Pest Management Regulatory Agency
Agence de réglementation de la lutte antiparasitaire

Regulatory Directive DIR2001-03

PMRA Re-evaluation Program

This regulatory directive outlines the Pest Management Regulatory Agency's (PMRA) re-evaluation program. It applies to technical active ingredients as well as to active ingredients in end-use products registered prior to December 31, 1994. The re-evaluation will include all end-use products associated with an active ingredient.

This document replaces regulatory proposal PRO99-01, *A New Approach to Re-evaluation*, published for public comments in December 1999. Comments received were taken into consideration in the final version of the document.

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Table of Contents

1.0 Introduction 1

2.0 Background 1

3.0 The re-evaluation program 2

4.0 Program structure 3

5.0 Re-evaluation documents 8

6.0 Establishing priorities 8

7.0 Roles of registrants and the PMRA 9

8.0 Time requirements 9

9.0 Summary 10

List of abbreviations 11

Appendix I Ongoing Canadian re-evaluations 12

Appendix II List of pesticides targeted for reassessments under the FQPA 13

Appendix III Flowchart for Pesticide Re-evaluation 2000 14

1.0 Introduction

Canadian agriculture, industry and other users rely on the availability of safe and effective products to manage pests. Today, close to 550 pesticide active ingredients are in products that are registered under the *Pest Control Products Act* (PCPA) for use in Canada. At the time of their registration, these pesticides were considered acceptable on the basis of an assessment of their safety, merit, and value. The scientific knowledge that forms the underpinning of these assessments is continually evolving and new methodologies and tools are being integrated into regulatory risk assessments. Also, the re-evaluation of older pesticides can take into consideration the full extent of the use patterns of the active ingredients, the diversity of their end-use products, and their market penetration. These parameters would not have been fully apparent at the time of initial registration. For these reasons, the PMRA has developed a re-evaluation program that uses current scientific approaches to examine the continued acceptability of older active ingredients and their end-use products. This regulatory directive describes the program.

2.0 Background

Approximately 550 pesticide active ingredients and their end-use products are currently registered in Canada, of which 405[1] active ingredients were registered or were in registered end-use products prior to December 31, 1994. These active ingredients and their currently registered end-use products are included in this program.

In its report of 1990, the Pesticide Registration Review Team,[2] in full recognition of the magnitude of the re-evaluation task, recommended a Canadian re-evaluation policy that would be heavily reliant on the outcomes of the pesticide reregistration program of the United States (U.S.).

The Canadian government responded to this recommendation in 1994[3] with the commitment to a cost effective re-evaluation on the basis of cooperation between the U.S. and Canada and with other Organisation for Economic Co-operation and Development (OECD) countries.

In 1999, the PMRA published a regulatory proposal[4] that described the Agency's proposal for a new approach to re-evaluation. A number of interested parties responded

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1 Not included in this number are pest control products (active ingredients and their end-use products) registered January 1, 1995 or later; devices; disinfectants that are currently reviewed by the Therapeutic Products Program; certain older active ingredients that have been subjected to recent extensive Canadian reviews; and active ingredients that are still in registered products, but where registrants have given notice of their intent to discontinue the registrations within the next two or three years.

2 *Recommendations for a Revised Federal Pest Management Regulatory System*, Final Report, December 1990

3 *Government Proposal for the Pest Management Regulatory System*, October 1994

4 PRO99-01, *A New Approach to Re-evaluation*

with detailed and extensive comments. These comments were considered and, where appropriate, are reflected in this regulatory directive.

3.0 The re-evaluation program

Re-evaluation is the review of pesticide active ingredients and their end-use products on the basis of updated data and information to determine whether, and under what conditions, their continued registration is acceptable.

Pesticide active ingredients, or active ingredients in end-use products, that were registered in Canada prior to December 31, 1994 and their currently registered end-use products will be re-evaluated, and the conditions of acceptability for active ingredients and their end-use products, including acceptable uses, rates, timing, methods of application, preharvest and re-entry intervals, appropriate cautionary and first aid statements, and limitations or risk reduction measures will be determined.

The PCPA provides the Minister of Health broad discretionary authority to determine information requirements, principles, policies and standards to be applied in the evaluation and re-evaluation of pest control products.

Foreign reviews, particularly those from the U.S. Environmental Protection Agency (EPA), where available and suitable, will be an important source of information that will keep Canadian resource needs as low as possible. This approach recognizes that the sheer volume of data to be reviewed could not be done in a timely or cost effective manner without reliance on existing acceptable reviews.

The PMRA's involvement in the activities of the North American Free Trade Agreement Technical Working Group on Pesticides and the OECD Working Group on Pesticides has given us the confidence that, where international reviews are available, the review work that will have to be carried out on a national basis can be reduced.

Thus, Canada will benefit significantly from the reviews resulting from the extensive data call-in by the EPA. Since 1986, mostly as a result of the reregistration initiatives in the U.S., registrants have generated and submitted a large number of studies on individual active ingredients and their associated products. These studies have brought pesticide databases closer to the modern standards that are required for new products.

The PMRA has recently developed policies and strategies that apply to the assessment and management of new pesticides, e.g., the PMRA's *Strategy for Implementing the Toxic Substances Management Policy* (TSMP),[5] and the proposed *Formulants Policy*.[6] These policies will also apply to pesticides under re-evaluation.

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5 Regulatory Directive DIR99-03, March 12, 1999

6 PRO2000-04, May 29, 2000

The PMRA has and continues to adopt policies and procedures that are being developed by the EPA in response to the requirements of the *Food Quality Protection Act* (FQPA). These policies apply to all new pesticides and those under re-evaluation. The PMRA has been providing input and is working with the EPA on the further development of these policies. Canadian registrants, user groups and other interested parties are advised to follow closely the development of these policies and to provide comments directly to the EPA.[7]

The priorities and the timely progress of the U.S. pesticide reregistration program will continue to exert a strong influence on the Canadian re-evaluation program. This is in part due to the strong reliance of Canadian re-evaluations on U.S. reviews and policies, but also because of the need to harmonize, as far as possible, the regulatory status and availability of pesticides.

The PMRA will base its re-evaluation decisions on the assessment of the currently available information and reviews. As an outcome of re-evaluation and where appropriate, however, the PMRA may require registrants to fill data gaps and to address areas of concern within prescribed time frames.

The strong reliance of the Canadian re-evaluations on the availability of U.S. reviews ties the completion of the Canadian program to that of the U.S. reregistration program. Since the EPA target is 2006, the PMRA will aim to complete re-evaluation of the 405 Canadian active ingredients within the same time frame. Although the U.S. has made enormous strides in meeting its commitments, the completion of these re-evaluations will remain an ambitious undertaking for both countries.

4.0 Program structure

The program consists of four distinct (sub)programs. They respond to the availability of foreign reviews (Program 1) and the need to do detailed in-house Canadian reviews for some pesticides (Program 2), take into account the need to align Canadian re-evaluation efforts to reassessments under the FQPA (Program 3), and provide room for targeted re-evaluations, which are also called Special Reviews (SR) (Program 4).

The following is a detailed description of the four programs; for a diagrammatic description, see Appendix III.

Program 1

Program 1 includes active ingredients and their end-use products for which a Risk Assessment Document or Reregistration Eligibility Decision (RED) document has been published by the EPA. These review documents (RDs) must be of such quality and detail to allow a Canadian regulatory decision to be made on the active ingredient and its end-

[7] Memorandum to Registrants, Applicants and Agents, January 25, 2001

use products registered in Canada. There must be, above all, a reasonable expectation that a Canadian regulatory decision could be based on the EPA review without substantial additional in-house work. Some recent reviews performed by regulatory bodies in the European Union and Australia may also be suitable to supplement the EPA RDs.

The broad criteria for inclusion in Program 1 are:

- A suitable RD from the EPA must be available. Other foreign reviews could also be considered to supplement the EPA review.

- The RD must address the main science areas that are necessary for Canadian regulatory decisions, i.e., human health and the environment. It is recognized that a RD may not cover the value assessment traditionally carried out as part of a Canadian review. This may not pose a significant problem, as value will not need to be reassessed unless there is a proposal to reduce the application rates.

- The RD must address the active ingredient itself and its main formulation types registered in Canada, and it must be relevant to Canadian uses.

- The RD must document in sufficient detail the data underlying its main conclusions to which Canadian content can be added, i.e., it must provide sufficient data on which to base Canadian environmental and human exposure assessments when Canadian use situations differ from those of the U.S.

- The product cannot already be included in one of the other three re-evaluation programs.

The assessment of mammalian toxicity studies and environmental toxicity studies will rely to a very large extent on the RD or other suitable foreign reviews. It is acknowledged that some detailed in-house work may be needed to adjust for differences in human and environmental exposures particular to the Canadian situation, and for differences in formulants that may affect the risk to Canadians and their environment. A reassessment of efficacy will not be done as a matter of routine. The decision whether to conduct a reassessment of efficacy will be triggered by marked differences between acceptable use rates in the U.S. and Canada, or the need to reduce identified risks to human health and the environment through the reduction of use rates or frequency of use. Other components of value will be assessed on the basis of information available to the PMRA from various sources such as the provinces and user groups.

The data necessary for the assessment of risks to human health and the environment will be available, since the identification of gaps in scientific data and a data call-in will have already been done in the context of the U.S. reregistration program. It is not expected that registrants will supplement recent U.S. reviews with a significant number of new studies that were not already part of the EPA review. When new studies are available that are crucial to the assessment and where these are not already included in the RD, they will be included in the Canadian review.

The outcome of the PMRA's assessment under Program 1 will be a proposed Canadian regulatory decision on the acceptability of the active ingredient and its end-use products for their continuing registration. It should be noted that under the current legislative framework the proposed decision documents cannot be published without the agreement of registrants if they contain confidential business information. This proposed decision will consider all aspects of the Canadian uses as they affect the human and environmental safety of the product. On the basis of the outcome of the assessment, the proposed decision could range from retaining registration with no changes, to amending label instructions, to modifying existing maximum residue limits (MRLs), to eliminating or phasing-out certain uses or formulations. An active ingredient and its end-use products could also be found to be unacceptable because of the risks they pose to the health of Canadians or to the Canadian environment.

The proposed regulatory decision document will identify the data gaps and will propose appropriate limitations and conditions of use while these gaps are being filled or, in the light of the importance of the gaps, whether registration of the product remains acceptable. The PMRA will discuss with registrants the time frame for filling data gaps and will include these time frames in a final decision document.

Program 2

Program 2 includes all products for which a Canadian regulatory decision requires a detailed in-house re-evaluation covering the full range of assessments of the risks to human health and the environment, as well as consideration of value. In particular, an assessment of efficacy will be done where there is the need to reduce identified risks to human health and the environment through the reduction of use rates or frequency of use. In contrast to Program 1, there is no fully suitable RD available on which the PMRA could rely to a substantial degree in its decision making. A RD may not be of sufficient detail or comprehensiveness, but it may still be of partial benefit to the re-evaluation of an active ingredient or a product. Therefore, even in Program 2, the PMRA will make use of relevant parts of these reviews wherever and to the fullest extent possible.

A number of re-evaluations were initiated previously and are currently ongoing. These re-evaluations involve detailed in-house reviews and they will be completed in Program 2.

Program 2 includes those pest control products for which there is one or more of the following:

- no suitable RD that covers the full range of assessments of the risks to human health and the environment as required for a Canadian registration decision;

- a unique use situation in Canada that requires a considerable Canadian review effort to supplement the RD; and

- an ongoing re-evaluation under previous re-evaluation efforts; see Appendix I.

The PMRA will base its assessment mainly on in-house reviews of the existing data and information available to the PMRA at the time of the initiation of the re-evaluation review and new data from registrants.

As under Program 1, the outcome of the PMRA's assessment under Program 2 will be a proposed Canadian regulatory decision on the acceptability of the continuing registration of the active ingredient and its end-use products. This proposed decision will consider all aspects of the Canadian uses as they affect the human and environmental safety of the product. On the basis of the outcome of the assessment, the proposed decision could range from retaining registration with no changes, to amending label instructions, to modifying existing MRLs, to eliminating or phasing-out certain uses or formulations. An active ingredient and its end-use products could also be found to be unacceptable because of the risks posed to the health of Canadians or to the Canadian environment.

The proposed regulatory decision document will identify the data gaps and will propose appropriate limitations and conditions of use while these gaps are being filled or, in the light of the importance of the gaps, whether registration of the product remains acceptable. The PMRA will discuss with registrants the time frame for filling data gaps and will include these time frames in the final decision document.

Program 3

Program 3 is focussed on the re-evaluation of pest control products that are scheduled for reassessment in the U.S. under the FQPA. Program 3 addresses the reassessment of pest control products, paying particular attention to pest control products with a common mechanism of toxicity, the aggregate exposures arising from all sources and from all uses, and the risks to susceptible subgroups in the exposed population, such as children.

Initially, Program 3 will include pest control products that are scheduled for a food tolerance reassessment under the FQPA. The timetable and priority ranking within Program 3 will follow that of the EPA as much as possible. Organophosphates, carbamates and probable human carcinogens are the first groupings that will be re-evaluated.

RDs from the EPA and consideration of the Canadian use patterns and rates will be the primary basis for the Canadian assessment and proposed regulatory decisions. When new studies are available that are crucial to the assessment and where these are not already included in the RD, they will be included in the Canadian review.

A proposed decision with respect to the regulatory status of a product re-evaluated under Program 3 will need to address the central issues of the FQPA, i.e., safety of food residues considering cumulative exposure from all sources, common mechanism of toxicity and susceptible subgroups. It is likely, therefore, that the proposed decisions might recommend changing use rates, methods and frequencies of application, preharvest, preslaughter and pregrazing, or feeding intervals, and limitations and conditions of use; eliminating or phasing-out certain uses (not necessarily limited to food uses); or changing existing MRLs.

A Canadian regulatory decision will be made on the active ingredient and its major end-use products registered in Canada. The proposed regulatory decision will address the acceptability for continuing registration of the active ingredient and its end-use products.

Program 4

Program 4 is a program of targeted re-evaluations, i.e., SRs. It includes those re-evaluations that are triggered by concerns arising from the reporting of serious adverse effects and national and international commitments and policies, e.g., Persistent Organic Pollutants and the federal TSMP, and that have a more narrowly defined focus on a particular aspect of a pest control product(s). Program 4 thus comprises SRs initiated to address particular concerns identified for specific pest control products and does not entail a complete re-evaluation of a product's database.

Program 4 includes pest control products for which:

- a potentially serious adverse effect has been identified in an RD, in an international forum or through submitted data;
- national or international commitments or policies require the PMRA to address a particular aspect of health or environmental safety; and
- emerging issues indicate that a regulatory follow-up is needed.

It is evident that the nature of the emerging concern associated with a product will strongly influence its priority ranking. Accordingly, priority within Program 4 cannot be preset.

The assessment of pest control products in Program 4 will be based on detailed in-house reviews. Substantial U.S. and other country reviews would not necessarily be available but they will be used wherever possible.

The outcome of a reassessment in Program 4 will be documented in an SR document. Its central issue will be the acceptability of continuing registration of a pest control product in light of the particular concern that triggered the SR. Depending on the nature and degree of concern, regulatory decisions could range from label changes to elimination or phase-out of certain uses. An active ingredient and its end-use products could also be found to be unacceptable because of the risks they pose to the health of Canadians or to the Canadian environment.

5.0 Re-evaluation documents

The re-evaluation document for each pest control product in Programs 1, 2, and 3 will be a Proposed Acceptability for Continuing Registration (PACR) document. As in the U.S., registrants will be allowed a brief period to review the document for factual errors. This is also the time when the Agency will seek a registrant's agreement for public release of the document as required under the current PCPA.

The PACR will contain summaries of the assessments and conclusions on the acceptability for continuing registration of an active ingredient and its end-use products and, where appropriate, proposed changes to the MRLs for food-use products. It will present proposed regulatory actions and will specify conditions and requirements for maintaining registration of end-use products. SRs conducted under Program 4 will be documented in a PACR-SR document. Where there are no legal impediments, the PACR will be a public document and a final decision document will be published after taking into consideration the comments received.

6.0 Establishing priorities

Active ingredients and their end-use products will be evaluated in four distinct programs within a multiyear time frame.

Programs 1 and 3 rely to a significant extent on the RDs and other U.S. reviews. The priority of Canadian reviews, therefore, is dependent to a large degree on the availability of U.S. documents. There is only limited room for modifying priorities within these two programs. Program 4 is driven by national and international commitments and policies, and issues and concerns as they emerge. Again, the opportunity for public input into priority setting is limited.

Program 2, which is based on detailed in-house Canadian reviews, is the only program that offers opportunity for stakeholder input into review priorities. The PMRA will consider suggestions from stakeholders and other government departments (OGDs) for priorities in Program 2.

7.0 Roles of registrants and the PMRA

Registrants

In the announcement of a re-evaluation of an active ingredient, the registrants will be asked to immediately notify the PMRA of their intention to maintain or discontinue the active ingredient or end-use product(s) under re-evaluation. It is also important that registrants flag or report information and studies on adverse effects and provide additional information as requested in the re-evaluation announcement and by letter (this may include a request to provide a bibliography of the published literature).

Registrants will also be asked to provide relevant new studies in their possession that are not already included in the U.S. review(s) and that have not already been submitted to the PMRA in the normal course of maintaining the database for their products. The PMRA may also request specific studies and information on particular aspects of concern.

The PMRA

The PMRA will announce each re-evaluation through a public announcement and a letter to each registrant whose product will be re-evaluated and will keep an updated list of priority for review within each of the programs.

The PMRA will also request input from OGDs, provinces and territories on relevant results from research and monitoring, and will carry out the re-evaluation, publish documents, consult where appropriate prior to regulatory decisions, and reach and implement final regulatory decisions.

OGDs, Provinces and Territories, and Stakeholders

At the announcement of each re-evaluation, OGDs, provincial and territorial regulatory bodies, as well as all other stakeholders, will be invited to provide relevant information.

During the re-evaluation, the Agency may need to obtain further information from these groups and organizations to fully understand current pesticide use practices and context, as well as clear and reliable information on the potential impact of various regulatory options under consideration.

Publication of a PACR will provide further opportunity for comments on proposed re-evaluation decision.

8.0 Time requirements

The PMRA will implement the new re-evaluation program immediately. Re-evaluations that were underway prior to this new program will continue and will be completed as soon as possible.

In Programs 1 and 3, faster progress can be made on the re-evaluation of active ingredients and their end-use products, since a large number of RDs are available.

The re-evaluation of active ingredients and their end-use products in Program 2 requires a longer start-up time because their assessment will be based on available data from registrants and detailed in-house reviews.

Program 4 must be responsive to emerging issues and national and international commitments and needs as they arise.

9.0 Summary

The re-evaluation program forms a key part of the PMRA's effort to ensure the continued safety and value of registered pest control products. The PMRA believes that the four-program approach to re-evaluation is comprehensive, timely and cost efficient. It allows more immediate progress on re-evaluation by building on suitable foreign reviews. Where no suitable foreign reviews are available, it allows the PMRA to carry out a detailed in-house review. It minimizes the potential that the Canadian regulatory status of pest control products will be incompatible with decisions taken by the EPA under the FQPA. It also strengthens the PMRA's ability to fulfill national and international commitments. For registrants, stakeholders and the public, the process will be clear and predictable. Re-evaluation enhances the PMRA's ability to ensure the continued safety and value of registered pest control products and is a major component of the strategy to reduce the risks of pesticides.

List of abbreviations

EPA	Environmental Protection Agency
FQPA	*Food Quality Protection Act*
MRL	maximum residue limit
OECD	Organisation for Economic Co-operation and Development
OGD	other government department
PACR	Proposed Acceptability for Continuing Registration
PCPA	*Pest Control Products Act*
PMRA	Pest Management Regulatory Agency
RD	review document
RED	Reregistration Eligibility Decision
SR	Special Review
TSMP	Toxic Substances Management Policy
U.S.	United States

Appendix I Ongoing Canadian re-evaluations

Pest Control Product	Announcement	Date
Chlorophenols	Memorandum to Registrants R-1-79	Aug. 7, 1979
2,4-D	Memorandum to Registrants R-1-201	Aug. 29, 1980
Fumigants	Memorandum to Registrants R-1-204	Oct. 27, 1980
MCPA	Memorandum to Registrants R-1-212	Nov. 4, 1981
Personal Insect Repellents	Announcement A90-01	June 1, 1990
Antisapstains	Announcement A92-01	July 2, 1992
Heavy Duty Wood Preservatives	Announcement A92-02	June 6, 1992

Appendix II List of pesticides targeted for reassessments under the FQPA

Priority Group 1: (started August 1996)

Organophosphates
Carbamates
Carcinogens (B1 and B2)
Reference dose exceeders
High-hazard inerts

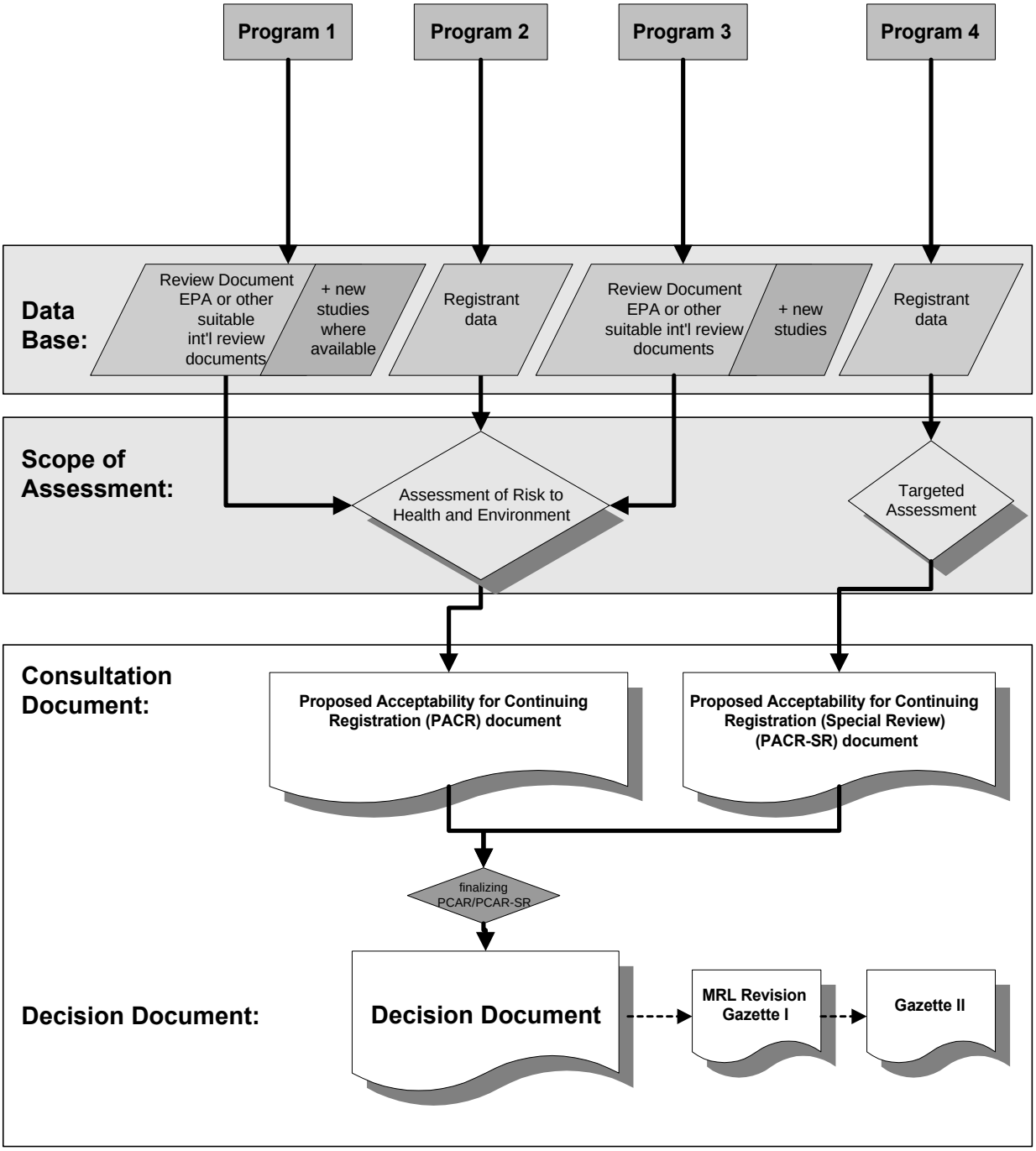
(includes the revocation of the 1200 tolerances)

Priority Group 2: (proposed to start August 2000)

Carcinogens (C)
All remaining reregistration chemicals

(to include tolerances from any remaining Priority Group 1 chemicals)

Priority Group 3: (proposed to start August 2003)

Remaining pre-FQPA chemicals with REDs
Remaining post-1984 chemicals
Biologicals
Remaining inerts
(to include tolerances from any remaining Priority Group 2 chemicals)

Appendix III Flowchart for Pesticide Re-evaluation 2000