Regulatory Directive DIR2012-02

# Re-evaluation Program
# Cyclical Re-evaluation

*(publié aussi en français)*

**21 June 2012**

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

Publications
Pest Management Regulatory Agency
Health Canada
2720 Riverside Drive
A.L. 6604-E2
Ottawa, Ontario K1A 0K9

Internet: pmra.publications@hc-sc.gc.ca
healthcanada.gc.ca/pmra
Facsimile: 613-736-3758
Information Service:
1-800-267-6315 or 613-736-3799
pmra.infoserv@hc-sc.gc.ca

Canada

ISSN: 1197-7396 (print)
1498-5926 (online)

Catalogue number: H113-3/2012-2E (print version)
H113-3/2012-2E-PDF (PDF version)

# Table of Contents

# 1.0 Introduction

Re-evaluation is the cyclic review of pesticide active ingredients and their associated uses on the basis of updated data and information to determine whether, and under what conditions, their continued registration is acceptable. Health Canada's Pest Management Regulatory Agency's (PMRA) proposed new approach to re-evaluation was published for consultation in Re-evaluation Note REV2010-18, *Re-evaluation Program*, in December 2010. A number of comments were received. These comments were taken into consideration in this final version of the document and are summarized in Appendix I. Section 4.0 *Special Review* from REV2010-18 and any comments received with respect to special review have not been included here. The special review process will be addressed separately in a forthcoming document.

In 2001, the PMRA implemented the four-program re-evaluation approach[1] for pesticides registered prior to January 1995. This approach is now reaching completion. As of October 2011, over 95% of the 401 active ingredients covered under the original approach have been addressed, with the vast majority of assessments resulting in changes to the conditions of use. A significant proportion of the active ingredients (over 20%) have been identified for phase-out (i.e. discontinuation) as a result of the PMRA's review or voluntary discontinuation by their manufacturers. Very few active ingredients have been accepted for continued use without any label changes.

The *Pest Control Products Act* 2006, came into force 5 years after the original re-evaluation approach was articulated. It specifies the legal foundation for re-evaluation and prescribes that the re-evaluation of all pesticides be initiated on a 15-year cycle to ensure that they continue to meet current scientific standards. Since 15 years have now passed for pesticides first registered in 1995, the new legislated approach of cyclical re-evaluation came into effect in 2010. Currently, 572 active ingredients are found in approximately 5000 end-use products registered under the *Pest Control Products Act* in Canada. At the time of their initial registration, these pesticides were considered acceptable (i.e. met health, environment and value standards of the time). Since then, science has evolved, and additional information may be available which could affect the risk and value profile of a pesticide. It is incumbent on the PMRA to re-evaluate registration and post-registration decisions on a 15-year cyclical regular basis to determine whether the use of these previously registered pesticides continues to be acceptable according to current standards.

This regulatory directive presents the renewed approach to cyclical re-evaluation which is in line with the requirements of the *Pest Control Products Act*. This directive will apply to all active ingredients initiated under cyclical re-evaluation. Regulatory Directive DIR2001-03, *PMRA Re-evaluation Program*, continues to apply to those active ingredients initiated under the original four-program approach to re-evaluation.

[1] Described in the Regulatory Directive DIR2001-03, *PMRA Re-evaluation Program approach.*

## 2.0 Key Considerations that Led to the Development of the New Approach

### 2.1 Requirements of Legislation

The *Pest Control Products Act* requires the PMRA to initiate re-evaluations for each registered pesticide on a 15-year cycle, based on the date of either its initial registration or the most recent major decision affecting the registration. The re-evaluation must be initiated no more than one year after 15 years have elapsed since the most recent major decision. The Act also requires that a scientifically based approach be applied in evaluating the health and environmental risks and in determining whether those risks are acceptable. This provides for the regular review of registered products and supports the ongoing incorporation of new methodologies, data and regulatory approaches into the evaluation and assessment of pesticides. This may include, for example, new methods of risk evaluation and assessment, new methods of risk mitigation and new information about specific pesticides. Policy approaches regarding the consideration of the unique characteristics of sensitive subpopulations among humans are now also entrenched in the new legislation.

The PMRA is required to initiate a re-evaluation as per section 16 (2) of the *Pest Control Products Act*:

> *"...the Minister shall initiate a re-evaluation of that product no later than one year after fifteen years have elapsed since the most recent decision"*, of a type referred to in the paragraph 28 (1) (*a*) or (*b*),
>
> *28(1)(a): "to grant or deny an application*
> *(i) to register a pest control product that is or contains an unregistered active ingredient, or*
> *(ii) to register, or amend the registration of, a pest control product if the Minister considers that registration or amendment of the registration may result in significantly increased health or environmental risks;*
>
> *28(1)(b): "about the registration of a pest control product on completion of a re-evaluation or special review".*

Re-evaluation of a pesticide is conducted as per section 16 (6):

> *"...After the re-evaluation is initiated , the Minister shall, in accordance with the regulations, if any, conduct any evaluations that the Minister considers necessary with respect to the health or environmental risks or the value of the pest control product and shall carry out the consultations required..."*

The PMRA may initiate a re-evaluation before the fifteen year statutory deadline as per section 16 (1):

> *"...The Minister may initiate the re-evaluation of a registered pest control product if the Minister considers that, since the product was registered, there has been a change in the information required, or the procedure used, for the evaluation of the health or environmental risks or the value of pest control products of the same class or kind."*

## 2.2 International Cooperation

In 1994, the Canadian government proposed a cost-effective re-evaluation program on the basis of cooperation between Canada and the United States, and with other members of the Organisation for Economic Co-operation and Development (OECD).[2]

The PMRA is committed to continuing co-operation with international regulatory bodies regarding re-evaluation activities. Where appropriate, the PMRA will participate in joint reviews or work-sharing of documents and information relating to the review of a pesticide with other countries.

In order to maximize efficiency, the PMRA will align Health Canada's re-evaluation schedule with that of the United States Environmental Protection Agency (USEPA), wherever appropriate.

## 2.3 Lessons Learned From the "First Round" of Re-evaluation

While the original re-evaluation program has succeeded in ensuring that older pesticides meet modern standards, there have been challenges and lessons learned.

The original re-evaluation program addressed products registered from the late 1920's through to 1995. Owing to the long time lapse between the initial registration of older active ingredients and their re-evaluation, science standards had generally evolved considerably since the last major review of these active ingredients, resulting in extensive data and review requirements. In addition, many of these active ingredients were registered before the existence of electronic databases, so the research and assessment of archived files was resource intensive. These demands are expected to lessen in subsequent re-evaluations as the PMRA begins to address active ingredients with more up-to-date databases and study methods, and the supporting data are more likely to be available in electronic form.

Lastly, there existed a wide range of timelines for re-evaluations conducted under the initial re-evaluation program. This was challenging from both the stakeholder (predictability) and Agency (work planning) perspectives. The new process will seek to bring greater clarity and predictability to the scope and timelines for each re-evaluation.

[2] *Government Proposal for the Pest Management Regulatory System - October 1994*

## 3.0 The New Approach

### 3.1 General

This regulatory directive describes a focussed re-evaluation approach where the breadth and depth of the review will be commensurate with the complexity of issues associated with a given pesticide.

Early in the re-evaluation process the PMRA will complete a screening review to determine the information and data available to the Agency. Risk assessment(s) previously conducted will be verified to determine if they are considered to meet the standards of modern science and current policy in all the review areas (i.e. health, environment and value). Screening reviews will also include scans for new information (for example, relevant developments reported in the scientific literature and incident reports) and information on the status of the active ingredient in other jurisdictions.

If previous risk assessments on file, in one or more areas (for example, occupational exposure, environment, etc.) do not meet current requirements, a new or revised evaluation may be required for each of the affected areas. For example, new scientific approaches, PMRA policies, or new scientific data and models could potentially result in modifications to the conditions of registration. On the other hand, the screening review may indicate that a previous risk assessment in a specific area (for example, dietary risk assessment) is acceptable as measured against current standards. The PMRA will also verify that the conditions of use assessed in the previous evaluation remain reflective of the current situation–that is, nothing major has changed that would alter the previous registration decision. If this is the case, this component of the re-evaluation may be considered complete and the previous risk assessment will stand. If further evaluation is required in one or more areas, a project plan will be published specifying the area(s) to be re-evaluated. If necessary, additional information and/or new data required to proceed with the re-evaluation will be specified at this time.

Alternatively, the PMRA may determine that all components of the re-evaluation are adequately addressed by previous reviews, and that additional evaluation is not warranted. In this situation, the PMRA will publish a proposed re-evaluation decision for public consultation, indicating that the pesticide does not pose unacceptable risk to human health and the environment, and continues to be acceptable for registration.

This approach will permit the PMRA to focus its review resources on those areas of risk assessment that require updates. In accordance with the *Pest Control Products Act*, the PMRA will provide a public summary of the assessment, conclusions, and any proposed risk management measures for consultation prior to finalizing a re-evaluation decision.

### 3.2 Process

The process is as follows:

Step 1 assess the information available to the PMRA including any information suggesting a change in risk or value; determine the scope of additional risk analyses and information required for the PMRA to make a re-evaluation decision;

Step 2 if further evaluation is required, develop and publish a project plan specifying areas to be re-evaluated; if necessary, additional information and/or new data required to proceed with the re-evaluation will be specified;

Step 3 conduct re-evaluations of targeted areas;

Step 4 publish a proposed re-evaluation decision for public consultation;

Step 5 publish a final re-evaluation decision;

Step 6 implement the decision.

**Steps 1 and 2**

Clearly defining the scope of a re-evaluation is key to an efficient and targeted approach. Consequently, the first step is to complete a screening review and assess information available on an active ingredient. This information can include, but is not limited to, information already on file with the PMRA, information obtained in the published literature, information from other jurisdictions, and incident reports. The PMRA will outline the anticipated focus of the re-evaluation and the associated time lines and share this information with stakeholders by publishing it to the Pesticides and Pest Management portion of Health Canada's website.

During Steps 1 and 2 the PMRA may request additional information from registrants to supplement the existing information on file. This could include information on the use pattern and extent of use, new science, incident reports, and risk mitigation measures.

**Steps 3, 4 and 5**

Scientific re-evaluations are conducted during Step 3. In some cases, all components of the re-evaluation may be adequately addressed by previous reviews, and an additional evaluation is not warranted.

A re-evaluation could result in one or more outcomes. On the basis of the completed scientific evaluations the proposed regulatory decision could be that continuing registration is acceptable with no changes. On the other hand, continued registration could require amendments to the label (for example, by adding additional protective measures to label instructions) or removal of certain uses or formulations from registration. A re-evaluation could also identify additional information requirements as a condition of continued registration to confirm or refine the conclusions drawn. A pesticide registration could also be proposed for cancellation because of unacceptable risks to human health or the environment of Canadians or unacceptable value.

Where there are significant changes to the risk profile associated with a pest control product, the PMRA may publish a preliminary risk assessment for consultation. Additional information requirements may be identified which must be satisfied in order to confirm, refine or complete the scientific evaluations. The PMRA may publish an interim re-evaluation decision and/or require interim risk mitigation, pending submission of this requested information.

Under the *Pest Control Products Act*, a registration may be cancelled or amended prior to the conclusion of the re-evaluation, if there are reasonable grounds to believe that there is an imminent risk to human health or safety, or the environment.

In accordance with the *Pest Control Products Act*, the PMRA will consult the public and stakeholders on proposed re-evaluation decisions, including any proposed risk management measures.

### 3.3 Scheduling

The initiation date of the re-evaluation for an active ingredient will be generally based on the date of the most recent major regulatory decision of a type referred to in section 28(1) of the *Pest Control Products Act*.

Other factors may result in the scheduling of re-evaluation earlier than the statutory deadline. For example, a cluster of similar active ingredients might be re-evaluated as a group instead of strictly according to the statutory time requirements.

Scheduling may also be advanced, but not delayed, to permit work-sharing with other regulatory jurisdictions or other parts of the Canadian federal government. The PMRA will continue to inform the public of upcoming re-evaluations by publishing a schedule.

# Appendix I Comments and Responses

The PMRA received comments in response to Re-evaluation Note REV2010-18, *Re-evaluation Program*, from stakeholders including registrants, non-governmental organizations with interests in human health or the environment, municipal governments, and the general public. The PMRA has consolidated and summarized the comments received and provides responses below.

## 1.0 Comment relating to the consultation process

There should have been broader public consultation on the PMRA's new approach to re-evaluation, and better advertising of the consultation process.

### PMRA Response

The PMRA posts documents for consultation to the Pesticides and Pest Management portion of Health Canada's website which is accessible to the general public. In response to comments received from stakeholders, the consultation period for REV2010-18 was extended by one month. Stakeholders may subscribe to the PMRA Really Simple Syndication (RSS) feed, which notifies subscribers of key new postings, including all documents available for consultation. To sign up for the PMRA RSS feed, go to www.hc-sc.gc.ca/cps-spc/pubs/pest/index-eng.php.

## 2.0 Comments relating to the re-evaluation process

### a) Comment relating to the need and impact of a new re-evaluation approach

Why is the PMRA developing a new approach to re-evaluation if the original 4-program approach was so successful? The new approach, specifically the internal scoping stages, will weaken the PMRA's mandate to protect the public and the environment as it appears less transparent than the present program. It would also be useful to know how the outcomes of the new re-evaluation approach compare to the original re-evaluation approach.

### PMRA Response

The original four-program approach was required based on the magnitude of the re-evaluation task (i.e. re-evaluation of over 400 pesticide active ingredients within a relatively short period of time). This approach relied heavily on the pesticide re-registration program of the United States (i.e. the Reregistration Eligibility Decision (RED) documents published by the USEPA).

Now that the PMRA is entering the first phase of cyclical re-evaluation, a more targeted approach is possible. This more targeted approach strives to provide increased transparency through the publication of a project plan for each active ingredient under re-evaluation. The project plan will clearly indicate the areas of focus for re-evaluation in consideration of all available information, such as recent PMRA assessments and re-evaluations of other OECD countries, including the United States.

Since the PMRA is simply building on, and improving, the original approach, the outcome of the re-evaluation (i.e. ensuring that risk to human health and the environment continues to be acceptable) will remain the same.

**b) Comment relating to registrant involvement throughout the re-evaluation process.**

Registrants should be engaged throughout the re-evaluation process and have the opportunity to provide additional information and/or propose changes in the use pattern, especially when significant changes are expected as a result of the re-evaluation. Recommend that registrants should have the opportunity to provide feedback prior to the initial publication of the proposed re-evaluation decision (i.e. during Steps 2, 3, 4 and 5) in order to discuss any pending issues or data gaps.

**PMRA Response**

Registrants will be engaged throughout the re-evaluation process. During Steps 1 and 2 the PMRA may request additional information from registrants to supplement the existing information on file. This could include information on the use pattern and extent of use. The PMRA will consider more dialogue with registrants when major changes are proposed to the use pattern. In certain cases, a preliminary risk assessment may be published for public comment (i.e. prior to Step 4) when more input is needed from stakeholders. Step 4, the publication of a proposed re-evaluation decision, will be open for public consultation as it has been in the past.

**c) Comment relating to timelines**

It is recommended that timelines for all the re-evaluation stages be communicated at the beginning of the process, once the scope of work is determined. The timelines should be specified for Step 1 through 6 and PMRA performance should be measured against those timelines. An 18 month timeline is typical for a new product review and a re-evaluation should take no longer then the registration of a new active ingredient.

**PMRA Response**

Although it may not be possible to specify timelines for Step 1 through 6 at the start of the process, the intent is that the project plan, published in Step 2, will improve the predictability of the process by outlining the anticipated focus of the re-evaluation and the associated timelines for each active ingredient. Timelines will depend on the complexity of the re-evaluation and on the amount of work anticipated. Section 3.0 of the Regulatory Directive has been revised to clarify the fact that timelines will be included in the project plan.

### d) Comment relating to sensitive subpopulations

In REV2010-18, Section 2.1 *Requirements of Legislation*, it is stated that "In addition, the approach considers the unique characteristics of sensitive subpopulations among humans and other organisms.". How does this differ with respect to the original re-evaluation approach?

**PMRA Response**

Considering the unique characteristics of sensitive subpopulations among humans and other organisms remains consistent with the original re-evaluation approach. The only difference is that it is now required under the *Pest Control Products Act* (s. 19(2*b*)). The text in Section 2.1 of the Regulatory Directive has been revised to clarify this point.

### e) Comment relating to the reading room

The PMRA should be clear as to what is an interim versus a final decision. If a decision is final then the public should have access to the related material in the reading room, including reports of data extraction and toxicological assessment.

**PMRA Response**

A decision is final once a final re-evaluation decision has been published. Under the *Pest Control Products Act*, interested persons may inspect confidential test data submitted by registrants in support of recent major regulatory decisions in the reading room.

## 3.0 Comment relating to the initial scoping stage.

The initial two-step review (Steps 1 and 2) to determine adequacy of existing information should be open for public consultation/publicly accessible and not an "internal file" review. Steps 1 and 2 appear secretive and unnecessary; they greatly decrease the transparency and accountability of the re-evaluation process. Scoping does not appear to be arms-length, independent or transparent because PMRA scientists will be reviewing work done by PMRA scientists to determine its quality.

**PMRA Response**

The purpose of the screening review is not to assess the reviews that are on file for quality, but to determine the information and data available to the Agency to ensure that it continues to meet modern regulatory and scientific requirements. Risk assessment(s) previously conducted will be verified to determine if they are considered to meet the standards of modern science and current policy. Based on the screening review, the PMRA will outline the anticipated focus of the re-evaluation and the associated timelines in a project plan which will be published. Furthermore, the proposed re-evaluation decision will continue to be available for consultation. Section 3.1 of the Regulatory Directive has been revised to clarify this process.

## 4.0 Comments relating to types of information to be considered during re-evaluation

### a) Comment relating to consideration of activities of other jurisdictions.

Re-evaluation should be coordinated with other government jurisdictions where possible (for example, USEPA, OECD, NAFTA, Chemicals Management Plan (CMP)) and joint re-evaluations should be considered. There is significant uncertainty about when a pesticide re-evaluation will occur and whether and how the CMP assessment results are considered in the pesticide re-evaluation.

**PMRA Response**

As in the past, the PMRA will continue to take into consideration reviews and other information from other government jurisdictions, specifically from other OECD countries. Joint re-evaluations will be considered when re-evaluation commitments and the scope of work are comparable.

The PMRA will continue to review the list of CMP substances to identify all pesticide active ingredients, with the objective of coordinating the CMP review with PMRA's re-evaluation schedule wherever possible. When alignment is not possible, the PMRA will consider the results of the CMP assessment in the proposed re-evaluation decision. The PMRA will also share the results of its re-evaluation decisions with Health Canada and Environment Canada partners, for consideration in CMP reviews.

The PMRA will publish initiation schedules for re-evaluation on a regular basis. The first schedule was published on 17 March 2011, indicating the initiation schedule for re-evaluation for the next 3 years (REV2011-03, *Pest Management Regulatory Agency Re-evaluation Initiation Schedule*). Target completion dates for each active ingredient will be published in a project plan once a screening review has been completed.

### b) Comments relating to the adequacy of information considered during re-evaluation.

Re-evaluation should take into consideration independent literature, incident reports and evaluation results from other jurisdictions (for example, USEPA, EU countries, etc.) when available. Will the independent literature be listed on the data-call-in if it is not performed by the registrant? If not, will the registrant be informed of what literature will be examined in the re-evaluation process?

**PMRA Response**

As in the past, the PMRA will continue to take into consideration reviews and other information from other government jurisdictions, specifically from other OECD countries such as the United States, the EU, New Zealand and Australia. The PMRA also has a mandatory incident reporting program which will be consulted during re-evaluation.

Independent literature will be taken into consideration but will not be listed on the data-call-in. The data-call-in only lists what is required from registrants by the PMRA. However, independent literature used during the re-evaluation will continue to be included in the reference list in the proposed regulatory decision, and comments with respect to the literature cited used can be submitted to the PMRA at that time.

**c) Comment relating to further information to be considered during re-evaluation.**

Empirical and sociological information about actual instances of pesticide poisoning, contamination or environmental impacts, patterns of pesticide use, cultural attitudes of users, levels of compliance with the labels, etc. should be considered during re-evaluation.

**PMRA Response**

Information about instances of pesticide poisoning, contamination or environmental impacts is collected under Health Canada's mandatory incident reporting program (*Pest Control Products Incident Reporting Regulations*). Patterns of pesticide use are collected under the mandatory sales reporting program (*Pest Control Products Sales Information and Reporting Regulations*). The PMRA will consider this information during re-evaluation.

There are also compliance programs and enforcement activities in place at the PMRA which are aimed at protecting human health and the environment from the risks of non-compliance with the *Pest Control Products Act* and Regulations (see DIR2007-02, *Compliance Policy*).

**d) Comment relating to the depth of re-evaluation**

Concern that the re-evaluation process could limit itself to only a very cursory examination of the new US re-evaluation data (or other quality new data) that is readily available.

**PMRA Response**

The re-evaluation process will not be cursory. The screening review will determine the depth of re-evaluation that will be needed for each active ingredient. In depth assessments will be conducted by the PMRA where required. The PMRA will consider information from other jurisdictions such as the USEPA and other OECD countries, provincial monitoring programs and other federal departments taking into consideration Canadian conditions. In addition, data from registrants, independent literature, the incident reporting database, and any other relevant information may also be taken into consideration.

**e) Comment relating to older studies and guideline requirements**

How will the quality of data be determined and will original data be re-checked for quality since data guidelines can change over time? Older studies should not be scrutinized with the same standard as today's. Guideline requirements change with time. A study that met guidelines at the time it was conducted should be evaluated based on the guidelines under which it was conducted. The application of new information may be appropriate where the generally accepted conclusions from certain observations have since been shown to be incorrect.

**PMRA Response**

The PMRA will review previous risk assessments in light of current scientific standards and policy. Consideration will be given to the guidelines under which studies were originally conducted. New studies will be required only if necessary.

**f) Comment relating to new data that registrants would like to submit but may not be required under targeted re-evaluation.**

It is recommended that the PMRA allow registrants to provide a list of any new studies that may be available during the re-evaluation. Under the proposed guidelines, registrants would not have the opportunity to submit new data during the re-evaluation unless it is required by the PMRA (i.e. the data does not fall within the scope of the proposed re-evaluation). This prevents the registrant from providing new studies that could further refine a risk assessment. For example, a registrant may have new ecotoxicology data that could reduce buffer zones but the PMRA is only focussing the re-evaluation on dietary risk. Another scenario could be that the database is not complete and the registrant would like to submit data to complete the database. Or, a registrant may have conducted a new study to replace an older study that was non-GLP, or that had some deficiencies.

**PMRA Response**

The PMRA will issue a request for additional information and/or new data when considered necessary for the conduct of the re-evaluation. Additional data may be required to refine the risk assessment. If a registrant has new studies to further refine a risk assessment which may result in a label amendment (for example, reduced buffer zones), but the study is not considered necessary to the re-evaluation, then that information may be submitted with a request to amend an existing registration. Any information/data subject to the incident reporting program must be submitted to that program.

**g) Comment relating to demonstration of product safety.**

The safety of a product may be demonstrated by long term use with no incidents and/or by epidemiology or biomonitoring studies. If a product has been safely used since initial registration there may be no need to request additional information even if the database has not been updated between the initial registration and re-evaluation.

**PMRA Response**

Although incident reporting data, and epidemiology and biomonitoring studies may be used as part of the decision making process during re-evaluation, the PMRA does not determine acceptability of an active ingredient for continued registration based on this information alone.

**5.0 Comment relating to an applicant's ability to modify the use pattern while an active ingredient is under re-evaluation.**

The PMRA needs to clarify how re-evaluation will affect an applicant's ability to amend a registration or make notifications with respect to a product.

**PMRA Response**

During the original re-evaluation program (2001 to 2010), the use pattern of an active ingredient was generally frozen once the re-evaluation was initiated. During the revised approach to re-evaluation, the PMRA will take a practical, pragmatic approach to requests for use expansion of an active ingredient to amend registrations based on the timing of the reviews.

**6.0 Comments relating to additional considerations which should be included in the re-evaluation process.**

**a) Comment relating to toxicity of formulants on a pesticides overall toxicity**

The PMRA should consider the toxicity of inactive ingredients and/or adjuvant additives on a pesticides overall toxicity.

**PMRA Response**

When an end-use product is considered for registration, the PMRA requires the submission of acute oral, dermal, inhalation, primary eye irritation, primary dermal irritation and dermal sensitization studies conducted with the end-use product. Depending on the use pattern, short-term studies or other special studies may be required if any component of the end-use product may increase absorption of the active ingredient(s) or increase toxic or pharmacologic effects.

Furthermore, formulants (i.e. any substance, other than an active ingredient, intentionally added to a pest control product) are regulated under Regulatory Directive DIR2006-02, *Formulants Policy and Implementation Guidance Document*.

### b) Comments relating to cumulative risk assessment

The PMRA should acknowledge that combined, multiple active ingredient use is possible and investigate the increase in toxicity from potential synergistic effects *in situ*. Will the PMRA consider cumulative risk assessment during the re-evaluation process? A new approach to re-evaluation should specify how cumulative risk will be addressed and how the PMRA will make progress in this area in conjunction with activities occurring within the USEPA. Details and a timetable for meeting obligations to consider information about cumulative effects of groups of similar pesticides is needed.

**PMRA Response**

When pesticide active ingredients are known to have a common mechanism of toxicity, a cumulative risk assessment will be conducted. Development of a cumulative risk assessment policy is currently underway by the PMRA. Furthermore, the assessment of risk by the PMRA is conservative in order to allow for uncertainties in a risk assessment.

### c) Comment relating to endocrine disruption and developmental neurotoxicity

Greater consideration during re-evaluation is needed to assess developmental neurotoxicity and endocrine disruption. Evaluation of endocrine disruption potential needs to address the challenges of non-monotonic dose-response curves and the related issue of evidence of effects at extremely low doses. For developmental neurotoxicity, greater consideration is needed in the assessment of functional end-points (behaviour, learning) as a result of early life exposure, particularly in utero.

**PMRA Response**

For the new approach to re-evaluation, the toxicology database and hazard assessments available will be considered during the screening review. In addition, scans for additional sources of information (for example, from other jurisdictions) will occur at this step. Where required, additional information and/or data will be requested to address potential concerns related to endocrine disruption or developmental neurotoxicity prior to proceeding with the re-evaluation.

The potential for a given pesticide to elicit endocrine-modulating (hormonal) effects is currently assessed from animal studies such as multigeneration reproductive toxicity assays and chronic toxicity/carcinogenicity assays. These studies form part of the data requirements for pesticide registration and have the potential to reveal numerous endpoints that may be directly or indirectly related to endocrine disruption. With respect to adequately characterizing dose-response curves, greater efforts to incorporate dose-response modelling in regulatory toxicology are currently underway. These *in silico* methods combined with targeted dose selection in animal toxicity studies will lead to a more accurate characterization of the shape and slope of the dose-response curve. In addition, the PMRA is in contact with the USEPA regarding the data call in for Tier I endocrine assays on pesticides.

Additional data to characterize neurotoxicity in developing animals will be required if risks of concern related to the potential for developmental neurotoxicity are triggered by the overall toxicity profile of a given active ingredient. These Developmental Neurotoxicity Tests (DNT) are based on animals dosed in utero and then assessed for gross neurologic and behavioural abnormalities, including physical and behavioural development, motor activity, motor and sensory function, and learning and memory.

### d) Comment relating to an adaptive management framework and updating of systematic reviews.

The PMRA needs to invest in scientific information infrastructure to systematically review information regarding pesticides. Ongoing updating of systematic reviews should be largely automated, with alerts when new reports become available. New data should be incorporated along with previous reports and a single research report should not be discarded because it does not single-handedly overturn an evaluation decision.

A framework for adaptive management should be instituted, particularly as research is progressing quickly in a rapidly changing environment.

**PMRA Response**

The PMRA continually adapts its data requirements and risk assessment methods to new data and evolving regulatory science in its assessments of registrants' applications to register new uses and label amendments for established pesticides. However, the PMRA does not have the resources to proactively incorporate new data and update previous regulatory decisions on an ongoing basis. Rather, the PMRA will conduct cyclical re-evaluations to update its reviews of registered pesticides and reassess their acceptability.

The cyclical re-evaluation program allows regulators and the regulated community to efficiently organise the conduct and review of updated studies and information for each and every active ingredient and the associated end-use products. PMRA evaluators search for new information at the time an active ingredient is under re-evaluation.

The PMRA Pesticide Incident Reporting Program also provides a mechanism for the ongoing collection of information on pesticides after they have been registered. Incident reports help the PMRA identify any potential risks to human health or the environment from the use of pesticides and to take corrective actions when necessary. Additional regulatory action may be taken at any time if new information provides sufficient grounds to believe the safety or value of the pesticide are no longer considered acceptable.

**e) Comment relating to relative risk of active ingredients for domestic use.**

The PMRA should implement immediate discontinuation of high-risk active ingredients when lower toxicity/risk alternatives are registered.

**PMRA Response**

The PMRA is not authorised to cancel a pesticide when there is a lower risk alternative registered, as long as that pesticide meets current requirements with respect to the protection of human health and safety and the environment. However, reducing the use of the highest-risk pesticides, encouraging the registration of lower-risk pesticides and promoting the use of alternative approaches to pest control are ways in which the PMRA strives to reduce the risk to Canadians from pesticides. The PMRA works with stakeholders to foster initiatives that, among other things, will support the development and availability of reduced risk pesticides and sustainable pest management practises that lead to reductions in human health and environmental risks, help increase grower awareness and adoption of biopesticides and increase public awareness of sustainable pest management practises. In addition, the Agency is developing an innovative and flexible approach for non-conventional pest control products with favourable risk profiles (Regulatory Proposal PRO2010-06, *Guidelines for the Registration of Non-Conventional Pest Control Products*).

**f) Comment relating to harmonization of MRL's and adding new uses.**

Recommend that the PMRA consider harmonization of MRL's and adding new uses (for example, minor uses) during the re-evaluation process.

**PMRA Response**

Re-evaluation will assess the existing registered uses of a pest control product, but will not be a mechanism to seek the addition of new uses to the product label or for the harmonization of MRL's. Applications for new uses and harmonization of MRL's should continue to be brought through the new product evaluation process.

**g) Comment relating to compliance with respect to packaging labels**

Domestic pesticide packaging labels, warnings and directions tend to be inadequately followed by the public. Compliance with labels is assumed despite little available evidence. As a result, increasing number of municipalities are adopting restrictive cosmetic pesticide use bylaws. The PMRA should consider options to improve readability of packaging label directions and warnings to the public to ensure proper use.

**PMRA Response**

The PMRA is always looking for ways to improve labels and to reach the public with regards to proper pesticide use. The pesticide label specifies the correct use of a pesticide product so that it poses no health or environmental concerns. The label is a legal document that must be followed. The PMRA does take initiatives to help consumers use pesticide products properly. In 2010, Regulatory Directive DIR2010-02, *Label Improvements for Spot-on Pesticides Used for Flea and Tick Control on Companion Animals* was published. Currently on the PMRA website there is a section on the *Proper Use of Pesticides* for the public, this section includes information on *Healthy Lawns, Mosquito Control, Swimming Pools* and *Homeowner Guidelines for Pesticide Use*. There is also a video on the proper use of rodenticides. As well, compliance and enforcement activities promote compliance with pesticide usage instructions.

## 7.0 Comment relating to data protection

Data used during a re-evaluation should be compensable between existing registrants. The proposed joint review and/or work-sharing of re-evaluations may have a significant negative impact on the data owners' ability to receive fair compensation for their investments. The PMRA's approach may discourage the proactive approach that many companies take to generating data to continually update product databases. The PMRA needs to clarify the treatment of data that the PMRA has in house and/or with joint review partners during joint reviews, work sharing or etc. The use of compensable data by the PMRA during a re-evaluation needs to have a mechanism by which the owner of the data is contacted and an agreement is in place to allow for data access to other registrants.

**PMRA Response**

The PMRA is currently working on a process with respect to data protection for data used during re-evaluation. Guidance will be provided by the PMRA once an approach has been developed.