Pest Management Regulatory Agency
Agence de réglementation de la lutte antiparasitaire

Regulatory Directive DIR2004-01

Formulants Program

This Regulatory Directive outlines the Pest Management Regulatory Agency's (PMRA) policy on the regulation of formulants contained in pest control products. It will apply to registration decisions in relation to formulants in manufacturing concentrates and registered end-use products, applications for research permits and in relation to the re-evaluation of products.

This document replaces Regulatory Proposal PRO2000-04, *Formulants Policy*, published for public comment in May 2000. Comments received were taken into consideration in the final version of the policy directive.

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Foreword

The Pest Management Regulatory Agency (PMRA, Agency) is implementing a program on the regulation of formulants. A formulant is any substance, other than an active ingredient, intentionally added to a pest control product. The program is based on the approach followed by the United States Environmental Protection Agency (USEPA)[1] and represents another step leading towards harmonization of pesticide regulation. Formulants will be assigned to several lists. List 1 includes formulants of toxicological concern (as on current and previous USEPA Inert List 1[2,3,4]), those meeting criteria of the federal Toxic Substances Management Policy (TSMP) and those subject to the Montreal Protocol on Substances that Deplete the Ozone Layer. List 2 contains formulants considered to be potentially toxic. List 3 contains formulants that do not meet criteria for the other lists. List 4A formulants are of minimal toxicologic concern. List 4B contains formulants of minimal concern under specific conditions of use. As a starting point, most formulants have been categorized using the U.S. Lists. Where the list number assigned for a particular formulant in Canada differs from that assigned by the USEPA, regulatory action as outlined in this regulatory directive is based on the PMRA list number. Formulants unique to Canadian-registered products will be assigned to the various lists as information is received. For a consolidated listing of all formulants found in Canadian registered pest control products and categorized according to the five lists, refer to Regulatory Note REG2004–01 or the latest version.

To update available information, statement of product specification forms (SPSFs) of control products are required to be submitted with each submission to register, to amend, to renew or to conduct research with a control product.

Current List 1 formulants are to be phased out of all control products by December 31, 2004. Only products for which registrants have provided safety data to support the continued use of a List 1 formulant or made an application to replace the List 1 formulant were able to be sold after December 31, 2002. As of that date, no other products containing List 1 formulants could be sold. Label disclosure of List 1 formulants has been required on product labels since December 31, 2001.

List 2 formulants must be listed on pest control product labels by January 9, 2006, and will be subject to reassessment and possible data call-in, in accordance with the USEPA reassessment activities. Labelling will be required for formulation preservatives and for allergens known to cause anaphylactic-type reactions.

The program also sets forth acceptance criteria for dyes, colourants and fragrances and criteria for notifiable changes to product labels and formulations.

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1 U.S. 52 Federal Register (FR) Notice 13305, April 22, 1987

2 Ibid

3 U.S. FR June 24, 1998, pp. 34384–34290

4 http://www.epa.gov/opprd001/inerts/lists.html

New requirements established under this program are being phased in over a three-year period beginning January 9, 2005.

Note: The new *Pest Control Products Act* (new PCPA) was given Royal Assent on December 12, 2002. Paragraph 43(5)(*b*) of the new PCPA indicates that a list of formulants and contaminants that are considered to be of health or environmental concern will be established. This list will comprise all of the formulants on Lists 1 and 2 of Regulatory Note REG2004-01, *PMRA List of Formulants*, as well as the formulants that are allergens known to cause anaphylactic type reactions as indicated in section 4.14 of this Regulatory Directive, and contaminants of concern found in pesticide active ingredients. The list will be published in the *Canada Gazette* and posted on the PMRA Web site. Once the new Act is in force, the identity and concentration in a product of any formulant or contaminant on the list, will not be confidential and will be available to the public on request.

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1.0 Introduction

This program outlines how formulants in pest control products will be regulated. The Pest Management Regulatory Agency (PMRA, the Agency) is taking action to ensure that information on formulations and identification of formulants are accurate and meet current standards. The Agency requires either elimination of certain toxic formulants from products or appropriate data to support the safety of their continued use. The PMRA also encourages the use of the least toxic formulants available that are appropriate to the formulation. In addition to data/information that is required for an individual formulant, as per current policy, for applications to register new products or for product amendments, data (e.g., acute toxicity, efficacy, etc.) may also be required on the end-use formulation which contains the formulant.

The high degree of concordance between formulants used in Canadian pest control products and those used in products in the U.S. has allowed the Canadian program to be based on and to be directed towards harmonization with the USEPA policy on inerts (also referred to as other ingredients).

By implementing this directive, the PMRA will have a formulants program that is similar to the USEPA policy. Further steps towards harmonization will take place under the North American Free Trade Agreement Technical Working Group on Pesticides. The PMRA recognizes that a step-wise process is required for the implementation of the formulants program. To optimize efficiency and reduce resource requirements, the Agency will utilize the USEPA reviews for decisions on Canadian formulants wherever possible.

1.1 Key elements of the PMRA formulants program

This formulants program:

- will lead to increased harmonization of Canadian regulatory approaches for formulants with those of the USEPA by adopting and building on their lists of inerts (formulants);
- requires applicants and registrants to submit updated statement of product specification forms (SPSFs) with all submissions to register, to amend, to renew or to conduct research with a control product, with identification of individual formulants by Chemical Abstracts Service (CAS) Registry Numbers, where one exists;
- applies the directives of the TSMP and Montreal Protocol to formulants that meet the criteria of these policies;
- requires data and label identification of formulants and, in selected cases, removal or substitution of formulants, that have potential or identified toxicological concerns;
- requires label identification of active ingredients that are present in the end-use formulation as formulation preservatives;
- sets acceptance criteria for formulants that are dyes, fragrances or oils; and

- requires label identification of formulants that are common allergens known to be associated with anaphylactic reactions.

1.2 Definitions

Active ingredient: the ingredient(s) of a pest control product to which the effects of the product are attributed, including any synergist, not including a solvent, diluent, emulsifier or ingredient that by itself is not primarily responsible for the effect of the product.

Adjuvant: a formulant used by the end user for in-tank mixing with a control product. Adjuvants whose intended use is to directly improve the efficacy or enhance the biological performance of the control product are registered under the authority of the *Pest Control Products Act* (PCPA) and Regulations.

Formulant: any substance or group of substances other than the active ingredient that is intentionally added to a pest control product to improve its physical characteristics (e.g., sprayability, solubility, spreadability and stability).

Formulant mixture: a formulant composed of more than one substance.

Inert (other) ingredient: USEPA terminology equivalent to the term formulant.

New formulant: any formulant that is not in a currently Canadian registered pest control product and is not on the USEPA Inerts Lists.

New use of a formulant: the formulant has not been identified for that purpose in an approved pesticide formulation in Canada or the U.S.

Pest control product: any product, device, organism, substance or thing that is manufactured, represented, sold or used as a means for directly or indirectly controlling, preventing, destroying, mitigating, attracting or repelling any pest and includes:

1. any compound or substance that enhances or modifies or is intended to enhance or modify the physical or chemical characteristics of a control product to which it is added, and

2. any active ingredient used for the manufacture of a control product.

Reactant: a component formulated into a pesticide formulation that reacts chemically with an active ingredient to modify its form, e.g., a reactant added to a formulation containing an acid form of an active ingredient to make a corresponding amine form of the same active ingredient. Reactants are generally completely used up in the chemical reaction with the active ingredient. Therefore, they are not normally considered to be formulants and are outside the scope of this policy. Such compounds must be identified as reactants on SPSFs.

Safener: a formulant in some herbicidal pest control products that mitigates the effects of the product on specific economically important crops. Safeners, since they are biologically active, are subject to the same data requirements as for an active ingredient.

1.3 Effective Date

New requirements established in the Formulants Program are being phased in over a three-year period beginning January 9, 2005. (A guidance document on how to comply with the Formulants Program will be available shortly and will include the implications of the Program on submissions in process and applications received within the pre-implementation period.)

2.0 Legal authority and related policies

All pest control products that are used, sold or imported into Canada are regulated by the PMRA. In Canada, the federal legislative authority for the regulation of pest control products including their formulants is derived from the PCPA and Regulations and the *Food and Drugs Act* (FDA) and Regulations.

2.1 Formulants determined to be of concern according to other federal legislation/policies (including the TSMP)

Appropriate regulatory action may need to be undertaken in order to manage/eliminate the use of formulants which are identified as being of concern with respect to human health or the environment under other federal legislation or policies. For example, the PMRA is applying its Regulatory Directive DIR99-03 (*The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*) to formulants. The TSMP was developed to provide a common approach for developing and implementing measures to minimize or reduce the use and release of substances added to Schedule 1 of the *Canadian Environmental Protection Act* 1999 (CEPA 1999). The PMRA is coordinating these activities for the pesticide sector. Formulants that meet TSMP Track-1 criteria are included in List 1.

2.2 Formulants subject to the directives of the Montreal Protocol

In 1980, the Canadian federal government established regulations under the *Environmental Contaminants Act* to prohibit the use of chlorofluorocarbons (CFC) in aerosols for certain personal products. In 1987, Canada became a signatory to the Montreal Protocol, which sets out a schedule to control ozone-depleting substances.

In keeping with the goals of the Protocol, as of April 1989, the CFCs -11, -12, -113, -114 and -115 were no longer permitted for use in pest control products (see Regulatory Directive DIR93-11, *Chlorofluorocarbons in Pesticide Products*).

A subsequent amendment to the Protocol incorporated other ozone-depleting chemicals, including CFCs, carbon tetrachloride, 1,1,1-trichloroethane (TCE), hydrochlorofluorocarbons (HCFCs) and methyl bromide. The PMRA no longer supports the use of ozone-depleting chemicals as formulants and no new registrations or renewals will be issued for products containing them. Registrants with products that currently contain these chemicals as formulants are required to reformulate or discontinue the product. A list of possible alternatives or substitutes is found at Environment Canada's Web site, www.ec.gc.ca/ozone.

3.0 Categorization of formulants currently in use in Canada

Existing formulants contained in registered pest control products in Canada will be assigned to one of the following five lists ranked in descending order of concern to establish priorities for regulatory activities. The regulatory actions proposed for formulants on each list are described in detail in Section 4. For a complete listing of formulants found in Canadian registered pest control products and their associated list numbers, refer to Regulatory Note REG2004-01 or the latest version. The most recent USEPA Inerts Lists are available on the USEPA Web site, www.epa.gov/opprd001/inerts/lists.html.

3.1 List 1, formulants of toxicological concern

List 1 consists of formulants identified as being of significant concern with respect to their potential adverse effects on health and the environment. As a starting basis, List 1 includes all formulants presently or previously listed on the USEPA List 1 and any additional formulants in Canadian products that meet any criteria for any one of the following categories:

Carcinogenicity:

1. a rating as a human carcinogen or probable or possible human carcinogen by the International Agency for Research on Cancer (rating 1, 2A or 2B)
2. characterized by the U.S. National Toxicology Program (NTP) as an animal carcinogen in at least one species and one sex
3. regulated by a Canadian or U.S. federal agency as a carcinogen

Neurotoxicity and chronic effects:

1. identified in U.S. *Occupational Diseases, A Guide to their Recognition* (1977), as causing neurotoxicological and chronic effects in the workplace environment
2. regulated by a Canadian or U.S. federal agency as a neurotoxin
3. peer reviewed study, included in the Toxicology Data Bank of the U.S. National Library of Medicine, reporting neurotoxic or chronic effects

Adverse reproductive effects:

1. regulated by a Canadian or U.S. federal agency as causing adverse reproductive effects
2. peer reviewed study, included in the Toxicology Data Bank of the U.S. National Library of Medicine, reporting adverse reproductive effects

Ecological effects:

1. a lethal concentration 50% (LC_{50}) of less than one part per million (This USEPA criterion refers to aquatic toxicity, i.e. potential for persistence and an aquatic $LC_{50} < 1$ mg/L)
2. a potential for bioaccumulation (The PMRA, like the USEPA, will consider persistence as a factor in this criterion, i.e., potential for persistence and bioaccumulation)

Formulants that meet the Track-1 criteria of the TSMP
See Section 2.1 above.

Formulants that meet the criteria of the Montreal Protocol
See Section 2.2 above.

The goal of the PMRA is to have List 1 formulants removed from products or supported with data to demonstrate no unacceptable risk. Registrants with List 1 formulants in their product are subject to the regulatory actions outlined for List 1 in Section 4.3.

3.2 List 2, potentially toxic formulants with a high priority for testing

List 2 contains formulants that are considered to be potentially toxic, based on either structural similarity to List 1 formulants or data suggestive of toxicity. Most of the chemicals on the USEPA List 2 were designated for testing through the U.S. NTP, the USEPA Office of Toxic Substances and other U.S. regulatory or government bodies. Reassessment of List 2 chemicals is underway in the U.S. Those formulants in Canadian products that are subject to reassessment and possible data call-in by the USEPA will also be subject to appropriate regulatory action in Canada. Regulatory action for List 2 formulants is described in Section 4.4.

3.3 List 3, formulants that do not meet the criteria of Lists 1, 2, 4A and 4B

List 3 contains the formulants in use in registered pest control products that do not meet the criteria of any of the other lists. Regulatory action for List 3 formulants is described in Section 4.5.

3.4 List 4A, formulants of minimal toxicological concern

List 4A contains formulants that appear on the U.S. Minimum Risk Inerts List that are generally regarded to be of minimal toxicological concern as well as substances commonly consumed as foods.[5,6] Based on their known properties, formulants on List 4A are considered acceptable in pest control products for both food and non-food uses with no further data necessary for the formulant alone. Regulatory action planned for List 4A formulants is described in Section 4.6.

3.5 List 4B, formulants of minimal concern under specific conditions of use

List 4B includes formulants, some of which may be toxic, but for which there are sufficient data to reasonably conclude that the specific use pattern of the pest control product (as listed in the U.S. Code of Federal Regulations, 40 CFR Protection of Environment, Subpart D, Section 180.000(*c*), (*d*) and (*e*)) will not adversely affect public health or the environment. List 4B includes formulants that meet the following criteria:

1. they were approved by the United States Food and Drug Administration (USFDA) or under the Canadian FDA and Regulations for use as direct food or drug additives; concentration restrictions are applicable;
2. they are polymers considered not to pose an unacceptable risk owing to such characteristics as size and lack of absorbability (Section 4.9); or
3. they were evaluated within an approved use pattern and determined to be of minimal risk for that use only.

Regulatory action proposed for List 4B formulants is described in Section 4.6. If the use pattern or proposed use pattern of a 4B formulant is beyond that approved by the USEPA, the PMRA will require an independent review.

3.6 Formulants unique to Canada

Formulants are unique to Canada if they:

1. are not listed on the USEPA Lists; or
2. are proprietary formulants or mixtures where individual components require identification and placement on the appropriate list.

Regulatory action proposed for formulants unique to Canada is described in Section 4.7.

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5 U.S. FR Document 94-23890, September 28, 1994

6 U.S. FR December 4, 1998, pp. 66999–67001

3.7 Formulants no longer used

Previously listed chemicals that are determined to no longer be used in pest control products will be removed from the lists of formulants.[7] If a registrant wishes to reactivate their use, these formulants will be considered "new" and will be subject to the appropriate requirements that would allow determination that the use would not pose an unacceptable risk to human health or the environment.

4.0 Regulatory actions on formulants currently in use in Canada

Irrespective of the initial placement of a formulant on a specific list, if information becomes available to indicate a significant concern, the formulant is immediately subject to regulatory action that may include removal, substitution, or data call-in to allow a risk assessment.

4.1 Statement of product specification form update

To ensure that information on formulations and identification of formulants is accurate and meets current standards, the Agency requires registrants to provide an updated SPSF for each submission to register, to amend, to renew or to conduct research with a control product or as outlined in the following sections, using a new SPSF (available electronically at the PMRA's Web site, www.hc-sc.gc.ca/pmra-arla/). This requirement becomes effective January 5, 2005. The information on the new SPSFs must:

1. accurately represent the product currently being formulated, including alternative formulations where acceptable; and
2. include all relevant information for each product component, supplier(s) name and address, percent weight per weight, certified limits, CAS number, Formulant List Number, and its purpose in the formulation.

If registrants are already aware that changes have been made to their product formulations that are not reflected on the SPSF currently on file with the Agency, a formal application for amendment should be submitted along with the updated SPSF, appropriate data and fees.

4.2 Conversion of guarantee statement from minimal to nominal

To harmonize with the USEPA, the Agency is working with registrants to convert guarantees from minimal to nominal values. Although the focus of this program is to update information on formulations and to eliminate certain formulants from products, it also provides opportunity for the simultaneous conversion of product specifications from minimal to nominal values.

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[7] Consistent with U.S. 52 FR Notice 13305, April 22, 1987

If the information to make the conversion from minimal to nominal is not immediately available, the new SPSF for formulant program purposes should be submitted with a minimal guarantee.

If the conversion to nominal results in a change in the guarantee statement, an application for label amendment, new draft labels showing the nominal guarantee and the application fee will be required if this activity is occurring simultaneously with the submission of an updated SPSF. Please note that conversion of guarantee statements from minimal to nominal for end-use products (EPs) and manufacturing concentrates can only be accommodated at registration renewal if the source of technical grade active ingredient (TGAI) is registered in nominal. Conversion of guarantee statements from minimal to nominal for TGAIs cannot be done at registration renewal and requires a separate application for product amendment.

Requirements and time frames for submission of updated specification forms, label amendments and data are described in detail within each of the following sections.

4.3 Regulatory action on pest control products that contain List 1 formulants

Current List 1 formulants are to be phased out of all control products by December 31, 2004. Only products for which registrants have provided safety data to support the continued use of a List 1 formulant or made an application to replace the List 1 formulant were able to be sold after December 31, 2002. As of that date, no other products containing List 1 formulants could be sold.

Since 1990, it was the practice, on receipt of an application to amend a formulation or register a new formulation, to ask the applicant to substitute or remove formulants that are on the USEPA Inerts Lists 1 and 2 (memorandum to Crop Protection Institute of Canada and Canadian Manufacturers of Chemical Specialties Association, August 7, 1990). In the case of List 1 formulants, label disclosure requirements were imposed where no suitable substitute could be found, as recommended in the Canadian Pesticide Registration Review (December 1990, p. 15). Consistent with the intent to progress towards harmonization with the USEPA Inerts Policy, the PMRA undertook an initiative to remove all List 1 formulants from pest control products in September 2001. Registrants of products containing List 1 formulants were given three options:

- immediate voluntary discontinuation of the product registration; OR
- substitution/removal of the List 1 formulant and interim disclosure labelling (with an application to amend the product formulation to be submitted by December 31, 2002); OR
- supporting the continued use of the List 1 formulant and interim disclosure labelling (with submission of safety data by December 31, 2002).

Failure to select and act upon one of the options would result in cancellation of product registration.

As formulants are reclassified from other Lists to List 1, products containing them will be dealt with in the same manner and within the same time-frames, as outlined below:

(a) Options for registered products with future List 1 formulants (except those subject to the Montreal Protocol)

When a formulant is reclassified to List 1, registrants of products containing that formulant will be subject to the following options within the timelines given which are set from the date of notification of reclassification:

(i) Immediate voluntary discontinuation of a product containing the List 1 formulant

Registrants may opt to voluntarily discontinue the product containing a List 1 formulant. Registrants must notify the PMRA if they choose to discontinue the product within four months of the date of notification of reclassification and no further sale by the registrant will be allowed.

(ii) Retain the product but substitute for the List 1 formulant

Registrants selecting this option have the responsibility to submit information demonstrating that the formulant used for substitution has no unacceptable health or environmental risks and that the product is still efficacious with the new formulant. Within 16 months of notification of reclassification, registrants must submit an application to amend their registered product.

Immediate substitution: Registrants may have sufficient information to apply immediately to amend the formulation of the product containing a List 1 formulant by the removal of the List 1 formulant and substitution with a formulant from other than List 1 and preferably not List 2. At the time of application to amend the formulation, the registrant is expected to immediately cease manufacturing the product containing the List 1 formulant. Four months after notification of reclassification, any remaining old product containing the List 1 formulant not already in the channels of trade is subject to the disclosure labelling requirement as described in Section 4.3(b). Where a List 2 formulant is substituted, Section 4.4 applies.

Substitution with disclosure labelling: It is recognized that formulation changes may require new developmental work to verify the safety and efficacy of the amended EP. The registrant will be required to label the existing product not already in the channels of trade to indicate that it contains a List 1 formulant until application to amend the formulation is approved. Formulations with List 1 formulants will not be permitted to be sold by registrants or retailers after 28 months of notification of reclassification (except as according to (iii) below).

In view of the fact that a certain amount of the work on many new formulations (e.g., to generate efficacy data) must be carried out in the field, a use-season will be allowed for such work. Application for amendment with the required data must be received by the PMRA within 16 months of notification of reclassification or the registration will be cancelled, and all sale/import and use of the product will end.

(iii) Data submission to support the use of the List 1 formulant

Registrants may submit data to verify the safety of a product containing a List 1 formulant within 16 months of notification of reclassification, or the registration of the product will be cancelled. The data may be specific to the formulant or conducted with the formulation. (Submission of data on the formulation only would not allow an independent assessment of the formulant itself and thus would only support the particular product formulation.) Such data must be sufficiently comprehensive to allow the PMRA to conduct a complete risk assessment to determine that there are no unacceptable risks to health and the environment. Dependent on the use pattern to be supported, the data requirements may be as extensive as those for the active ingredient or may be tailored to the specific use scenario. Formulations with List 1 formulants will not be permitted to be sold after 28 months of notification of reclassification unless supported by an acceptable risk assessment.

(b) Disclosure of List 1 formulants on product labels

Label disclosure is required for all products containing a List 1 formulant. Label disclosure changes may be carried out by notification and will apply to products in the hands of the registrants. Labels may be printed or overstickered. The following statement must appear within four months of notification of reclassification on the labels of any product containing a List 1 formulant that continues to be available as described above.

> "This product contains the toxic formulant (insert name of chemical) at (insert percent weight/weight) %."

This statement must be placed on the same panel as, and in proximity to, the guarantee statement, in a type comparable to others of the panel text.

(c) New products with a List 1 formulant

Applications to register new products or to amend existing products containing List 1 formulants will not be accepted, unless information or data to specifically support the safety of the product containing the List 1 formulants accompanies the application.

(d) Regulatory action on pest control products that contain formulants subject to the Montreal Protocol

The production of ozone-depleting chemicals is being phased out in accordance with the provisions of the Montreal Protocol. As this process continues, registrants with products currently containing ozone-depleting chemicals will be required to discontinue or reformulate them.

(i) Disclosure of ozone-depleting formulants

Until phased out, all products containing ozone-depleting chemicals governed by the Montreal Protocol must be labelled with the following statement if they are sold or distributed in Canada.

> "WARNING: This product contains (insert name of chemical), which harms public health and the environment by destroying the ozone in the upper atmosphere."

This statement must be placed on the same panel as, and in proximity to, the guarantee statement, in a type comparable to others of the panel text.

4.4 Regulatory action on pest control products that contain List 2 formulants

As previously noted in Section 3.2, List 2 formulants may have structural similarity to List 1 chemicals and are considered to be potentially toxic. Accordingly, the PMRA will be working with the USEPA to gather and review information on potential adverse effects of formulants on the USEPA Inert List 2, and to determine the necessary course of action for these formulants. **Should a List 2 formulant be found to meet List 1 criteria, it will be subject to the options and time frames as outlined in section 4.3(a)**.

The PMRA will be reassessing List 2 formulants and where possible will be coordinating reassessment activities with those of the USEPA, where the same formulant is being reassessed as part of the USEPA's reassessment of List 2 inert ingredients. Registrants with List 2 formulants in their products are strongly encouraged to consider amending formulations by substituting more acceptable alternatives such as those on Lists 3, 4A and 4B (if the use scenario applies) or submitting data/information to support the continued use of List 2 formulants. Registrants have the responsibility to submit information demonstrating that the List 2 formulant they wish to continue to use, or the formulant proposed for substitution, poses no unacceptable health or environmental risks and that the product is still efficacious with the new formulant.

(a) Labelling of products containing List 2 Formulants

Until the status of all List 2 formulants is resolved via reassessment, all products containing List 2 formulants must be labelled with the List 2 statement provided

below by January 9, 2006. Products not conforming with this will not be amended or renewed.

These label changes may be carried out by notification and will apply to all product labels. Labels may be printed to show the statement below or may be overstickered.

> "This product contains (insert name of chemical) at (insert proportion by weight) %, which requires further toxicological testing."

This statement must be placed on the same label panel as, and in proximity to, the guarantee statement, in a type comparable to others on panel text.

If registrants wish to continue to use List 2 formulants, they are encouraged to submit supporting information/data as outlined in section (b) (iv) below as soon as possible. If information/data are submitted and reviewed before January 9, 2006, and the PMRA determines that the List 2 formulant is acceptable for use, the formulant will be reclassified to List 4B and the List 2 labelling statement will not be required.

As of January 9, 2006, applications for new products containing List 2 formulants or product amendments involving the addition of List 2 formulants will be subject to the same labelling requirements described above as a requirement for obtaining registration/amended registration.

(b) Options for registered products with List 2 formulants

The reassessment process will define the time frames for final resolution of List 2 formulants. For the List 2 formulants subject to data call-in, registrants have the following options:

(i) Demonstrate the absence of the List 2 formulant

Registrants may opt to provide evidence that a List 2 formulant is no longer contained in the formulation. If there have been changes to the product formulation that are not reflected on the SPSF currently in the product register, registrants should apply for an amendment with appropriate data and fees. All formulants must be identified by CAS number where one exists. When formulants are mixtures, registrants should follow the directions described in Section 4.10 to ensure that the mixture does not contain List 2 formulants. If the information for changing to a nominal guarantee is readily available, this should also be submitted with the updated SPSF.

(ii) Voluntary discontinuation of the formulation with the List 2 formulant

Registrants may opt to voluntarily discontinue the product. Registrants should notify the PMRA according to the provisions of the data call-in notice if they choose to discontinue the product. Reinstatement of these discontinued products will not be permitted without supporting data.

(iii) Amendment of the formulation to remove or substitute the List 2 formulant

Registrants may choose to make an application (with supporting data as required) to remove or substitute for a List 2 formulant that is subject to or pending data call-in. Preferably, any substitution should be with a formulant from List 3, 4A or 4B (if the use conditions apply). Registrants have the responsibility to provide any necessary information to demonstrate that the formulant used for substitution poses no unacceptable health or environmental risks and that the product is still efficacious with the new formulant.

(iv) Data submission to support the use of the List 2 formulant

Registrants have the option of supplying data to support safety in the use of the product containing the List 2 formulant subject to the data call-in. The data may be specific to the formulant or conducted with the formulation. Such data must be sufficiently comprehensive to allow the PMRA to conduct a risk assessment to determine that there are no unacceptable risks to health and the environment. Dependent on the use pattern to be supported, the data requirements may be as extensive as those for the active ingredient or may be tailored to the specific use scenario.

(c) New products with List 2 formulants

As of the date of the data call-in, applications to register new products or to amend existing products containing List 2 formulants subject to the announced data call-in will not be accepted without supporting data. As of the data call-in, submissions currently with the PMRA that lack the supporting data will be returned to the registrant.

New products with List 2 formulants not yet subject to data call-in will continue to be accepted; however, registrants should be aware that reassessment and possible data call-in are pending for all of the List 2 formulants. It is recommended that registrants plan early and make necessary formulation changes to minimize or avoid potential regulatory action. New products containing List 2

formulants that have not yet been reassessed are subject to the labelling requirements outlined in (*a*) above.

4.5 Regulatory action on pest control products that contain List 3 formulants

The USEPA List 3 formulants have been subjected to a quantitative structure activity relationship (Q-SAR) analysis for structural alerts and do not have information available to demonstrate they meet the criteria of any of the other lists.

Registrants should be aware that as additional data become available, formulants on List 3 may meet the criteria of List 1 or List 2 and will be subject to the requirements described for Lists 1 and 2, including the submission of data to support continued or new use. In the future, formulants remaining on List 3 will be subject to reassessment and possible data call-in to complete their database once the issues associated with the Lists 1 and 2 formulants are approaching resolution. Registrants will be informed of the timing for the data call-in as work is completed on the higher priority Lists 1 and 2 formulants. If new information comes to light on any List 3 formulant that raises concern, the formulant will immediately be subject to the appropriate data requirement to support continued use.

4.6 Regulatory action on pest control products that contain Lists 4A and 4B formulants

List 4A contains formulants that appear on the U.S. Minimum Risk Inerts List that are generally regarded to be of minimal toxicological concern as well as substances commonly consumed as foods. Based on their known properties, formulants on List 4A are considered acceptable in pest control products for both food and non-food uses with no further data necessary for the formulant alone. When a formulant is on List 4A, no further regulatory action is anticipated.

List 4B includes formulants, some of which may be toxic, but for which there are sufficient data to reasonably conclude that the specific use pattern of the pest control product (as listed in the U.S. Code of Federal Regulations, 40 CFR Protection of Environment, Subpart D, Section 180.000(*c*), (*d*) and (*e*)) will not adversely affect public health and the environment. When a formulant reaches List 4B, no further regulatory action is anticipated unless the use pattern for which it is being considered is beyond that approved, in which case the PMRA will require an independent review.

4.7 Regulatory action on formulants unique to Canada

A number of formulants in Canadian products appear to be unique to Canada, as they do not appear on the USEPA lists or are proprietary mixtures whose individual components may or may not be on the USEPA lists.

As per current practice, all new submissions to register or amend products will continue to require identification of all formulant components prior to review of the submission. It is the responsibility of the applicant to ensure that components of the formulant mixtures

be supplied to the PMRA. Applicants can request that formulant manufacturers submit proprietary information to the PMRA Formulant Section under separate cover to support review of the submission as described in Section 4.10. As the components of the formulant mixtures are identified, the formulant mixture will be placed on the appropriate list and be subject to the regulatory action and requirements for that list. The list number for a mixture is based on the components, i.e., the list number would be the one representing the highest level of concern. The order for formulants of most concern to least concern is 1, 2, 3, 4B, 4A. For example, if a mixture contained components from List 2, 3 and 4A, the mixture would be categorized to List 2. Formulants or formulant components that do not appear on a current USEPA List will be subject to the appropriate data/information requirements to support continued use of existing products or any applications for new products.

4.8 Regulatory action for formulants in products under re-evaluation

As a part of the re-evaluation of TGAIs and their EPs, registrants have been informed of the proposed direction the Agency will be taking with formulants. Registrants have been advised to take this into consideration when determining the course of action for their products under re-evaluation.

The regulatory requirement for individual formulants will be handled according to the outline in this Regulatory Directive and separately from the re-evaluation of TGAIs and EPs. Registrants will not be asked to submit data on individual formulants as part of the re-evaluation of their active ingredients and EP, unless they wish to retain registration of a product containing a List 1 formulant, or a List 2 formulant subject to the data call-in.

4.9 Regulatory action on pest control products that contain polymers as formulants

In the U.S., certain polymers are exempt from data requirements when used as formulants in a pest control product formulation. Canada has adopted the same approach and these polymers will be exempted from data requirements if they:

1. conform with the international definition of a polymer as adopted by the Organisation for Economic Co-operation and Development (OECD) in May 1993 (*Polymer Exemption Guidance Manual*, USEPA 744-B-97-001, 1997, p. 3); and
2. are eligible for use as an inert ingredient according to the USEPA requirements.

The terminology adopted and the USEPA policy regarding polymers is accessible through the internet at www.epa.gov/oppt/newchems/polyguid.pdf.

Formulants claiming polymer status that do not conform with the accepted international definition of a polymer described above will be subject to data requirements.

4.10 Regulatory action on pest control products that contain proprietary formulants or mixtures

Some formulants are claimed to be proprietary trade secrets and the manufacturer may not wish to disclose the constituents of such formulants to a registrant or formulator. It is the responsibility of the registrant to arrange for the manufacturer of a proprietary formulant or mixture to disclose the composition of the proprietary formulant or mixture directly to the PMRA Formulants Section. The constituents of a proprietary formulant or mixture are subject to the provisions of the program on formulants.

The fact that the applicants use a proprietary formulant ingredient or mixture whose composition is not known to them does not remove their responsibility for maintaining the composition of each of those formulants within its certified limits and assuring that the composition of the proprietary formulant or mixture will not change over time. The PMRA believes that a contractual arrangement between a formulator and supplier or manufacturer is the best way to ensure that the formulator can rely on the composition of the material received. Registrants or formulant manufacturers are responsible for notifying the PMRA when the composition of a formulant mixture used in a pest control product is altered.

(a) Registered products

If a product with an existing registration contains a formulant of toxicological concern comprising part of a proprietary formulant or mixture, the PMRA will notify the registrant that the formulant contains a proprietary formulant or mixture of concern. It will be the responsibility of the registrant to contact the supplier or manufacturer of the proprietary ingredient or mixture to determine the identity of the formulant(s) of toxicological concern present in the pest control products and to take appropriate action as outlined above for each of the lists of formulants.

(b) New and amended products

The PMRA will notify the registrant if the proposed new or amended pest control product contains a proprietary formulant or mixture with ingredients of concern. It will be the responsibility of the registrant to contact the supplier or manufacturer of the proprietary ingredient or mixture to determine the identity of the formulant(s) of toxicological concern present in the proposed new or amended pest control product and to take appropriate action as outlined above for each of the lists of formulants.

4.11 Research permits

Formulants in products proposed for research are subject to this program. In the case of a new formulant, the data/information required would depend on the proposed use of the product and the potential exposure. Sufficient data/information to allow for a quantitative

risk assessment may be necessary to evaluate the risks posed by the presence of a new formulant in a pest control product for which a research permit is requested.

4.12 Adjuvants added to pest control products prior to application (tank-mix adjuvants)

Adjuvants are formulants which are sold and used separately for in-tank mixing by the end-user. Adjuvants which are intended to directly improve the efficacy or enhance the biological performance of a pest control product by modifying or enhancing physical or chemical characteristics, are subject to the PCP Regulations as outlined in Regulatory Directive DIR93-15, *Registration Requirements for Adjuvant Products*.

While such adjuvants are subject to the data requirements described in DIR93-15, all the individual ingredients of these adjuvants are also subject to the conditions laid out in this program.

4.13 Labelling requirements for formulation preservatives

Certain registered EP formulations contain pesticidal active ingredients previously described as formulants. These active ingredients are generally included in a formulation in small amounts to protect the formulation from being denatured or degraded by pests. Examples include the addition of an insecticide at 0.1% to a rodenticide bait to prevent feeding by insects and the addition of formaldehyde to aqueous formulations to prevent bacterial growth. The past practice has been to consider such active ingredients as formulants and to not list them in the guarantee statements of product labels. The formulation preservatives that are active pesticidal ingredients include **but are not limited to** formaldehyde, paraformaldehyde, hexachlorophene, pyrethrins, malathion, chloropicrin and glutaraldehyde.

Any active ingredient whose function is to preserve or protect the formulation is to be so specified on the SPSF and on the product label with the following statement:

> "Contains (insert name of active ingredient) at (insert percent weight/ weight) % as a preservative."

This statement must be placed on the same panel as, and in proximity to, the guarantee statement, in a type comparable to others of the panel text.

If the preservative is an active ingredient that is registered in Canada, only a registered source may be used.

Registrants of formulations containing preservative ingredients are required to submit an application to amend the label and SPSF by July 9, 2005. Where the preservative is a registered product, each application is to be accompanied by a Letter of Confirmation of Source from the supplier/registrant of the preservative.

As of July 9, 2005, applications for new products containing formulation preservatives or product amendments involving the addition of formulation preservatives will be subject to the same labelling requirements described above as a requirement for obtaining registration/amended registration.

4.14 Labelling requirements for formulants that are allergens known to cause anaphylactic type reactions

Registrants of products containing the following common allergenic substances known to cause anaphylactic type reactions as formulants must amend their product labels to add the following statement:

> "Warning, contains the allergen (insert name of allergen)."

Milk; eggs; fish, crustaceans, shellfish; peanuts, soy, tree nuts or their shells; sesame seeds; wheat; any hydrolyzed plant protein, starch or lecithin of any of the above; sulfites.[8]

This statement must be placed on the same panel as, and in proximity to, the guarantee statement, in a type comparable to others of the panel text.

Products containing the above allergenic formulants must be labelled with this statement by July 9, 2005. Label disclosure changes may be carried out by notification and will apply to all product labels. Labels may be printed to show this statement or may be overstickered.

As of July 9, 2005, applications for new products containing allergenic formulants or product amendments involving the addition of allergenic formulants received after the effective implementation period for the Formulants Program will be subject to the same labelling requirements described above as a requirement for obtaining registration/amended registration.

4.15 Acceptance criteria for dyes and colourants, fragrances or oils used as formulants

(a) Dyes and colourants

To be permitted for use in pesticide products, colourants or colourant ingredients must be on the PMRA or USEPA List 3 or 4, have an appropriate USEPA exemption from the requirements of a tolerance, and the pesticide product containing the colourant must meet the conditions associated with the exemption, or must be colourants or colourant ingredients that are approved in Canada for food or drug use (Section 16, FDA).

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[8] Zarkadas, M. et al. Common Allergenic Foods and Their Labelling in Canada: a Review, Canadian Journal of Allergy and Clinical Immunology, Vol. 4, No. 3, 1999.

Registrants of pest control products are required to replace colourants, that do not meet these criteria, with acceptable colourants by December 31, 2006.

Where the total percentage of the substituted colourant does not exceed 1% by weight of the formulation, the PMRA should be advised of the substitution by notification. If the total percentage of the substituted colourant exceeds 1%, the registrant must submit an application for amendment. Colourants in excess of 1% of the formulation may be subject to data review.

(b) Fragrances

Only fragrances or fragrance ingredients listed on the PMRA or USEPA List 3 or 4, or that are approved in Canada for food or drug use, as appropriate, may be used as formulants. Each component of a fragrance which is not on the PMRA or USEPA List 3 or 4 or approved for food and drug use and is present at greater concentration than 0.1%, may be subject to review. If a fragrance has identified toxicological concerns, it may be subject to data requirements and risk assessment. The total amount of fragrance may not exceed 1% by weight of the formulation.

Registrants are required to replace fragrances that do not meet the acceptability criteria described above and are currently used in pest control products with acceptable fragrances by December 31, 2006. Where the total percentage of the substituted fragrance does not exceed 1% by weight of the formulation, the PMRA may be advised of this substitution by notification. If the total percentage of the substituted fragrance exceeds 1%, the registrant must submit an application for amendment.

(c) Mineral oils

To be considered a List 4A formulant, a mineral oil must meet the United States Pharmacopoeia (USP) requirements for purity (Class 5, USFDA; Food Chemical Codex [*Codex Alimentarius*]), or equivalent. An oil not meeting these criteria will not be considered to be a List 4A formulant and will be subject to the requirements of the list to which it is categorized.

4.16 Changes concerning formulants allowable by notification

Changes to a label or a formulation of a control product generally require an application for amended registration and necessary supporting documentation and data. Specific changes to labels and formulations outlined in this regulatory proposal, however, will be allowable by notification if they meet the following criteria: Please note that when notifying the PMRA of the following changes, a label or SPSF should not be submitted.

(a) Disclosure labelling for a formulation containing a List 1 formulant where:

(i) a letter of notification is received prior to the specified deadline date;
(ii) the registrant commits in the letter of notification, to remove the List 1 formulant or to provide the data to support the continued use of the List 1 formulant by the specified deadline date; and
(iii) the registrant attests that the following statement has been added to the label and appears on the same label panel as, and in proximity to, the guarantee statement, in a type comparable to others on panel text:

> "This product contains the toxic formulant (insert name of chemical) at (insert proportion by weight) %."

(b) Labelling for a formulation containing ozone-depleting formulants governed by the Montreal Protocol (except TCE) where:

(i) the registrant commits in the letter of notification to submit an application within the specified timeline to remove the ozone-depleting formulant from the formulation; and
(ii) the registrant attests that the following statement has been added to the label and appears prominently on the primary panel:

> "WARNING: This product contains (insert name of chemical), which harms public health and the environment by destroying the ozone in the upper atmosphere."

(c) Labelling for control products containing List 2 formulants where:

(i) a letter of notification is received by January 9, 2006; and
(ii) the registrant attests that the following statement has been added to the label and appears on the same label panel as, and in proximity to, the guarantee statement, in a type comparable to others on panel text:

> "This product contains (inset name of chemical) at (insert proportion by weight) %, which requires further toxicological testing."

(d) Labelling for control products containing common allergens where:

(i) a letter of notification is received by July 9, 2005; and
(ii) the registrant attests that the following statement has been added to the label and appears on the same label panel as, and in proximity to, the guarantee statement, in a type comparable to others on panel text:

"Warning, contains the allergen, (insert name of allergen)."

(e) Addition, deletion or substitution of colourants where:

(i) the total percentage of changed, new, added or deleted colourant does not exceed 1% by weight of the formulation;
(ii) the product is not intended for use on or mixing with seeds; and
(iii) the ingredient(s) of the colourant are on the PMRA or USEPA List 3 or 4, have an appropriate USEPA exemption from the requirements of a tolerance, and the pesticide product containing the colourant meets the conditions associated with the exemption, or the ingredient(s) of the colourant meet the requirements for food or drug use (Section 4.15) as appropriate.

(f) Addition, deletion or substitution of one or more fragrances where:

(i) the total percentage of the changed, added or deleted fragrance does not exceed 1% by weight of the formulation;
(ii) the composition of the fragrance has been provided to the PMRA by the supplier or manufacturer, or registrant; and
(iii) the ingredient(s) of the fragrance are on the PMRA or USEPA List 3 or 4 or the fragrance has been determined to be acceptable to the PMRA at the proposed concentration or the ingredient(s) of the fragrance meet the requirements for food or drug use as appropriate.

(g) Change in nominal concentration of formulant where:

(i) the nominal concentration falls within the certified limits for that ingredient as listed on the accepted SPSF;
(ii) the composition of the formulant is known to the PMRA;
(iii) the formulant is not on the PMRA or USEPA List 1 or 2; and
(iv) the formulant does not contain contaminants of toxicologic concern.

(h) Change in certified limits of formulant where:

(i) the certified limits fall within standard certified limits;
(ii) the PMRA has not previously determined that alternative or special certified limits apply; and
(iii) the nominal concentration has not previously been changed by notification (see item (g) above).

(i) Change in formulation process where:

(i) only a blending or dilution of product components is involved;
(ii) the nominal concentration and certified limits of the active ingredient(s) and formulants do not change; and
(iii) the physical, chemical and biological characteristics or the performance of the product remain unchanged.

NOTE: An application for amended registration is required when changes in the formulation process involve a chemical reaction.

(j) Change of supplier of a formulant where:

(i) the composition of the formulant is known to the PMRA;
(ii) the CAS registry numbers are the same;
(iii) the formulant is not on the PMRA or USEPA List 1 or 2;
(iv) the formulant does not contain contaminants of toxicologic concern; and
(v) the formulant is not proprietary.

5.0 Regulatory actions for new formulants in Canadian pest control products

Any formulant proposed for use in a pest control product is considered to be "new" if it is not currently identified as being present in a registered Canadian pest control product or on the USEPA lists. The requirements for new formulants are under consideration. The requirements listed in the Regulatory Proposal PRO2000-04, which at the time the proposal was released were harmonized with the USEPA, are no longer harmonized. The USEPA recently released a document entitled *Methodology for Lower Toxicity Pesticide Chemicals; Notice of Availability*, which describes their new method and data requirements for evaluating inert ingredients. It is the PMRA's intention to harmonize as much as possible with the USEPA's new approach and the PMRA will be releasing a regulatory proposal on new formulant requirements, for comment. In the meantime, applicants should contact the PMRA for guidance if they wish to propose a new formulant for use in pest control products.

List of abbreviations

CAS	Chemical Abstracts Service
CFC	chlorinated fluorocarbons
Codex	Codex Alimentarius
DACO	data code
EC_{50}	effective concentration 50%
EP	end-use product(s)
FDA	*Food and Drugs Act*
FR	Federal Register
HCFC	hydrochlorofluorocarbon(s)
K_d	adsorption coefficient (ratio of concentration in the soil phase to that in the aqueous phase under test conditions)
K_{oc}	adsorption coefficient (relates K_d to the organic carbon content of the soil sample)
K_{ow}	*n*-octanol–water coefficient
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
NTP	National Toxicology Program
OECD	Organisation for Economic Co-operation and Development
PCPA	*Pest Control Products Act*
pH	$-\log_{10}$ hydrogen ion concentration
pK_a	dissociation constant
PMRA	Pest Management Regulatory Agency
Q-SAR	quantitative structure activity relationship
SPSF	statement of product specification form(s)
TCE	1,1,1-trichloroethane
TSMP	Toxic Substances Management Policy
USEPA	United States Environmental Protection Agency
USFDA	United States Food and Drug Administration
USP	United States Pharmacopoeia