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A Decision Framework for Risk Assessment and Risk Management in the Pest Management Regulatory Agency

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Table of Contents

1.0 Introduction

Pesticides are designed to "control, prevent, destroy, mitigate, attract or repel" pests. Because of the properties and characteristics that make them effective for their intended purposes, they also may pose risks to people and the environment.

In developing a decision framework that is based on the assessment and management of risk, one must identify the types of risks to be controlled; the nature of the sources from which those risks may arise; the types of activities that may cause them to arise; the means available for assessing the magnitude of the risks; the means available to mitigate and minimize the risks; appropriate means to involve stakeholders in the decision-making process; and appropriate means to enable and facilitate interaction and cooperation with other jurisdictions and regulatory bodies.

This document describes framework that guides the Pest Management Regulatory Agency (PMRA) in the assessment and management of risk and in its regulatory decision making. A cornerstone of the framework is its strong reliance on a comprehensive body of scientific evidence and scientific methods to determine the nature and magnitude of the risks posed by pesticides. This allows application of appropriate and effective risk management strategies for the protection of both human health and the environment. The PMRA's risk-based approach to the regulation of pesticides reflects approaches of pesticide regulatory agencies in other countries. It is also consistent with approaches for regulation of other chemicals in Health Canada. The framework provides for a systematic application of science to support the PMRA's regulatory decisions. It enhances predictability and transparency of the process that protects the health of Canadians and their environment. By considering all relevant criteria in a comprehensive fashion, it also ensures completeness in risk management decision making.

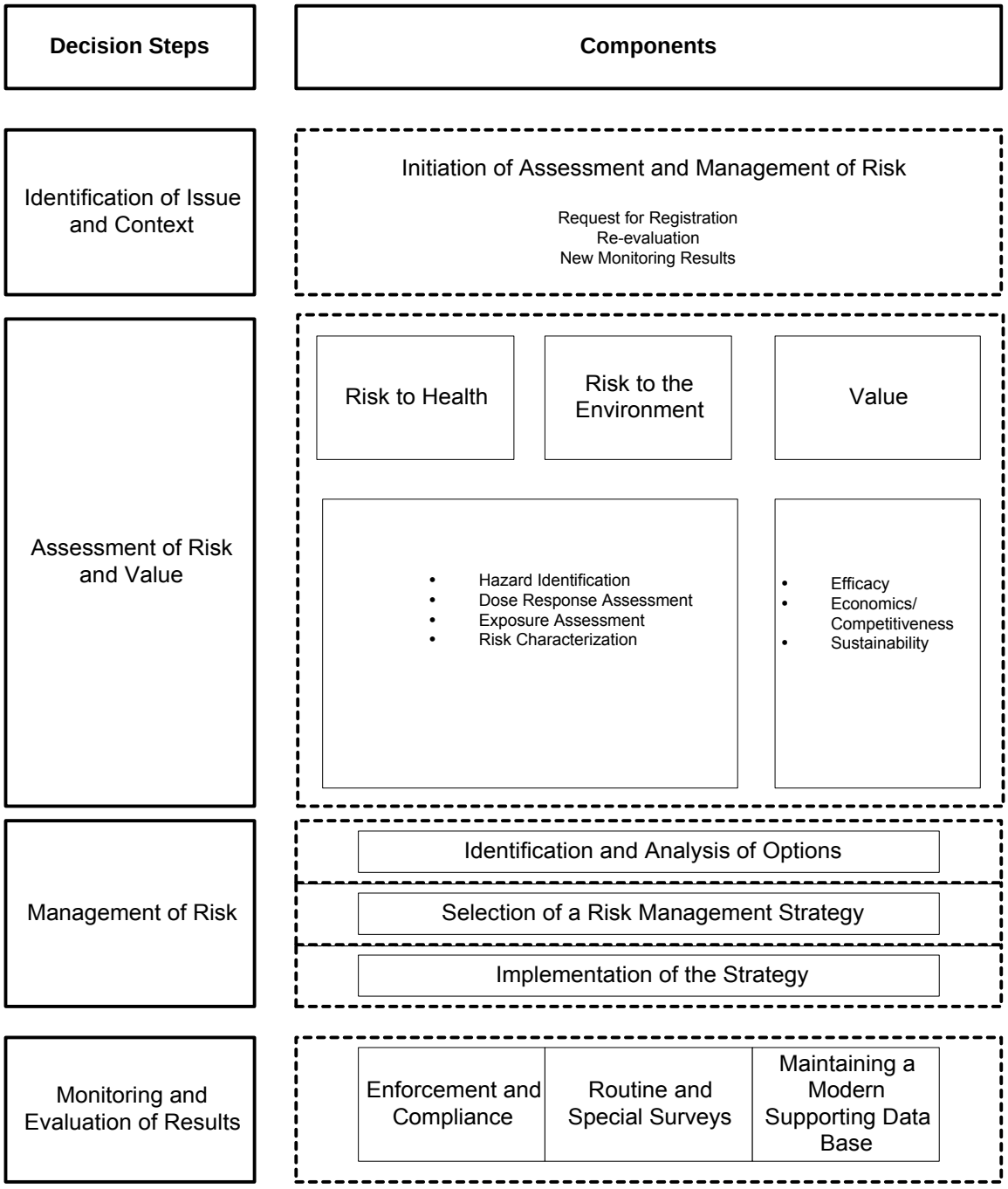
2.0 Overview of the framework

The decision framework is divided into a number of identifiable decision steps and components, as outlined in Figure 1.

Although the framework is presented as a series of sequential steps leading from a starting point, such as a request to register a new pesticide, to a defined end point, such as the decision to register, the underlying process is highly iterative and interactive. This is particularly evident in the development of risk management options. If there is a concern that the use of a product as proposed by the applicant may be associated with an unacceptable level of risk, PMRA will consider restrictions on use or other regulatory options to reduce the risk to acceptable levels. The process usually results in a number of possible management options. Each of these options must be elaborated on in sufficient detail to allow quantitative re-examination of the initially calculated risk. Typically, this requires several iterations of the assessment of risk and recalculation of risk under the different options considered.

The majority of registration decisions within the PMRA concern chemical pesticides. Accordingly, this framework is based to a large extent on the processes and approaches used to arrive at decisions about a new chemical pesticide or one under re-evaluation. With modifications specific to the situation, however, the framework also applies to registration decisions for microbial and pheromone pesticides.

Figure 1 Decision framework of the Pest Management Regulatory Agency



3.0 Identification of the Issue and its Context

All pesticides must be registered before they can be sold or used in Canada. Therefore, the most common trigger for initiating the decision-making process is a request for registration of a new pesticide or for amendments to an existing registration. The identification of the need for a re-evaluation will also trigger the decision-making process.

The *Pest Control Products Act* [1](PCP Act) and Regulations is the primary federal legislation for the regulation of pesticides in Canada and governs their importation, manufacture, sale and use. This legislation entrenches the authority for risk assessment and risk management based decisions, whereby the risks and value of a product must be considered acceptable by the Minister for it to enter and remain on the market in Canada. The legislation also includes provisions to facilitate enforcement of compliance with the PCP Act and Regulations. It should also be noted that provincial pesticide legislation plays an important role in the overall process of pesticide regulation in Canada.

The PCP Act provides the authority for decision making on the basis of risk assessment and risk management : it requires a risk based, proactive approach for new products which are subject to premarket approval, and it requires a continued regulatory vigilance to ensure that registered products remain acceptable.

Part of the regulatory context is consideration of the compatibility of pesticide registrations with federal policies, such as the Toxic Substances Management Policy (TSMP), and international agreements on Persistent Organic Pollutants (POPs), and the Montreal Protocol on ozone depleting substances. Substances identified as Track 1 under the federal TSMP, ozone depleting substances, such as methyl bromide identified in the Montreal Protocol, and POPs are considered unacceptable for registration as new pesticide active ingredients, and would not enter the decision-making process except in highly unusual and very restricted cases, such as emergencies[2] and critical need situations.[3] Their presence in existing pesticide products as active ingredients, formulants or contaminants could lead to a reassessment of their registration status and regulatory action consistent with pertinent federal policies and international commitments. It is also important to ensure that the use of a pesticide will not contravene other federal statutes before that use is approved under the PCP Act.

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1 Where a pesticide is used on food products, i.e., on food crops or directly on food products, the PMRA evaluates and establishes appropriate maximum residue limits (MRLs). Maximum residue limits are set for each pesticide used on food in Canada or present on food imported into Canada. The MRLs are established as a regulation under the *Food and Drugs Act* (FDA).

2 See Regulatory Directive DIR94-05, *Registration of Pesticides for Emergency Use*, March 30, 1994.

3 See Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*, March 12, 1999.

As in other Organisation for Economic Co-operation Development (OECD) countries, detailed risk and value assessment and risk management methodology or policies are not included in statute or regulation, but rather in directives and guidelines, so that they can be adapted quickly as scientific knowledge and public policy evolve.

4.0 Assessment of Risk and Value

Assessments of health risk, environmental risk and value are central to PMRA's decision-making process. They provide a solid factual and contextual basis for making sound registration decisions that protect human health and the environment from unacceptable risks from pesticides. Each of these three components must be acceptable before a pesticide is considered acceptable for registration. This means that products that do not work are considered to not have value and therefore would not be registered even if the health and environmental risks were acceptable. The converse is also true that if the product was very efficacious and useful to an important commodity, it would not be registered if there were unacceptable health and environmental risks.

4.1 The risk component (human health and environment)

There is broad international consensus amongst regulatory agencies that the acceptability of a pesticide should be predicated on the nature and degree of risk it poses. The PMRA employs a risk-based approach for assessment of pesticides that necessarily involves consideration of the toxicity and the level of exposure to fully characterize risk. The extensive premarket assessment of pesticides allows the PMRA to identify potential hazards and risks to health and the environment prior to making the registration decision.

The risk assessments carried out by the PMRA follow a structured predictable process that is consistent with international approaches. Assessments are based on a prescribed set of scientific data provided by registrants. These assessments provide best estimates of risk to defined populations exposed under defined exposure conditions. They are conducted in the context of well defined use scenarios, such as the use of a new pesticide on a particular field crop using specified application rates, methods and equipment. Potentially exposed populations and environments are also defined and considered in the risk assessment. The data required from registrants in support of a pesticide are tailored to provide the necessary information for the different proposed uses. The PMRA has specified extensive and detailed data requirements for over 30 different use scenarios.[4]

Only products with a database that includes all of the required studies are allowed to progress within the evaluation process and reach the decision stage. These data are generated in accordance with validated study protocols and must follow Good

[4] See Regulatory Proposal PRO98-02, *Organizing and Formatting a Complete Submission for Pest Control Products*, February 5, 1998.

Laboratory Practices.[5] Risk assessments can, and often do, use additional scientific data from other sources, particularly in the re-evaluation of older pesticides.

It is the nature of predictive toxicology and risk assessment that scientific uncertainties may arise even when the database is complete. For example, interpretation of the applicability of toxic effects in animals to humans, or extrapolation from small scale laboratory and field trials to actual pesticide use situations are both potential sources of uncertainty. These uncertainties are dealt with at each appropriate step in the framework. Where scientific uncertainties cannot be fully resolved through additional data, the PMRA applies "worst case" assumptions and uses increased safety factors in its risk assessment.

Re-evaluation entails assessing the risks associated with the use of currently approved pesticides and the acceptability of these risks in the light of current standards. The same steps as described for the premarket assessment are used within the process of re-evaluation and decision making. In addition, the re-evaluation program allows for placing pesticides with particular identified concerns under a "special review." Threats of serious or irreversible damage to health or the environment are triggers for special reviews and regulatory action. These actions could include severe restrictions of use, phase-out or cancellation of a pesticide.

4.2 The value component

Value is the third component assessed for determination of the acceptability of a pesticide. The primary consideration is whether the product is efficacious, i.e, 'does it do what it is claimed to do'. The assessment is based on results from field studies. These are conducted under typical use conditions and they must demonstrate that the pesticide provides effective control or suppression of a pest that is threatening animal and human life or health, or an agricultural and industrial commodity, process or product.

As will be discussed in Section 5.0 and 6.0 of this document, the assessment of value has an additional function. It allows for the development and evaluation of risk management options by providing information on the inherent cost of risk mitigation and impacts on economic benefits and competitiveness. It also can bring into the decision-making process, information for considering impacts on trade, such as the potential impediment to movement of commodities that may arise from differences between major trading partners with respect to the regulatory status of pesticides and allowable pesticide residue limits.

It must be emphasized that health and environmental risks must be acceptable before a product is considered eligible for registration regardless of the value of the product.

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[5] See Regulatory Directive DIR98-01, *Good Laboratory Practice*, July 27, 1998.

4.3 Assessment of Risks to Human Health

The purpose of conducting an assessment of risks to human health is to define the nature of the risk (hazard) and to provide a measure of the likelihood and the magnitude of the risk associated with a defined exposure. The assessment follows a four-step process:[6] (1) hazard identification, (2) dose–response assessment, (3) exposure assessment and (4) risk characterization.

The main source of information for identifying hazards (toxic end points or adverse health or environmental effects) and for determining the relationship between dose and response are animal toxicity studies. These are considered to be well understood predictors of toxicity in humans. The PMRA relies heavily on toxicological data to establish reference doses for acute (ARD) and chronic (ADI) effects and to derive estimates of potential cancer risks.

With few exceptions, i.e., carcinogenic and mutagenic effects, most toxic effects occur only when a dose threshold has been exceeded. These differences must be taken into account and as a result the PMRA is using two different approaches for assessing the acceptability of risks from pesticides to human health: a margin of safety approach for "threshold" effects and a quantitative risk assessment for non-threshold effects, such as cancer.

For toxic end points that have a threshold, the PMRA establishes a reference dose, taking into account both the acute and the chronic nature of the toxic effects. The lowest level of exposure in test animals that causes no adverse effects, the no observed adverse effect level (NOAEL), is the starting point for calculating the reference dose. The NOAEL is selected for a toxic end point observed in animals that is relevant to humans, and it is usually from a study in which animal exposure is representative of the route, frequency and duration of human exposure.

Furthermore, the establishment of reference doses must take into account uncertainties arising from the extrapolation of effects observed in animals to potential effects in humans. It also considers that some humans in the population are more sensitive to potential effects than others. Therefore, the reference dose incorporates two safety factors: a 10-fold factor to account for extrapolation from animals to humans (i.e., interspecies) and an additional 10-fold factor to account for the variation within the human population (i.e., intraspecies). In this way, the calculated reference dose for humans is a minimum of 100-fold lower than the dose that caused no adverse effects in animal studies.

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[6] This internationally accepted process was first introduced by the United States (U.S.) National Research Council in 1983 in the so-called "Red Book" on *Risk Assessment in the Federal Government: Managing the Process*.

In addition to these two 10-fold safety factors, additional safety factors are applied to the reference dose to address severity of toxicology end point, sensitive sub-populations and any concerns or uncertainties about the precision of toxicity and exposure estimates. Increased sensitivity of the young and exposure of infants and children, as well as pregnant women, to a pesticide are considered during the risk assessment process, with the goal of providing additional protection where warranted, consistent with the practice established by the U.S. *Food Quality Protection Act* of 1996. Where reliable scientific data are available, a case specific determination as to the size of the additional factor is used. This approach is consistent with that of the U.S. Environmental Protection Agency (EPA).

The determination of whether the exposure is acceptable is made by comparing the estimated human exposure to the reference dose. Exposures that fall below the reference dose are considered to provide sufficient margins of safety and are unlikely to be associated with unacceptable risk to health.

The assessment of a chemical's potential to cause cancer requires a different kind of assessment and expression of risk. Cancer risk assessment for pesticides is based on evidence from cancer studies in at least two species, usually the rat and the mouse, together with evidence from in vitro and in vivo genotoxicity studies. The cancer studies are evaluated on the basis of the number and type of lesions elicited in test animals. They are typically carried out at dose levels that are much higher than expected human exposures. These studies are in many cases complemented with studies that shed light on the mechanism by which the pesticide causes the carcinogenic effect. The outcome of the animal studies together with mechanistic considerations are used in a weight-of-evidence approach to decide if a pesticide is likely to pose a cancer risk to humans. This type of approach is used by the International Agency for Research on Cancer in identifying agents that may pose a cancer risk to humans.

The quantitative assessment of cancer risk requires the use of sophisticated statistical models to estimate potential cancer risks at the lower levels of exposure seen in humans. A model used widely for regulatory purposes is the linearized multistage (LMS) model.[7] This model results in an expression of a unit cancer risk, Q_1*, that allows for the calculation of the likelihood or probability of cancer (lifetime cancer risk) for an average daily lifetime exposure. For example, a $1 \times l0^{-6}$ cancer risk means that an individual has a one in a million chance of developing a cancer from an average daily lifetime exposure to a particular pesticide.

The acceptability of cancer risk is a risk management decision that cannot rely exclusively on a numerical standard, but needs to take into consideration all the factors that influence the risk. Given historical actions of regulatory agencies such as the EPA,

[7] The LMS model is based on the assumption that the dose–response curve is linear at low doses with no threshold. The LMS model is generally considered more appropriate for genotoxic than for nongenotoxic carcinogens.

it is recognized that areas of regulatory concern for lifetime cancer risk are in the neighbourhood of 10^{-4} to 10^{-6}. A lifetime cancer risk that is below 1×10^{-6} (one in a million) usually does not indicate an unacceptable risk for the general population when exposure occurs through pesticide residues in or on food, and to otherwise unintentionally exposed persons. In some instances, cancer risks in the range of 1×10^{-5} to 1×10^{-6} (one in one-hundred thousand to one in a million) have been tolerated for industrial workers exposed occupationally to carcinogenic chemicals. These risk ranges are used by the PMRA as a guide in reaching decisions about the acceptability of lifetime cancer risk.

Both types of risk assessment, the margin of safety approach and the quantitative cancer risk assessment, provide estimates of risk arising from defined exposures. Usually the estimate reflects a "typical" exposure and use situation taking into consideration whether exposure is occasional or frequent and of short or long (life-time) duration. The estimate is kept conservative by generally overestimating exposure and risk and by using many "worst case" assumptions, such as assuming that 100 percent of the crop would be treated at the maximum application rate, or that 100 percent of the pesticide deposited on the skin would penetrate through the skin.

The PMRA currently aggregates exposure for a single pesticide active ingredient by combining exposures from all food residues and drinking water. The Agency will also take into account exposure from residential activities. It should be noted that the aggregation of exposure is a concept only recently introduced by regulatory agencies.

There are only a few chemical groups that are toxicologically well enough understood to allow estimation of cumulative risk (the combined risk from several pesticides) on the basis of a common mechanism of toxicity. The development of a standardized approach and appropriate methods to conduct cumulative risk and aggregate exposure assessments for pesticides with a common toxic mechanism are still under development.[8] The EPA is awaiting the outcome of their Scientific Advisory Panel before being able to implement this approach.

4.4 Assessment of Environmental Risk

The assessment of environmental risk requires the integration of information on environmental exposure and effects. Although the environmental risk assessment is in principle similar to human health risk assessment, it poses a very different challenge. It requires identification of the potential toxic effects to a vast number of organisms in the environment, and is focussed on potential effects on individuals, but can also include potential effects on species, ecosystems and the food chain. It is necessary to consider not only local effects at the site where the pesticide is being used, but also the potential of the pesticide to move and to be transported to other sensitive environmental compartments

[8] Approaches to cumulative and aggregate exposure assessments are discussed by the U.S. National Research Council in their 1993 report on *Pesticides in the Diets of Infants and Children*.

such as groundwater or lakes and rivers, or via atmospheric transport and deposition into remote environments.

Since it is not possible to study all potentially affected organisms and ecological systems, it is important to specify at the outset of a risk assessment the parts or levels of the environment intended to be protected. The PMRA includes in its consideration the maintenance of biological diversity, ecosystem health, achievement of sustainable development and the protection of particular species of animals or plants. The characterization of environmental risk identifies which, if any, organisms or ecosystems (environmental compartments) are at risk, and also identifies any uncertainties in estimating risk. Based on this information, risk management strategies can be explored to see if any are available that might sufficiently mitigate the risk. It provides the basis for deciding if risk management strategies are necessary to ensure that there are no unacceptable environmental risks and provides a focus for protection of a particular environmental compartment.

Environmental risk assessment is thus based on effects on indicator organisms and expected environmental exposures for defined environmental compartments. A key component of the assessment is consideration of the persistence of a pesticide in the various environmental compartments and its potential for accumulation up the food chain.

Laboratory and field studies, including acute and chronic toxicity tests in a range of standard test organisms from different taxonomic groups, are used to characterize the toxic response and to determine the dose–effect relationship of the pesticide and its major transformation (degradation) products. These are used as predictors for effects on ecosystems. The adverse effects considered are lethal and sub-lethal effects, including mortality, organ toxicity and reduced growth. The median lethal dose or the median lethal concentration (LD_{50} or LC_{50}) and the median effective dose or the median effective concentration (ED_{50} or EC_{50}) are determined as well as the concentration at which there is no observed adverse effect, the No Observed Effect Concentration (NOEC).

Potential effects in non-target biota are assessed and characterized by using a series of internationally recognized indicator species. Terrestrial species used represent the following major taxonomic groups: birds, mammals, terrestrial invertebrate species including insects and terrestrial plants. Potential effects in aquatic biota can be characterized in both freshwater and, when necessary, marine species that include fish and aquatic invertebrates, as well as algal species and aquatic vascular plants, both sub-mergent and emergent. To estimate environmental exposure to pesticides, it is essential to know how, when and under what conditions a pesticide is being used and to predict from its behaviour and fate in the environment the extent of exposure (concentrations in soil, surface and ground water) at the use site and in other environmental compartments.

For a pre-market assessment, the estimation of exposure is based to a significant degree on modelling of Expected Environmental Concentrations (EECs). The modelling requires a detailed understanding of the physico-chemical properties and information on transformation rates. These rates give an indication of the transformation potential in the various environmental compartments, sometimes under a range of different conditions. This is necessary to predict fate and transport of a pesticide in soil, water and air, as well as the potential for uptake by plants or animals and the transfer from organism to organism through the food web to higher trophic levels. The reliability of the models can be enhanced with results from field trials under conditions that reflect the Canadian environment.

A standard method for expressing environmental risks quantitatively is the ratio of the highest concentration without any adverse effect in a relevant and sensitive species to the expected environmental concentration in a relevant environmental compartment (NOEC/EEC). The larger the ratio, the larger the margin of safety, and the more limited the environmental impact is expected to be. When the ratio of NOEC to EEC approaches 1 or falls below 1, it identifies that environmental effects are likely to occur. This allows PMRA to decide when additional risk management options need to be implemented to ensure that environmental concentrations do not approach or exceed effect concentrations.

The PMRA is following closely recent advances in methods for environmental risk assessments on the basis of probabilistic exposure assessments and will consider incorporation of these new methods in future adjustments of its approach to environmental risk assessments.

4.5 Assessment of Value

The determination of value is an important element of the pre-market evaluation of pest control products. Value assessments, as conducted by the PMRA, consist of three components: an assessment of efficacy, of economic benefits and competitiveness, and of a pesticide's contribution to sustainability.

The PMRA carries out a value assessment for all new pesticides corresponding to a new active ingredient or new formulation, or amendments to existing products proposing new uses, such as addition of new pests, new hosts or new application methods. The extent and focus of the value assessment is case specific. It may include a review of all the components of efficacy, of economics and competitiveness and of sustainability, or a review of efficacy only for an amendment to add a new pest to a registered pesticide.

The assessment of pesticide efficacy involves an evaluation of the pesticide's performance under field conditions. Pesticides that do not achieve an effective level of control or suppression of a pest are not candidates for registration, even if they do not pose risks to human health or the environment.

Where the efficacy of a pesticide is acceptable, the assessment serves to establish appropriate label claims or directions and the lowest application rate (or rate range) that is required to provide effective and consistent pest control, without unacceptable damage or injury to the host or crop and subsequent hosts or crops, under normal use conditions. In some cases, the objective is to attain the lowest overall amount of pesticide required to control the pest during a use season, rather than the lowest single application rate.

The efficacy of a pesticide is related to the concentration or amount of the pesticide that is used and the method and timing of use. These factors can also have a significant impact on the risks that are associated with the use. The required amount, method and timing of use for successfully dealing with a pest can lead to unacceptable risks, and thus preclude registration. There is also the possibility of modifying these factors while still maintaining an acceptable level of efficacy, thus providing a significant opportunity for developing risk management options.

Several aspects of product performance may be considered under the general category of efficacy assessment. These include the effectiveness of the pesticide in controlling the target pest, the tolerance of the host or crop to the pesticide applied and the tolerance of succeeding host(s) or crop(s) to the pesticide applied.

Some or all of these components may be considered during the review of a submission, dependent upon the type of pesticide involved and the proposed use. Data for an efficacy assessment are derived from field or laboratory trials. Field trials are carried out at different geographical locations and can extend over more than one use season to allow determination of the pesticide performance over a variety of conditions.

In most cases, proof of efficacy establishes the nature of the expected benefits, so that the PMRA would not normally engage in an in-depth or extensive evaluation of benefits. Assessment of economic benefits and competitiveness may be undertaken in particular cases where aggressive risk management options must be developed. A high economic value of the commodity to be protected usually allows consideration of a wider range of mitigation options than lower value commodities. In the case of high economic value, users may accept higher cost measures and thus more aggressive mitigation measures can be imposed. Otherwise, the product will not be registered.

The PMRA assesses the compatibility of a pesticide with sustainable agricultural or industrial practices and production systems. In particular, the assessment identifies existing alternative methods of control for the target pests, the fit of the pesticide with established integrated pest management (IPM) programs and the role of the pesticide in resistance management strategies.

The PMRA also considers the potential impact on resistance development and the role a pesticide plays in the management of pesticide resistance. The introduction of a pesticide with an existing mode of action may accelerate the development of resistance, while a pesticide with a new, unique mode of action may provide the opportunity to delay the development of resistance, thus increasing its value.

The assessment of the value of a pesticide during re-evaluation has a particular purpose. During re-evaluation, value is examined under current conditions and in light of alternative pest control methods (both chemical and nonchemical) that may have been developed since the pesticide was first registered. The efficacy component of the value assessment is not repeated during re-evaluation because product performance has been established through its history of use. With the development and implementation of IPM programs, however, the use of a pesticide may now be targeted to specific application times during the season, or the rate required for efficacy may be reduced owing to an IPM approach. In such cases, studies of pesticide efficacy from published sources may be incorporated in the reviews.

4.6 Outcome of the risk and value assessments

As discussed above, the outcome of the risk and value assessments can have various results which set the path for different regulatory decisions.

When the risks to health and the environment are acceptable and the pesticide has value, i.e., the pesticide can be used safely and effectively without any modifications to its proposed or existing uses, the registration of the new pesticide must be granted. In the context of a re-evaluation, the re-registration of an existing pesticide will be maintained.

When a pesticide has value but the risks to health or the environment are unacceptable, PMRA will identify and develop risk management options to reduce the identified risk(s) in such a manner and to such an extent that the pesticide can be used without unacceptable risks to health and the environment. These mitigation options will reduce exposure and could include protective clothing for applicators, buffer zones to protect environment, reduction of application rates, and lengthening preharvest intervals. The extent of these mitigation measures cannot reduce the efficacy beyond acceptable levels. If that is the case, the product is not registerable.

When the risks to the environment or health, *or* the pesticide's value are unacceptable, and the risks cannot be mitigated through modifications of the conditions of use, then the registration of a new pesticide will be denied and, in the context of a re-evaluation, the registration of an existing pesticide will be discontinued or its uses will be phased out.

When the use of the pesticide is incompatible with federal policies and international agreements, such as the TSMP, the Montreal Protocol on ozone depleting substances and international agreements on POPs, or the use of a pesticide would contravene other federal acts, a new pesticide can be refused and the registration of an existing pesticide can be discontinued or its uses may be phased out.

5.0 Identification and Analysis of Risk Management Options

The outcomes of the assessments of risks to health and the environment, and the assessment of value, are the basis for the next step: identification and analysis of risk management options. The goal is to identify a range of options that have the potential to reduce the extent of human and environmental exposures, and to analyse these options to determine if they can achieve acceptable risk standards for human health and the environment. The identification and analysis must be focussed and must be responsive to the nature and extent of risk, its source, the affected human population and the environmental populations and compartments that were identified in the risk assessment steps. It is essential that the scientists who assessed the potential risks and risk managers participate in the identification and analysis of management options.

As mentioned previously, the identification and analysis of risk management options is a dynamic process, requiring recalculation of risk under various risk mitigation scenarios. In many cases, the choice is not between individual risk management options, but the choice of a combination of options. There may be competing risks within the range of possible risk mitigation options: what may be a reasonable strategy to reduce risk to applicators/farmers may increase risks to the environment leaving the product unregisterable . Thus, development of options must provide a clear basis to ensure that all risk elements are considered and are acceptable.

The range of risk management options is constrained by legal and practical considerations. The risk management options must be consistent with the requirements of the PCP Act and must be legally enforceable. The development of risk management options, therefore, relies on mitigative measures that can be prescribed in the conditions of use, as prescribed on the legally binding label.

The risk management options available under these legal constraints can include denial of registration or imposition of conditions and restrictions with respect to: classification of use (domestic, commercial or restricted class), provincial permit requirement, professional qualification of applicator, specification of application technique and equipment, personal protective equipment, use conditions (use quantities, application rates, timing and frequency of application, pre-harvest intervals, re-entry intervals), crops, use scenario, buffer zones and other mitigative measures to protect sensitive environments and particularly vulnerable plant and animal species, and safe storage and disposal. Options can also consider changes to the pesticide product, such as changes to the formulation, or the physical and chemical make-up of the pesticide product.

The practicality of risk management options is guided by a thorough understanding of the use situation, use practices, application technology, extent of use, and geographical location. This level of detailed understanding is necessary to focus the development of options on those that are appropriate and can realistically be achieved.

The value assessment plays a significant role in defining some of the limits of management options because application rates, frequency, technology and practices influence the effective use of a pesticide. The efficacy assessment provides the basis for determining these practical limits.

The value assessment also provides an estimate of the cost to the user of implementing a particular option. Since no management option is without cost, excessive or disproportionate costs can influence the benefit to the user. It provides a measure for gauging the cost tolerance of the user and thus focuses the development of management options on realistic options. If the cost of reducing the risk to an acceptable level outweighs the benefit of the pesticide, it would not be registered.

There is a growing recognition that, in addition to these regulatory approaches to risk mitigation, there are a number of ways to further strengthen the label statements to influence the pesticide users in their practices and choice of dealing with pests. These additional management options have become increasingly important, particularly within the context of modern agriculture. They can significantly enhance regulatory measures and compliance. The PMRA is working with a variety of stakeholders, including user groups, to develop IPM programs to help reduce reliance on pesticides as a sole means of pest management.

6.0 Selection of a Strategy

The selection of a risk management strategy, including the selection of one or a combination of management options developed and elaborated in the previous step, involves a great deal of scientific expertise. Expertise has been built up in the PMRA over many years and on numerous practical examples. The selection of a strategy is to a significant degree based on data indicating that the anticipated risks to health and the environment are acceptable and that the pesticide is effective. It also includes experience in deciding if the selected strategy is practicable from both a use pattern and a compliance and enforcement perspective.

Part of the strategy selection process involves the recalculation of the margins of exposure or level of risk remaining under various possible management strategies. This recalculated level of risk provides a measure of how well a management option fulfills criteria of acceptable risk. Options that do not ensure that risks are within acceptable limits are not further pursued.

The choice of options can be further narrowed by considering their inherent cost and their impact on economic benefits and competitiveness. A high economic value of a commodity allows consideration of higher cost management options. Options for which the cost exceeds the economic value are not likely to be accepted by users and the pesticide would not be registered if there would be an expectation of low user compliance.

The consideration of practicality and expected compliance with management options is much more difficult to quantify. In-depth knowledge of user groups, their level of "sophistication" in pesticide use, their past record on compliance and an understanding of countervailing pressures are essential for this task.

The selection of management options, therefore, is case specific and is a search for the optimal combination of choices that achieve an acceptable level of risk while maintaining an acceptable value of the product.

7.0 Implementation of the Strategy

The selected risk management strategy forms an essential part of the regulatory decision. It is implemented as part of the registration or de-registration decision.

In the case of acceptable risks to health and the environment and value, the PMRA registers the pesticide and specifies the registration conditions on the legally binding label. Any use in contravention of the label is illegal under the PCP Act.

There are few pesticides that do not require safety precautions to achieve an acceptable level of risk. In fact, most pesticides require very specific measures to achieve an acceptable level of risk. In each case, the selected strategy provides the basis for specific registration conditions and restrictions. They are specified on the label and include domestic, commercial, restricted category, permit requirement, use conditions and restrictions, measures to protect users and the environment, re-entry and pre-harvest intervals, and buffer zones.

For pesticides used on food crops, MRLs are established and promulgated in regulations under the FDA. MRLs are an essential part of ensuring that the dietary intake of pesticide residues does not lead to unacceptable exposure and risks to human health.

All registered pesticides are thus restricted in that they can be used only for the specified purposes under specified use conditions.

8.0 Monitoring and Evaluation of Results

Decisions to register pesticides reflect the state of knowledge and regulatory practices at the time the decision is taken. Post-registration monitoring plays an essential role to ensure the continued safety and value of a registered pesticide.

There are three essential elements to post-registration monitoring: (1) the enforcement of compliance with the PCP Act and the FDA;[9] (2) the conduct of routine inspections and special monitoring (e.g., for environmental levels and effects[10]), food residue surveys and health surveys;[11] and (3) the maintenance of a modern database on the potential effects on human health and the environment including periodic up-dating of approaches to risk assessment and risk management.

The stronger the need for measures to manage the risks associated with pesticides, the stronger the need to monitor compliance with these measures. Inspection programs of the PMRA respond to this need . Additional support mechanisms for ensuring compliance are certification and training of users, Best Management Practices for pesticide user sectors and IPM programs. These support mechanisms are largely provincial responsibilities. They are encouraged and supported, and in some cases led, by the PMRA through the close interaction among all partners of the Federal/Provincial/Territorial Committee on Pesticide Management and Pesticides (F/P/T Committee).

Compliance with the PCP Act is mandatory. The PMRA enforces compliance through the National Pesticide Compliance Program, which is designed to promote and verify compliance with the PCP Act through inspections and investigations. This is achieved through a full range of compliance techniques and measures. PMRA inspectors encourage voluntary reporting of suspected infractions, inspect for compliance and respond to noncompliance situations. All suspected infractions are examined and action is taken, as provided by the PCP Act. This includes education, warning and criminal prosecution. The results of these activities are used by the PMRA in the risk assessment, particularly in special reviews and during re-evaluation.

The Canadian Food Inspection Agency (CFIA) enforces compliance with the MRLs for pesticide residue in food established by the PMRA and promulgated in regulations under the FDA.

Monitoring, particularly environmental presence and effects monitoring, is carried out by provincial and territorial agencies, other federal government departments and the registrants themselves. The monitoring can include a wide range of pesticides, can be regional, can apply to a part of the environment (e.g., groundwater), can be use specific (e.g., corn herbicides), or can be narrowly focussed on a single pesticide.

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9 The enforcement of MRLs of pesticides in or on food is the responsibility of the Canadian Food Inspection Agency (CFIA).

10 Environment Canada and provinces/territories.

11 Health Canada.

Post registration developments in scientific knowledge and in experience may indicate that the initially required studies and information on which the registration decision was based should be improved, and that additional information should be obtained and assessed to determine whether a registration can continue to be supported.

The following situations may indicate the need for a re-assessment: (1) new scientific knowledge of toxicological end points of concern, often combined with new investigative methods; (2) adverse effects reporting, incidence reporting, results from epidemiological studies, environmental monitoring and surveys; (3) age of supporting database (over time, data requirements have expanded, quality and scientific rigour have increased and a wider range of risks must be considered).

In recognition of these factors, particularly consideration of the age of the database for a large number of older pesticides, the PMRA has presented a Regulatory Proposal[12] for a comprehensive re-evaluation program for pesticides registered prior to 1995. Under this program, the assessment and management of risks of pesticides will follow the same steps that are outlined in this document.

Once a pesticide has been registered, there is a need to track its actual use. The National Pesticide Sales Database, which is currently being established by the PMRA, is a first step in collecting comprehensive pesticides sales data on a regular basis. The sales data will be useful for estimating pesticide use and will provide important information for the re-evaluation of pesticides and risk reduction activities.

9.0 Involvement of Interested and Affected Parties

The registration decisions of the PMRA affect users and registrants, and those exposed to pesticides and pesticide residues. They are also of interest to a large number of other parties, including the Canadian public in general, other federal departments and provincial agencies and departments with health and environmental protection mandates, and various organizations representing the interests of pesticide users, consumers and environmental and health advocacy groups.

The framework of decision making allows the PMRA to interact with these affected and interested parties in a manner that is commensurate to their degree of being affected by and interest in regulatory decisions.

[12] See Regulatory Proposal PRO99-01, *A New Approach to Re-evaluation*, December 3, 1999.

9.1 Interaction with registrants

The PMRA has published a Regulatory Proposal[13] for a Management of Submission Policy (MOSP) that sets out prescribed processes and procedures for both the PMRA and registrants of pesticides. Interaction and consultation with registrants occur frequently within this process: during the pre-submission phase, the screening for completeness of the submitted data, and the review of deficiencies in the initial stages of review. The PMRA further provides an opportunity for registrants to comment on the mitigation measures that the PMRA intends to impose as a condition of registration. This provides registrants an opportunity to decide if they are willing to accept the conditions or forego registration and marketing of their product.

9.2 Informing and consulting with the public and other interested parties

To document the basis for individual registration and re-registration decisions, and to consult and inform other interested parties and the public about the decision, the PMRA publishes a number of documents. Major decisions, such as the registration of a new pesticide and major new uses for an existing pesticide, are documented in a Regulatory Note (REG) or in a Proposed Regulatory Decision Document (PRDD) followed by a Regulatory Decision Document (RDD). Re-evaluation decisions are published in a Proposed Acceptability for Re-registration Document (PAR) followed by a Re-registration Decision Document (RRD).

Under the current provisions of the PCP Act, the PMRA must request permission from registrants before publishing PRDDs, PARs and other documents, e.g., REGs, that contain product specific information and (proposed) decisions. When requesting permission to publish a PRDD, the only changes that PMRA will entertain from registrants are corrections of factual errors that might have occurred.

It should be noted that PMRA also solicits public comment on new policies and programs through a mailing to PMRA's stakeholders and the posting on the internet of Regulatory Proposals. A comment period of 45 or 60 days allows for public input to be received. Responses are then reviewed and, where appropriate, changes are made to reflect public input and concerns.

9.3 Advisory bodies

The Pest Management Advisory Council (PMAC), established in November 1998, provides a forum for stakeholders to provide advice on policies and issues relating to the federal pest management regulatory system. The Council's membership includes environmental, health, labour and consumer groups, academics and pesticide manufacturers and users.

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[13] PRO96-01, June 7, 1996

The Economic Management Advisory Committee (EMAC) was established in April 1997 to advise the Executive Director of the PMRA on specific ways to improve efficiency and cost effectiveness without compromising health or environmental protection while maintaining industry competitiveness. Members of the EMAC include pesticide industry representatives, grower groups and officials from the PMRA.

The Federal/Provincial/Territorial Committee (F/P/T Committee), established in October 1997, brings together federal and provincial/territorial pesticide officials together to exchange information and expertise. The F/P/T Committee provides advice and direction to governments on programs, policies and issues relating to pesticides and actively pursues solutions to shared issues of concern through the activities of its working groups.

Other government departments. Memoranda of Understanding provide a mechanism for the Executive Director of the PMRA to consult on policy issues with Assistant Deputy Ministers from other federal government departments, such as Agriculture and Agri-Foods Canada, Natural Resources Canada, Environment Canada, and relevant branches of Health Canada.

10.0 Summary

In its decision making, the PMRA uses a well defined decision framework. The framework describes a multi-step process through which pesticide registration decisions are developed, implemented and monitored. They consist of (1) identification of the issue and its context, (2) assessment of risks and value, management of risk on the basis of (3) identification and analysis of risk management options, (4) selection of a risk management strategy and (5) implementation of the chosen strategy. The final step (6) is the monitoring and evaluation of results. Involvement of interested and affected parties (7) is integral to the overall process.

The PMRA decision making is designed to protect human health and the environment and only allow pesticides that provide value to users and the Canadian society to be registered. Decisions are made on the basis of a comprehensive body of scientific evidence and scientific methods to determine the nature and magnitude of the risks posed by pesticides and by applying appropriate and effective risk management strategies.

List of abbreviations

ADI	allowable daily intake
ARfD	acute reference dose
CFIA	Canadian Food Inspection Agency
EC_{50}	median effect concentration
ED_{50}	median effect dose
EEC	expected environmental concentration
EMAC	Economic Management Advisory Committee
F/P/T	Federal/Provincial/Territorial
FDA	*Food and Drugs Act*
IPM	integrated pest management
LC_{50}	median lethal concentration
LD_{50}	median lethal dose
LMS	linearized multistage
MRL	maximum residue limit
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
OECD	Organisation for Economic Co-operation Development
PAR	Proposed Acceptability for Re-registration Document
PCP Act	*Pest Control Products Act*
PMAC	Pest Management Advisory Council
PMRA	Pest Management Regulatory Agency
POP	persistent organic pollutants
PRDD	Proposed Regulatory Decision Document
RDD	Regulatory Decision Document
REG	Regulatory Note
RRD	Re-registration Decision Document
TSMP	Toxic Substances Management Policy
U.S. EPA	United States Environmental Protection Agency