 20460

Courier Address:
U.S. EPA-OPP
Biopesticides and Pollution Prevention Division
8th Floor, S-8956
2777 Crystal Drive
Arlington, VA 22202

Introduction

The purpose of this document is to inform applicants and other interested groups about the process for joint review of proposed biopesticides (i.e., microbial and biochemical pesticides) by the Canadian Pest Management Regulatory Agency (PMRA) and the United States (U.S.) Environmental Protection Agency (EPA) leading to simultaneous registration decisions in both Canada and the U.S.. For pre-registration testing (research authorizations, experimental use permits, or notification for small-scale testing), please contact the individual countries.

Definitions

Microbial: a naturally occurring or genetically modified micro-organism including but not limited to fungi, bacteria, and viruses.

Biochemical: a naturally-occurring substance or a functionally identified synthetic that controls pests by non-toxic mechanisms. Biochemical pesticides include, but are not limited to, semiochemicals (e.g., pheromones and kairomones) and plant extracts.

Criteria

a) Criteria for proposing new active substances and associated end-use product(s) for joint review

An applicant may request a joint review for a new active ingredient and associated end-use product(s).

The following criteria are used to determine whether the applicants' active ingredient and end-use product(s) are suitable for a joint review:

- the active ingredient is a microbial agent or a biochemical;
- the active ingredient must not be registered in either country;
- a complete database is available or will be available at the time of application;
- the proposed use pattern and formulation type are the same for both countries; and
- the timeline for dossier submission, as well as the marketing of the active ingredient and end-use product(s), is similar in both countries.

b) Criteria for proposing "second-entry" joint review

A second-entry joint review is the joint review of an application for a product (new or amended) which contains active ingredients already registered in both countries. At this time, for second-entry joint reviews, primarily the following types of applications which involve data review will be considered:

- new source of active ingredient
- use expansions for existing products including new uses, rate of application, number of applications, etc.
- new formulations of existing products
- new combination of active ingredients

- new products with new uses and/or new formulations

The criteria for determining whether the applicant's product is likely to be suitable for a "second entry" joint review are:

- active ingredient(s) must be registered in both countries;
- there must be a complete database by modern standards on file with each of the regulatory authorities for the active ingredient(s);
- proposed uses (that are applicable to all countries) and formulations must be new to both countries, i.e., can not have some uses or formulations already registered in one country and not in another;
- formulations should be the same for both countries;
- the timeline for dossier submission to both regulatory authorities should be the same;
- for applications involving formulation changes, corresponding label uses should be the same in both countries; and
- for new sources of registered active ingredients, the new source(s) of the active ingredient must be new to both countries and must be the same source(s).

In determining whether a joint review is possible, the data requirements (refer to Appendix I), submission timelines, and data protection requirements in each country will also be considered, i.e., if there are significant differences in data requirements and submission timelines, a joint review might not be feasible. In addition, where precedent products are cited to support registration of some or all uses in a proposed product, differences in the data protection/compensation provisions in the participating countries may be an obstacle to a joint review.

Process

a) Joint Review Pre-Submission Consultation

A joint review pre-submission consultation is required to determine:

- whether a joint review is possible;
- to establish joint data requirements for a specific product or the type of information required to support a data waiver; and
- to establish the review time-lines.

(Note: As part of the joint review process, participating regulatory authorities will decide, in advance of dossier receipt, which agency will act as the project lead (i.e., the primary regulatory contact point for the applicant) as well as on how the evaluation work of the submitted studies will be divided among agencies).

Proponents of microbial or biochemical pesticides that meet the general prerequisites for joint review (as noted above) will initiate a joint review pre-submission consultation, by submitting to both agencies an information package that includes:

- a completed pre-submission consultation request form;
- formal letters consenting to consultation between the EPA and the PMRA, including confidential business information, during joint review (contact either agency for model letters);
- a draft label;

- product specifications for the proposed product(s) including identity and amounts of active ingredient and formulants;
- short summaries of available data regarding efficacy, environmental and human health assessments, and any scientific rationales regarding waivers from the submission of data that the proponent would like to include in the formal submission;
- for microbial products only: the identity of the organism and its survival parameters, the manufacturing methods, information regarding any potential health or environmental issues, and the protocols of studies that will be submitted to support registration if these differ from the standardized protocols described in the guidelines; and
- for biochemical products only: as much chemistry information (as described in the registration guidelines) as possible and a description of the manufacturing methods.

The applicant also needs to indicate who the applicant's primary and secondary project contacts will be for all communications with regulatory authorities regarding the joint review.

Upon receipt of a pre-submission consultation request and adequate supporting information, the regulatory authorities will determine if a joint review is possible. If the proposed product(s) meets the criteria for a joint review, the regulatory authorities will work together to develop a joint table of data requirements and identify the project lead i.e., the regulatory authority who will serve as the overall administrative lead for the joint review. In most cases, key communications between the applicant and the regulatory authorities are through the project lead. At the same time, the primary (lead) reviewer for each science discipline is identified.

The data requirements will be shared with the applicant and the applicant will have an opportunity to meet with the regulatory agencies to discuss/clarify the data requirements. The project lead will also develop a project plan for the joint review (refer to Appendix 2) which will include the review work-split for the proposed product(s) as well as the review time-lines. The project plan is reviewed and agreed upon by both agencies. Review time-lines are negotiated between the regulatory authorities and the applicant in consideration of the EPA's *Pesticide Registration Improvement Act* time-lines and the size/complexity of the data package. During meetings (or teleconferences) between applicants and regulatory authorities, applicants are responsible for taking meeting notes and sharing these draft notes with the regulatory authorities for correction/clarification prior to being finalized. Additional technical pre-submission meetings may also be arranged in order to address specific technical questions, e.g. efficacy testing protocols.

The data requirements that are established during a joint pre-submission consultation will be considered valid for up to 24 months.

b) Joint Review Implementation

Dossier Submission

Applicants of products that meet the general prerequisites (as noted above) for joint review must submit simultaneously to the PMRA and the EPA:

- the same formulation type, packaging, and use pattern;
- a common data package, including U.S. and Canadian labels, to both countries. Note: Both agencies are able to accept a submission in OECD (Organisation for Economic Co-operation and Development) dossier format;
- the country-specific forms and fees, as required by each agency;
- a written request for a joint review (refer to date and file number of pre-submission consultation). Letters should identify a company contact in each country. If the technical and end-use submissions are from different applicants, the companies should indicate who is the "lead applicant"; and
- a letter permitting exchange of data and reviews, including confidential business information, between the PMRA and the EPA.

Various guidance documents are available on the Pesticides and Pest Management portion of Health Canada's website to help applicants prepare a complete application package. Instructions regarding applying for registration can be found in DIR2006-05: *Requirements for Submitting Data Index, Documents and Forms*.

For information on biopesticide regulation in the US, please check the following web sites:

http://www.epa.gov/pesticides/bluebook/
http://www.epa.gov/oppfead1/labeling/lrm/
http://www.epa.gov/pesticides/biopesticides/regtools/index.htm

For electronic submission:

http://www.epa.gov/pesticides/regulating/registering/submissions/index.htm

Dossier Receipt and Completeness Check

Upon receipt of the dossier, each regulatory authority will conduct a completeness check to determine whether the appropriate forms, fees, data, and information have been submitted in order to allow the review of the products to proceed.

Evaluation

If the dossier is complete, the regulatory authorities will continue with the primary review of the data parts as designated in the project plan. Once completed, the primary reviews will be passed to the other regulatory authorities for a peer review. With the consideration of comments resulting from the peer review, the primary reviewer will finalize the reviews. These finalized evaluations will serve as the basis for the independent risk assessments conducted by each regulatory authority.

If deficiencies or data gaps are identified during the review of the data, the project lead agency will draft a deficiency letter and forward it to the other agency for review and concurrence before sending it to the applicant. The applicant will be given 75 days to submit the additional information required to adequately address the deficiencies.

If the additional information received within the timeframe allotted adequately addresses the deficiencies or data gaps, then the review will continue. However, the participating regulatory authorities reserve the right to renegotiate the due date if it is determined that additional review time is required to complete the review of the application.

If the additional information requested is not received within the timeframe allotted or is inadequate/insufficient, then the applicant may be provided additional time to address the deficiencies. In this case, the due date must be renegotiated.

A decision regarding the acceptability of the proposed products for registration will be made independently by each regulatory authority in accordance with the date specified in the project plan. The actual dates of registration may vary among regulatory authorities depending on their specific legislative requirements, e.g., public consultation requirements.

Appendix 1: Data Requirements

The data requirements for microbials and biochemicals (including pheromones) in the U.S. and Canada are essentially harmonized, except in the area of efficacy. The documents providing information on protocols and data requirements for the registration of these products can be found at:

1. U.S. EPA 40CFR 158.2000 Biochemical Pesticides Data Requirements, and U.S. EPA 40CFR 158.2100 Microbial Pesticides Data Requirements, both at http://www.epa.gov/pesticides/regulating/data_requirements.htm#requirements

2. OCSPP Harmonized Test Guidelines, at http://www.epa.gov/ocspp/pubs/frs/home/guidelin.htm

3. Biochemicals Test Guidelines, at http://www.epa.gov/ocspp/pubs/frs/publications/Test_Guidelines/series880.htm

4. Microbial Pesticide Test Guidelines, at http://www.epa.gov/ocspp/pubs/frs/publications/Test_Guidelines/series885.htm

5. Health Canada Regulatory Directive: Guidelines for the Registration of Microbial Pest Control Agents and Products, DIR2001-02 at http://www.hc-sc.gc.ca/cps-spc/pubs/pest/_pol-guide/dir2001-02/index-eng.php

6. Health Canada Regulatory Proposal: Guidelines for the Research and Registration of Pest Control Products Containing Pheromones and Other Semiochemicals, PRO2002-02 at http://www.hc-sc.gc.ca/cps-spc/pest/part/consultations/_pro2002-02/index-eng.php

For further information on Biopesticides at the EPA, refer to http://www.epa.gov/pesticides/biopesticides

For further information on the PMRA, refer to the Pesticides and Pest Management portion of the Health Canada website: http://www.hc-sc.gc.ca/cps-spc/pest/index-eng.php

Appendix 2: Template for a Joint Review Project Plan (3 Parts)

Date Created:
Date Last Modified:

Joint Review Project Plan: (*Insert active ingredient name*)
Applicant: *(Insert applicant name)*
Regulatory Participants: *(Insert as required)*
Project lead: *(Insert name of appropriate regulatory authority)*

FOR USE BY EPA/PMRA

Overall Negotiated Timeline: x months (dossier receipt to decision-making date)

Scope of Joint Review (e.g., TGAI, End-use Products/Formulations):

Part 1/3: Summary of Work Allocation to Participating Regulatory Authorities

Science Discipline (Work Area)	***Lead Regulatory Authority for the Primary Review***
Product Chemistry & Product Identity (Product Characterization and Analysis)	
Human Health Toxicology (*TGAI and EPs*)	
Environmental Fate	
Ecotoxicology	
Metabolism and Core Residue Studies (Tolerance Exemption Petition or Numerical Tolerance)	
Efficacy, Crop Tolerance	

Part 2/3: Overall Summary of Joint Review Project Timelines

Project Stage	**Description**	**Completion Date (Ending at Decision-Making Stage)**
OVERALL (Dossier Receipt to Decision-Making (x months)		
Dossier Receipt	Receipt in Canada: Receipt in USA: U.S. PRIA date:	
Completeness Check/Screening	Each regulatory authority to screen package and share identified deficiencies with each	

	other to determine course of action for soliciting a response from the applicant if required (i.e., project lead should prepare a consolidated letter of deficiencies to the applicant on behalf of both agencies). Project lead will organize a conference call for the teams to confirm the results of the screen and if necessary to discuss documents, format, timelines, potential issues. (For EPA: Allow 21 days from time the package is in-house to determine if the package is complete, i.e., inform applicant if package is deficient. PRIA due date will be established when record of receipt of payment or fee waiver is granted.)	
Primary Review	Each regulatory authority will conduct a primary review of the data for which they have been assigned the lead according to the work-split agreement. Reviews will be documented using NAFTA DERs in Word format. Primary reviewers will e-mail the designated secondary reviewers the completed primary reviews and will c.c. the project leads in both jurisdictions. (Note: Completed primary reviews for Product Characterization & Analysis [or Product Chemistry/Identity], which is considered to be CBI, can only be e-mailed to the secondary reviewers if the applicant has consented. Otherwise that information will have to be sent via fax or CD). When EPA sends data to a contractor for review, the EPA will review the contractors work and send an approved version of the reviews to the PMRA for secondary review. PMRA will send primary reviews of Efficacy to EPA for information purposes only. E-mails or conference calls will be used as appropriate to discuss issues/clarifications. At the end of the Primary Review Stage, the project lead will organize a conference call to ensure that all primary reviews have been completed and forwarded to the	

	secondary reviewers.	
Secondary Review	Evaluators (Reviewers) designated as secondary reviewers will review the appropriate primary reviews and provide comments to the primary reviewers. Comments by secondary reviewers will be annotated on the primary reviews (DERs) using the Word "comment" feature. Secondary reviews will be e-mailed to the primary reviewers (with a c.c. to the project leads). Note: Completed secondary reviews for Product Characterization & Analysis [or Product Chemistry/Identity], which is considered to be CBI, can only be e-mailed to the primary reviewers if the applicant has consented. Otherwise that information will have to be sent via fax or CD. Secondary reviews are to be provided to the primary reviewers no later than 2 weeks before the end of the Secondary Review stage to permit consideration/clarification/discussion and integration of comments into the final DER. E-mails or conference calls will be used as appropriate to discuss issues/points of disagreement pertaining to the integration of the secondary review comments into the DERs. **Note**: Outstanding issues that must be addressed by the applicant should be communicated to the applicant (i.e., to the primary company contact) by the regulatory authority designated as project lead. At the end of the Secondary Review stage, the project lead should organize a call to ensure that all secondary reviews have been completed and that there are no outstanding issues.	
Preparation of Independent Risk Assessments and Proposed Regulatory Options	Each agency will conduct independent risk assessments and may share them with each other as completed.	
Independent Decision-Making regarding the acceptability of the	-Independent decision-making by each regulatory jurisdiction. -Communication of either a proposed or final regulatory decision (supported by	

proposed products for registration (could be a proposed decision)	appropriate documentation as required). - Any public consultation, if required, would be initiated independently by the participating regulatory authorities on or after this date.	

Part 3 / 3: Primary and Secondary Project Contacts

Organization	Name (primary and secondary contact)	Contact details (address, telephone and fax numbers, e-mail)
Health Canada's PMRA	Primary: Pre-Dossier Receipt: Post-Dossier Receipt:	
	Secondary : Pre-Dossier Receipt: Post-Dossier Receipt:	
US EPA	Primary: Pre-Dossier Receipt: Post-Dossier Receipt:	
	Secondary : Pre-Dossier Receipt: Post-Dossier Receipt:	.
Applicant	Primary:	
	Secondary:	

Addendum to Appendix 2: Template for Detailed Contact Information for Evaluators (Primary Reviewers and Secondary Reviewers) for each Science Discipline (For Use by Regulatory Authorities Only)

	Product Chemistry & Product Identity (or Product Characterization and Analysis)	Toxicology (Inc. Health Exposure contact if different)	Metabolism and Core Residue Studies (Tolerance Exemption Petition or Numerical Tolerance)	Env. Fate	Eco-Tox.	Efficacy / Crop Tolerance
Canada						
USA						