Pest Management Regulatory Agency
Agence de réglementation de la lutte antiparasitaire

Regulatory Directive DIR2003-02

Harmonization of Regulation of Pesticide Seed Treatment in Canada and the United States

The purpose of this document is to provide information on how seed treatment products are currently regulated in Canada and the United States and to demonstrate the degree of regulatory harmonization of **pesticides used for seed treatment** in the two countries. The harmonization of registration data requirements and test protocols for these commodities between Canada and the United States are substantially in agreement.

Consultation documents were published simultaneously August 30, 2000 by the Pest Management Regulatory Agency (PMRA) as Regulatory Proposal PRO2000-05 and the United States Environmental Protection Agency (U.S. EPA) as OPP Docket #OP-00675. This Regulatory Directive has considered the comments received as a result of this consultation.

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1.0 Objective

The harmonization of pesticide regulatory requirements being carried out under the auspices of the North American Free Trade Agreement (NAFTA) Technical Working Group (TWG) on Pesticides is important for achieving the goal of one North American market for pesticides. This goal is articulated in the document known as the North American Initiative (NAI). The NAI commits Canada's Pest Management Regulatory Agency (PMRA) and the EPA to harmonize pesticide regulatory tools so that work sharing and joint review activities become routine. It is also an objective of the TWG to clearly communicate the status of the harmonization process.

Regulatory Proposal, PRO2000-05, *Harmonization of Regulation of Pesticide Seed Treatment in Canada and the United States*, published in 2000, provided information on how seed treatment products are currently regulated in both Canada and the U.S. and reviewed the degree of regulatory harmonization of these commodities in the two countries.

For the purposes of this document, seed treatments include products that are primarily intended to provide protection against soil fungi and insect damage. Seeds for propagation may be treated domestically or imported as treated seed, may be treated domestically for subsequent export, or may be planted to produce crop that is to be exported.

2.0 Current legal framework in the United States

2.1 The *Federal Insecticide, Fungicide and Rodenticide Act*

Under the *Federal Insecticide, Fungicide and Rodenticide Act* (FIFRA), a pesticide generally must be registered with the EPA in order to be distributed, sold or imported into the U.S. To be registered, the EPA must determine that the pesticide will not pose unreasonable adverse effects to humans or the environment. The EPA has the authority, however, under FIFRA Sec. 25(b) to exempt a pesticide from any provisions of FIFRA including registration, if the pesticide is "adequately regulated by another Federal agency" or "of a character that is unnecessary to be subject to [FIFRA] in order to carry out the purposes of the Act."

For the purposes of FIFRA, pesticide-treated seeds are considered to be pesticides themselves because they are a mixture of substances that are intended to prevent, destroy, repel or mitigate a pest. In 1988, the EPA promulgated regulation 40 Code of Federal Regulations (CFR) 152.25(a) exempting certain treated articles (including treated seeds) from regulation under FIFRA provided that both of the following conditions are met:

(a) the pesticide used for the treatment is registered for such use; and

(b) the treatment is for the protection of the article or substance itself.

In issuing this regulation, the EPA reasoned that the risks of treated seeds that meet the above criteria could adequately be regulated by means of registration of the treating pesticide. In evaluating the risks of the seed treatment, the EPA could also evaluate the risks from exposure to the seed treated according to the label instructions and forgo the need for a separate evaluation and registration of the treated seed.

The term "registered for such use" in 40 CFR 152.25(a) refers to registration in the U.S. under FIFRA, and not to registration processes in other countries. Seeds treated in foreign countries are not eligible for the exemption unless they are treated with a pesticide also registered in the U.S.

The term "for the protection of the [seed] itself" means that the pesticidal protection imparted to the treated seed does not extend beyond the seed itself to offer pesticidal benefits or value attributable to the treated seed. Unless claims of pesticidal benefit or value attributable to the treated seed and extending beyond the treated seed are made in conjunction with the distribution or sale of the treated seed within the U.S., the EPA will presume that the seed will have been treated "for the protection of the seed itself." The EPA does not regard a statement that seed has been treated (e.g., Seed has been treated with [a particular pesticide active ingredient] as a protectant) as a pesticidal claim that would negate the exemption outlined in 40 CFR 152.25(a).

In general, seed treated with a pesticide that is to be sold or distributed in the U.S. must be coloured to prevent diversion for animal feed or other non-planting uses. EPA regulations in 40 CFR 153.155 require that a pesticide registered for treating seeds must contain a suitable dye unless the treatment is applied at planting (e.g., in the hopper box) for which dye is not necessary, or unless the pesticide label requires the user treating the seed to separately add a dye during the seed treatment process.

Seeds for planting which are treated with pesticides registered in the U.S. are exempt from registration as pesticides, and may be freely distributed and sold within the U.S. sellers, distributors and importers of treated seeds should maintain sufficient documentation of the treatment to demonstrate that the treating pesticide is registered in the U.S.

2.2 The *Federal Food, Drug and Cosmetic Act*

Under the *Federal Food, Drug and Cosmetic Act* (FFDCA) sec. 408, the EPA evaluates the risks posed by pesticide residues in food and feed to a standard of "a reasonable certainty of no harm." Before registration, a pesticide tolerance (or exemption) must be established if the intended use of the pesticide may result or may reasonably be expected to result, directly or indirectly, in residues in a food crop. Treated seed for planting of food crops requires a tolerance unless it can be shown that residues are not carried forward to the crop grown from the seed. Generally, tolerances established as a result of the assessment of a foliar use for a particular crop are adequate to cover use as a seed treatment.

Under the FFDCA, the Food and Drug Administration has established a policy with respect to the colouration of grain seeds to prevent the diversion into animal feed. Grain seed treated with pesticides for which there are no tolerances set or in excess of an established tolerance is required to be coloured or discoloured to avoid being considered adulterated. Although the policy applies only to certain grain seeds, it is widespread practice for other treated seed to be so coloured to indicate the presence of a pesticide.

2.3 The *Federal Seed Act*

The *Federal Seed Act* (FSA) and its regulations establish labelling requirements for seeds treated with toxic pesticides, both domestic and imported. Treated seeds must be labelled or tagged, or information concerning the treatment of bulk seed must be provided in invoices. In general, the following information is required: (1) a statement that seeds have been treated; (2) the common name of the treating pesticide; (3) a warning not to use for food, feed or oil purposes; and (4) if toxic, a skull and crossbones and the word POISON. The regulations outline exceptions and other provisions and should be consulted for complete information.

3.0 Current legal framework in Canada

3.1 *Pest Control Products Act*

In Canada, the PMRA administers the *Pest Control Products Act* (PCPA) which regulates all pest control products and requires those products subject to registration to be assessed as to their safety, merit and value.

The PCPA exempts from registration seeds (including seed-like fruits, bulbs, corms and rootstock) that have been treated with pest control products under certain conditions specified in Schedule II of the regulations, as follows:

(a) the product used to treat seed is registered in Canada for that specific purpose; and

(b) the seed is sold and shipped in bulk and shipping documents bear information setting forth the common name or chemical name of the active ingredient of the control product used to treat the seed; and

(c) where the seed is packaged, the package bears a label with the words “This seed is treated with” followed by the name of the control product including the common name or chemical name of its active ingredient together with the appropriate precautionary symbols and signal words selected from Schedule III and such other statements as are required by these regulations and applicable to the control product used to treat the seed.

In addition, Section 42 of the PCP Regulations requires that, "Where the physical properties of a control product are such that the presence of the control product may not be recognized when used and is likely to expose a person or domestic animal to a severe health risk, the control product shall be denatured by means of colour, odour, or such other means as the Minister may approve to provide a signal or warning as to its presence."

The PMRA has published Regulatory Directive DIR94-06 which gives specific instruction on expected colour standards and the labelling of treated seed.

3.2 *Food and Drugs Act*

In Canada, the *Food and Drugs Act* (FDA) prohibits the sale and distribution of contaminated and adulterated food. Regulations indicate when an adulterant is 'unacceptable', e.g., in the case of agricultural chemicals, whenever the residue exceeds the prescribed maximum residue limit (MRL). In the absence of a specific MRL for a pesticide, a maximum limit of 0.1 part per million is used, as per subsection B15.002(1) of the *Food and Drugs Act* and Regulations. The use of this provision of the FDA is currently under discussion in Canada.

In the case of pesticide-treated seed, the seed is not considered a food (due to colouration, labelling and packaging which prevent its diversion to food); therefore, MRLs are not set for treated seeds. However, crops grown from treated seeds may potentially have a residue, and so there remains a need to evaluate potential residues as part of any risk assessment.

3.3 *Seeds Act*

The *Seeds Act* (SA) regulates all seeds, including those treated with pest control products. The SA defines seed as any plant part of any species belonging to the plant kingdom, represented, sold or used to grow a plant.

Section 20 of the SA regulations requires that any seed treated with a pest control product "shall be thoroughly stained with a conspicuous colour to show that the seed has been so treated," unless the seed has been coated with any material that itself renders the seed conspicuous. Where seed has been treated with a pest control product, the precautionary symbol and signal word prescribed by the regulations made under the PCPA to indicate the degree and nature of risk inherent in that product, together with the following statement marked on the package of the seed or on a conspicuous label attached to the package, are required:

"Do not use for food or feed. This seed has been treated with… (common or chemical name of pest control product)."

4.0 Comparison of U.S. and Canadian legal framework

Both Canada and the U.S. require registration of seed treatment products used for domestic seed treatment. Both countries allow exemptions for imported pesticide-treated seeds providing the seed is treated with a pesticide registered in the host country for that specific purpose and where certain other conditions are met (e.g., compliance with colouration and labelling requirements). As summarized in the attached Appendix I which compares the legal framework in the U.S. and Canada, both countries have essentially similar legislation, regulatory frameworks, labelling, colouration and packaging requirements to mitigate risk associated with handling of the treated seed and to prevent its diversion to use as a food or feed.

5.0 Comparison of U.S. and Canadian data requirements

The general data requirements for a new seed treatment formulated with an unregistered active ingredient are provided in the attached Appendix II. This table is a side-by-side comparison of requirements of the EPA Terrestrial Food Crop Use Group and the PMRA Use Site Category (USC) # 10, *Seed Treatments, Food and Feed*. It should be noted that, although the EPA categorizes seed treatments as a Terrestrial Food Crop, for the purposes of this table, the EPA has, where possible, evaluated those requirements as they apply to seed treatments only. The table demonstrates that U.S. and Canadian data requirements are essentially harmonized, although there remain some differences (see below). Many of the remaining differences are non data components. For example, the PMRA has included separate data code (DACO) numbers for data summaries, applicant addresses and other studies, data or reports which applicants may include as part of a scientific rationale or waiver request. Although the EPA has not published a requirement for these items, they are recognized as important and are provided by applicants. Remaining differences are not significant barriers to registration.

Requirements for both the EPA and the PMRA of each of the major data categories are discussed below and any significant difference between the two agencies rationalized. The EPA and the PMRA are continuing to work to resolve outstanding differences. Where a foliar food use is also proposed or already registered for a particular active ingredient, the specific data requirements for a new seed treatment product are also briefly discussed.

5.1 Product chemistry

The PMRA and the EPA product chemistry requirements are essentially identical. With the exception of storage stability data, the properties listed as "R" (requirement) for the PMRA and "CR" (conditional requirement) for the EPA under 2.14 (technical grade of active ingredient [TGAI]) and 3.5 (end-use product [EP]) in Appendix II (e.g., properties such as pH, viscosity, flammability, corrosion characteristics) are equivalent. The PMRA requires that each DACO number for these properties be addressed either by the provision of data or a waiver request rationale. The basis for waiver requests (as per notes in the Regulatory Directives DIR98-03, *Chemistry Requirements for the Registration of a Manufacturing Concentrate or an End-Use Product Formulated from Registered Technical Grade of Active Ingredients or Integrated System Products*, and DIR98-04, *Chemistry Requirements for the Registration of a Technical Grade of Active Ingredient or an Integrated System Product*) **are consistent** with the EPA's proprietary conditions (as per 40 CFR 158.190 notes).

5.2 Toxicology

Toxicology data requirements are essentially the same in Canada and the United States. Whereas microbial and mammalian point mutation studies are both required in the United States, Canada requires only one of these studies along with in vitro and in vivo chromosomal aberration genotoxicity studies. The U.S. requires a short-term neurotoxicity study while Canada only conditionally requires this study if there is potential for neurotoxicity. The PMRA would currently accept a seed-treatment product for review that meets EPA toxicology requirements.

5.3 Exposure (occupational and bystander)

Canada requires occupational exposure data. Options include passive dosimetry data, biological monitoring data or acceptable data from the Pesticide Handlers' Exposure Database (PHED). These data are only conditionally required by the EPA.

5.4 Food and feed residue studies

In the U.S., registration of a product as a seed treatment requires a tolerance unless it can be shown using a radio-labelled study that there is no residue uptake (<5 parts per billion) in the plant grown from the treated seed. Consequently, Appendix II indicates a number of residue chemistry data requirements associated with the need to establish a tolerance, including multiresidue analytical methods, supervised residue trials, temporal residue data and analytical residue reference standards. If the required radio-labelled study indicated no uptake, no tolerance would be required and these data would not be required. Such data are only conditionally required in Canada.

In Canada, if the results of three metabolism studies on dissimilar crops indicate a similar metabolic route in the three crops, then additional metabolism studies will not be required. When radio-labelled data for a crop grown from treated seed show no uptake of residues to the aerial portion and root portion of the crop (both human and livestock consumption), i.e., total radioactive residues (TRRs) in all plant tissues are less than 5 ppb, no further studies are required. However, the analytical methodology is always required (as per Appendix II). An MRL would then be established based on the analytical method's limit of quantitation (LOQ), provided that it is sufficiently low from an analytical chemistry standpoint and for risk assessment purposes. If TRRs are greater than 5 ppb, normal data requirements would apply. However, uses resulting in no quantifiable residues can be eligible for a reduction in the number of field trial data requirements if certain conditions are met (DIR98-02; Section 9.8)."

5.5 Environmental fate and ecological effects

The environmental data requirements are similar for both countries. Subsequent to the publishing of this document as a Regulatory Proposal, the PMRA now only requires terrestrial field dissipation studies for seed treatment on a case-by-case basis (i.e., conditionally) based on laboratory transformation, mobility, and toxicity data and the potential exposure. This is now harmonized with the U.S. EPA requirements. With respect to ecotoxicology, the EPA requires non-target plant data, while the PMRA does not for seed treatments.

5.6 Value data

Applicants in both the United States and Canada must generate similar efficacy trials to support the claims of their products, however only the PMRA requires such data to be submitted. In the context of a joint review, the EPA will use the results of the PMRA efficacy review.

5.7 Addition of a seed treatment use to an existing registration

The data requirements discussed above represent the full data package for a seed treatment formulated with a new, unregistered active ingredient. Registration of a product for use as a seed treatment is frequently requested subsequent to or in addition to other proposed food uses and may therefore only require a reduced subset of the data outlined above.

Many of the data requirements will have been satisfied where a seed treatment use is requested for a pesticide which is already registered as a foliar use on a particular crop. Addition of a seed treatment use to an existing foliar registration would require only data associated with registration of the specific end-use product intended for the seed treatment, typically product chemistry, acute toxicology, plant metabolism, analytical reference standards (U.S. only), efficacy (Canada only), environmental chemistry and fate. In both the U.S. and Canada, a tolerance for the foliar use will, in most cases, cover residues resulting from seed treatment; thus, additional data will not be needed to establish a tolerance. However, depending on the active ingredient and previously registered uses, data may be conditionally required in the U.S. and Canada for worker exposure, food residues, field dissipation and avian toxicity (see Appendix II).

In conclusion, data outlined in Appendix II which has already been submitted and reviewed to support a foliar application of a particular active ingredient or end-use product to a food crop may be cited in support of an application for use of the same product as a seed treatment on that same crop.

5.8 Seed treatment for export only market

In order to facilitate registration of seed treatment products for use on seed for export only, a reduced set of data requirements has been identified in Appendix II. In Canada, DACOs identified with the symbol NX would **not** be required if the end-use seed treatment product was for use on seed for export only.

6.0 Programs to facilitate registration of seed treatment products

The PMRA has several programs which may facilitate registration of active ingredients, seed treatment end-use products and seed treatment uses. The User Requested Minor Use Registration (URMUR) program encourages sponsor/user groups, in cooperation with registrants, to apply for the registration of products containing active ingredients which have been recently registered (i.e., within the last 5 years) in the United States or other OECD countries. The PMRA ensures that by making use of acceptable foreign reviews completed by other countries that the procedures for the technical review of URMUR applications are as efficient as possible.

The User Requested Minor Use Label Expansion (URMULE) program considers the registration of a new minor use of a pesticide for which the active ingredient(s) and the end-use product are currently registered in Canada (see DIR2001-01). Many seed treatment uses may be considered minor uses.

The PMRA and the U.S. EPA, in cooperation with Mexico's CICOPLAFEST, have established a process for the joint review of pest control products that contain conventional chemical pesticides, and for the joint review of pest control products in which the new active ingredient is a microbial or an arthropod semiochemical (including pheromones). Joint reviews, which offer applicants reduced timelines for review, increase the efficiency of the registration process, facilitate simultaneous registration in participating countries and increase access to new pest management tools in participating countries. Joint review is a process which both Agencies strongly encourage registrants to pursue. Pre-submission consultations are required in the joint review process to establish case-specific data requirements (including possible data waivers) and differences resolved or justified prior to a submission being made. Typically, minor differences in data requirements for seed treatment products are resolvable through a pre-submission consultation either in the context of an independent application to the PMRA or in a joint review submission.

Reduced-risk pesticides

In May 2002, the PMRA introduced an initiative whereby the North American Free Trade Agreement (NAFTA) Joint Review Programs for Reduced-Risk Pesticides will be extended by the PMRA to include submissions made to the PMRA only. The program is designed to encourage pesticide manufacturers to apply for Canadian registration of reduced-risk products that are currently available in the United States (U.S.); Canada will use the same criteria as the U.S. EPA to determine eligibility of chemicals for the reduced-risk program and recognize the U.S. EPA's biopesticide designation, thus further harmonizing the respective approaches of the two countries. Through this program, the PMRA will also commit to shorter review timelines for products that have been shown to qualify as reduced-risk chemicals or biopesticides. Refer to Regulatory Directive DIR2002-02 *The PMRA Initiative for Reduced-Risk Pesticides* for more details and guidance on preparation of submissions to the PMRA.

7.0 Conclusions

The legal framework for the registration of seed treatment products in Canada and the U.S. are essentially harmonized. Although data requirements are not identical, they are essentially harmonized in most areas, and the EPA and the PMRA continue to work to resolve differences.

Trade irritants are most frequently the result of dissimilar registrations in the two countries. Commodity grower groups and users are encouraged to work with pesticide registrants to ensure that full use is made of existing joint review and work sharing mechanisms between the two agencies, as well as other regulatory streams which can facilitate registration (e.g., minor use programs).

List of abbreviations

a.i.	active ingredient
CR	conditionally required
DACO	data code
EP	end-use product
EPA	Environmental Protection Agency (U.S.)
FDA	*Food and Drugs Act*
FFDCA	*Federal Food, Drug and Cosmetic Act* (U.S.)
FIFRA	*Federal Insecticide, Fungicide and Rodenticide Act* (U.S.)
FSA	*Federal Seed Act* (U.S.)
ISP	integrated system product
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LOQ	limit of quantitation
NAFTA	North American Free Trade Agreement
NAI	North American Initiative
NX	not required
OECD	Organisation for Economic Cooperation and Development
OPP	Office of Pesticide Programs (U.S.)
PCPA	*Pest Control Products Act*
PHED	Pesticide Handlers' Exposure Database
PMRA	Pest Management Regulatory Agency
R	required
ROC	residue of concern
SA	*Seeds Act*
TGAI	technical grade of active ingredient
TRR	total radioactve residue
TWG	Technical Working Group
URMULE	User Requested Minor Use Label Expansion
URMUR	User Requested Minor Use Registration
U.S.	United States
USC	Use Site Category

Appendix I Comparison of U.S. and Canadian legal framework

United States	Canada
***Federal Insecticide, Fungicide and Rodenticide Act* (FIFRA)**	***Pest Control Products Act* (PCPA)**
Pesticide-treated seeds are considered to be pesticides themselves because they are mixtures of substances used to prevent, destroy, repel or mitigate a pest. Regulation 40 CFR 152.25(*a*) exempts certain treated articles (including treated seeds) from regulation under FIFRA provided the following conditions are met: (*a*) the pesticide used for the treatment is registered for such use. (*b*) the treatment is for the protection of the article or substance itself. Treated seeds that are to be sold or distributed in the U.S. must be coloured to prevent diversion for animal feed or other non-planting uses. Regulation 40 CFR 153.155 requires that a pesticide registered for treating seeds must contain a suitable dye **unless** the treatment is applied in the hopper box at planting or **unless** the pesticide label requires the user treating the seed to separately add a dye to the seed treatment process.	The PCPA requires that all pest control products be assessed as to safety, merit and value. Seeds (including seed-like fruits, bulbs, corms, and rootstock) treated with a pest control product be registered unless exempted from registration under conditions specified in Schedule II of the Regulations: (*a*) the product used to treat seed is registered in Canada for that specific purpose **and** (*b*) where the seed is sold and shipped in bulk that shipping documents bear information setting forth the common name or chemical name of the active ingredient of the control product used to treat the seed **and** *(c)* where the seed is packaged, the package bears a label with the words “This seed is treated with” followed by the name of the control product including the common name or chemical name of its active ingredient and the appropriate precautionary symbols and signal words. Section 42 of the Regulations requires that “Where the presence of the control product may not be recognized when used; the control product shall be denatured by means of colour, odour, or such other means.” The PMRA has also published Regulatory Directive DIR94-06 which gives specific instruction regarding the colouration and labelling of treted seed.

United States	Canada
***Federal Food, Drug and Cosmetic Act* (FFDCA)**	***Food and Drugs Act* (FDA)**
Under Sec. 408 of the FFDCA: The risks posed by pesticide residues in food and feed is assessed under a standard, "reasonable certainty of no harm." Before registration, a food crop must have a pesticide tolerance (or exemption). Treated seed for planting of food crops must have a tolerance unless it can be shown that residues are not carried forward to the crop grown from seed. Generally, tolerances established as a result of assessment of a foliar use are adequate to cover seed treatment use. Grain seed treated with pesticides for which there are no tolerances set or in excess of an established tolerance must be coloured or discoloured to avoid being considered adulterated. (Although the policy applies only to certain grain seeds, it is widespread practice for other treated seed to be so coloured to indicate the presence of a pesticide.)	Prohibits the sale and distribution of contaminated and adulterated food and requires that MRLs be established for agricultural chemicals. MRLs are not set for pesticide-treated seed, as the seed is not considered to be a food due to colouration, labelling and packaging which prevent its diversion to food. Crops grown from treated seeds may contain residues so there remains a need to evaluate potential residues as part of any risk assessment.
***Federal Seed Act* (FSA)**	***Seeds Act* (SA)**
Treated seeds must be labelled or tagged, or for bulk seed, invoices must provide information concerning the pesticide treatment. Required information includes: (1) a statement that seeds have been treated; (2) the common name of the treating pesticide; (3) a warning not to use for food, feed or oil purposes; (4) if toxic, a skull and crossbones and word POISON.	Section 20 of the SA regulations requires that any seed treated with a pest control product "shall be thoroughly stained with a conspicuous colour to show that the seed has been so treated," unless the seed has been coated with any material that itself renders the seed conspicuous. The precautionary symbol and signal word prescribed by the PCPA regulations together with the following statement marked on the package of the seed or on a conspicuous label attached to the package, is required: "Do not use for food or feed. This seed has been treated with… (common or chemical name of pest control product)."

Appendix II Seed treatment data requirements for Canada (Seed Treatments, Food and Feed, PMRA USC # 10) and the U.S. (EPA Terrestrial Food Crop Use Group)

Seed Treatment Data Requirements				
Canada PMRA Data Code[1]		**Title**	**PMRA USC # 10**	**EPA Terrestrial Food Crop**
0		**Index**	**R***	**R***
1		**Label**	**R***	**R***
2		**Chemistry requirements for the registration of a TGAI or an integrated system product (ISP)**		
2.1		Applicant's Name and Office Address	R*	R*
2.2		Manufacturer's Name and Office Address and Manufacturing Plant's Name and Address	R*	R*
2.3		Product Trade Name	R	R
2.3.1		Other Names	R	R
2.4		Common Name	R	R
2.5		Chemical Name	R	R
2.6		Chemical Abstracts Service Registry Number	R	R
2.7		Structural Formula	R	R
2.8		Molecular Formula	R	R
2.9		Molecular Weight	R	R
2.11		**Manufacturing Methods for the TGAI**		
2.11.1		Manufacturing Summary	R	R
2.11.2		Description of Starting Materials	R	R
2.11.3		Detailed Production Process Description	R	R
2.11.4		Discussion of Formation of Impurities	R	R
2.12		**Specifications**		
2.12.1		Establishing Certified Limits	R	R
2.12.2		Statement of Product Specification Form	R	R
2.13		**Preliminary Analysis**		
2.13.1		Methodology/Validation	R**	CR
2.13.2		Confirmation of Identity	R**	CR
2.13.3		Batch Data	R	R
2.13.4		Impurities of Toxicological Concern	CR	CR
2.14		**Chemical and Physical Properties**		
2.14.1		Colour	R	R
2.14.2		Physical State	R	R
2.14.3		Odour	R	R
2.14.4		Melting Point/Melting Range	R**	CR
2.14.5		Boiling Point/Boiling Range	R**	CR
2.14.6		Density or Specific Gravity	R	R
2.14.7		Water Solubility (mg/L)	R	R
2.14.8		Solvent Solubility (mg/L)	R	R
2.14.9		Vapour Pressure	R	R
2.14.10		Dissociation Constant	R	R
2.14.11		Octanol/Water Partition Coefficient	R	R
2.14.12		UV/Visible Absorption Spectra	R	R
2.14.13		Stability (Temperature, Metals)	R	R

Seed Treatment Data Requirements				
Canada PMRA Data Code[1]		**Title**	**PMRA USC # 10**	**EPA Terrestrial Food Crop**
2.14.14		Storage Stability Data	CR	CR
2.15		Sample(s) of Analytical Standards and ROC	R	CR addressed by 860.165
2.16		Other Studies/Data/Reports	CR***	CR
3		**Chemistry Requirements for the Registration of Manufacturing Concentrates and EPs Formulated from Registered TGAIs or ISPs**		
3.1		**Product Identification**		
3.1.1		Applicant's Name and Office Address	R*	R*
3.1.2		Formulating Plant's Name and Address	R*	R*
3.1.3		Trade Name	R	R
3.1.4		Other Names	R	R
3.2		**Formulation Process**		
3.2.1		Description of Starting Materials	R	R
3.2.2		Description of the Formulation Process	R	R
3.2.3		Discussion of the Formation of Impurities of Toxicological Concern	CR	R
3.3		**Specifications**		
3.3.1		Establishing Certified Limits	R	R
3.3.2		Statement of Product Specification Form	R	R
3.4		**Product Analysis**		
3.4.1		Enforcement Analytical Method	R	R
3.4.2		Impurities of Toxicological Concern	CR	R
3.5		**Chemical and Physical Properties**		
3.5.1		Colour	R	R
3.5.2		Physical State	R	R
3.5.3		Odour	R	R
3.5.4		Formulation Type	R*	R*
3.5.5		Container Material and Description	R*	R*
3.5.6		Density or Specific Gravity	R	R
3.5.7		pH	R	CR
3.5.8		Oxidizing or Reducing Action (Chemical Incompatibility)	R	CR
3.5.9		Viscosity	R	CR
3.5.10		Storage Stability Data	R	CR
3.5.11		Flammability	R	CR
3.5.12		Explodability	R	CR
3.5.13		Miscibility	R	CR
3.5.14		Corrosion Characteristics	R	R
3.5.15		Dielectric Breakdown Voltage	R	CR
3.6		Sample(s)	CR	CR
3.7		Other Studies/Data/Reports	CR***	CR
4		**Toxicology**		
4.1		Summaries—Toxicology Profile	R***	
4.2		**Acute Studies—TGAI**		
4.2.1		Acute Oral	R	R
4.2.2		Acute Dermal	R	R
4.2.3		Acute Inhalation	R	R
4.2.4		Primary Eye Irritation	R	R

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4.2.5		Primary Dermal Irritation	R	R
4.2.6		Dermal Sensitization	R	R
		Acute Neurotoxicity—rat	CR	R
4.3		**Short-Term Studies—TGAI**		
4.3.1		Short-Term Oral (90-day) (rodent)	R	R
4.3.2		Short-Term Oral (Non-rodent, e.g. dog)	R	R
4.3.6		Short-Term Inhalation (90-day)	CR	CR
		21-Day Dermal (rodent)	R	R
		90-Day Dermal	CR	CR
		28-Day delayed neurotoxicity—hen	CR	CR
4.4		**Long-Term Studies TGAI**		
4.4.1		Chronic (rodent)	R (4.4.1 and 4.4.2 can be combined as 4.4.4)	R
4.4.1		Chronic (non-rodent)	R	R
4.4.2		Oncogenicity (rodent species 1 e.g. mouse)	R (see 4.4.1)	R
4.4.3		Oncogenicity (rodent species 2 e.g. rat)	R	—
4.4.4		Combined Chronic/Oncogenicity (rodent)	CR (see 4.4.1)	R
4.5		**Special Studies TGAI**		
4.5.1		Multigeneration—Reproduction (rodent)	R	R
4.5.2		Teratogenicity (rodent)	R	R
4.5.3		Teratogenicity (non-rodent)	R	R
4.5.4		Genotoxicity: Microbial Point Mutation	CR	R
4.5.5		Genotoxicity: Mammalian (cell) Point Mutation	CR	R
4.5.6		Genotoxicity: In vitro Chromosomal Aberrations	R	—
4.5.7		Genotoxicity: In vivo Chromosomal Aberrations	R	R
4.5.8		Other Genotoxicity Studies	CR	—
4.5.9		Metabolism/Toxicokinetics in Mammals (laboratory animal)	R	R
4.5.10		Acute Delayed Neurotoxicity	CR	CR
4.5.11		Short-Term Neurotoxicity	CR	R
		Domestic Animal Safety	—	CR
		Dermal Penetration	—	CR
4.6		**Acute Studies—EP**		
4.6.1		Acute Oral	R	R
4.6.2		Acute Dermal	R	R
4.6.3		Acute Inhalation	R	R
4.6.4		Primary Eye Irritation	R	R
4.6.5		Primary Dermal Irritation	R	R
4.6.6		Dermal Sensitization	R	R
4.7		**Short-Term Studies—EP**		
4.7.1		Short-Term Oral (90-day)	CR	—
4.7.3		Short-Term Dermal (90-day)	CR	—
4.7.4		Short-Term Dermal (20-day, 30-day)	CR	—
4.7.5		Short-Term Inhalation (90-day)	CR	—
4.7.6		Short-Term Inhalation (21-day, 30-day)	CR	—

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4.8		Other Studies/Data/Reports	CR***	—
		Domestic Animal Safety	—	CR
		Dermal Penetration	—	CR
5		**Exposure (Occupational and/or Bystander) (EP)**		
5.1		Summaries	R***	—
5.2		Use Description/Scenario (Application and Post-Application)	R	CR
5.3		Pesticides Handlers' Exposure Database Assessment (or other database)	CR (one of 5.3, 5.4, or 5.5 is required	—
5.4		Mixer/Loader/Applicator—Passive Dosimetry Data	CR (see 5.3)	CR
5.5		Mixer/Loader/Applicator—Biological Monitoring Data	CR (see 5.3)	CR
5.6		Post-Application—Passive Dosimetry Data (Includes dermal and inhalation exposure)	CR (one of 5.6. or 5.7 required)	CR
5.7		Post-Application—Biological Monitoring Data	CR (see 5.6)	CR
5.8		Dermal Absorption	CR	CR
5.9		Dislodgeable Residues (Foliar, Soil and Surface)	—	CR
5.11		Glove/Clothing Penetration Data	CR	—
5.13		Package Integrity Study	CR	—
5.14		Other Studies/Data/Reports	CR	CR
6		**Metabolism/Toxicokinetics Studies (TGAI or EP)**		
6.1	NX	Summaries	R***	
6.2	NX	Livestock	CR	CR
6.3	NX	Plants	R	R
6.4	NX	Other Studies/Data/Reports	CR***	CR
7	**NX**	**Food, Feed and Tobacco Residue Studies EP**		
7.1	NX	Summaries	R***	—
7.2	**NX**	**Analytical Methodology (Food Crops and Tobacco)**		
7.2.1	NX	Supervised Residue Trial Analytical Methodology	R	R
7.2.4	NX	Analytical Methodology (Multi-Residue Analytical Methodology)	R	R
7.3	NX	Freezer Storage Stability Tests	CR	CR
7.4	**NX**	**Crop Residue Data**		
7.4.1	NX	Supervised Residue Trial Study	CR	R
7.4.2	NX	Temporal Residue Study	CR	R
7.4.3	NX	Confined Crop Rotation Trial Study	CR	CR
7.4.4	NX	Field Rotation Crop Data	CR	CR
7.4.5	NX	Processed Food/Feed	CR	CR
7.4.6	NX	Residue Data for Crops Used as Livestock Feed	CR	CR
7.5	NX	Livestock, Poultry, Egg and Milk Residue Data (from feeding of treated crops)	CR	CR

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7.8	NX	Other Studies/Data/Reports	CR***	CR
		EPA ONLY		
		Analytical Reference Standards	addressed by DACO 2.15	R
8		**Environmental Chemistry and Fate**		
8.1	NX	Summaries	R***	—
8.2		**Laboratory Studies of Physicochemical Properties**		
8.2.1		Summary to Include: Solubility in Water, Vapour Pressure, Octanol/Water Partition Coefficient, Dissociation Constant, UV/Visible Absorption, Density or Specific Gravity (See parts 2 and 3)	R	R
8.2.2		**Analytical Methodology (parent compound and transformation products)**		
8.2.2.1		Soil	R	R
8.2.2.4		Biota	R	CR
8.2.3		**Laboratory Studies of Transformation (TGAI)**		
8.2.3.1	NX	Summary	R***	—
8.2.3.2		Hydrolysis	R	R
8.2.3.3		**Phototransformation**		
8.2.3.3.2	NX	Water	R	R
8.2.3.3.3	NX	Air	CR	—
8.2.3.4	**NX**	**Biotransformation in Soil (TGAI)**		
8.2.3.4.2		Aerobic Soil 20–30°C	R	R
8.2.3.4.4	NX	Anaerobic Soil 20–30°C	R	R
8.2.3.6	NX	Special Studies Related to Use-Pattern or Formulation	CR***	—
8.2.3.5		**Biotransformation in Aquatic Systems (TGAI)**		
8.2.3.5.2	NX	Aerobic Water 20–30°C	CR	CR
8.2.4		**Laboratory Studies of Mobility (TGAI)**		
8.2.4.1	NX	Summary	R***	—
8.2.4.2		Adsorption/Desorption	R	R
8.2.4.5	NX	Volatilization	CR	CR
8.2.4.6	NX	Special Studies Related to Use-Pattern or Formulation (EP) e.g., special seed leaching study	CR	CR
8.3		**Field Studies of Dissipation/Accumulation (May be Small or Large-Scale) (EP)**		
8.3.1	NX	Summary	R***	—
8.3.2	NX	Terrestrial	CR***	CR
8.3.4	NX	Special Studies Related to Intended Use Pattern	CR***	—
8.4		**Storage, Disposal and Decontamination (TGAI and EP)**		
8.4.1		Summary	R***	—
8.5	**NX**	**Other Environmental Fate Studies (TGAI and EP)**		
8.5.1	NX	Summary	CR***	—
8.6	NX	Other Studies/Data/Reports	CR***	CR

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9		**Environmental Toxicology**		
9.1	NX	Summary	R***	—
9.6	**NX**	**Wild Birds**		
9.6.1	NX	Summary[1]	R***	—
9.6.2	**NX**	**Acute Studies**		
9.6.2.1	NX	Oral (LD_{50}) Bobwhite Quail	R	R
9.6.2.2	NX	Oral (LD_{50}) Mallard Duck	CR	—
9.6.2.3	NX	Oral (LD_{50}) Other Species	CR	—
9.6.2.4	NX	Dietary (LC_{50}) Bobwhite Quail	R	R
9.6.2.5	NX	Dietary (LC_{50}) Mallard Duck	R	R
9.6.2.6	NX	Dietary (LC_{50}) Other Species	CR	—
9.6.3	**NX**	**Chronic Studies**		
9.6.3.1	NX	Avian Reproduction Bobwhite Quail	R	R
9.6.3.2	NX	Avian Reproduction Mallard Duck	R	R
9.6.3.3	NX	Avian Reproduction Other Species	CR	—
9.6.4	NX	Laboratory Studies with End-Use Product (EP)	CR	CR
9.6.5	NX	Field Studies (EP)	CR	CR
9.6.6	NX	Special Studies Related to the Intended Use-Pattern	CR***	—
9.7	**NX**	**Wild Mammals (TGAI)**		
9.7.1	NX	Summary	CR***	—
9.7.2	NX	Field Studies (EP)	CR	—
9.9	NX	Other Studies/Data/Reports	CR	—
9.5.2	**NX**	**Non-Target Freshwater Organisms**		
9.5.2.1	NX	Coldwater Fish (rainbow trout)	R	R
9.5.2.2	NX	Warmwater Fish (bluegill sunfish)	R	R
9.3.2	NX	*Daphnia* sp. Acute	R	R
9.3.3	NX	*Daphnia* sp. Chronic (Life-Cycle)	CR	CR
		Fish early Life Stage	CR	CR
9.4	**NX**	**Non-Target Estuarine/Marine Organisms (TGAI)**		
9.4.2	NX	Acute (Crustacean)	CR	CR
9.4.5	NX	Chronic (mollusk or crustacean)	CR	CR
9.5.2.4	NX	Acute Estuarine Fish	CR	CR
9.5.3.2	NX	Chronic Fish Life Cycle	CR	CR
9.8	NX	Non-Target Plant Studies (10 terrestrial species)	—	R (Tier I)
10		**Value (applicable to each pest/site or host combination)**		
10.1	NX	Value Summaries	R***	—
10.2	**NX**	**Efficacy Studies**		
10.2.1	NX	Mode of Action	R	—
10.2.2	NX	Description of Pest Problem	R	—
10.2.3	**NX**	**Efficacy Trials**		
10.2.3.1	NX	Summaries	R***	—

[1] Summary should include number of seeds/unit weight of seeds, weight of a.i./unit weight of seeds and number of seeds applied/unit area"

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10.2.3.2	NX	Efficacy: Laboratory, Growth Chamber Trials —may be required to support 10.2.3.3	CR	—
10.2.3.3	NX	Efficacy: Small-scale Trials (Field, Greenhouse)	R	—
10.2.3.4	NX	Efficacy: Operational Trials —may be required in lieu of/in addition to 10.2.2.3	CR	—
10.3	**NX**	**Adverse Effects on Use Site**		
10.3.1	NX	Summaries	CR***	—
10.3.2	NX	Non-Safety Adverse Effects (e.g., to crop, host animal, site of application [discolouration, corrosion], etc.)	CR	—
10.3.3	NX	Damage to Rotational Crops	CR	—
10.4	NX	Economics	CR	—
10.5	**NX**	**Sustainability**		
10.5.1	NX	Survey of Alternatives (chemical and non-chemical)	CR	—
10.5.2	NX	Compatibility with Current Management Practices Including IPM	CR	—
10.5.3	NX	Resistance Management	CR	—
10.5.4	NX	Contribution to Risk Reduction	CR	—
10.6	NX	Other Studies/Data/Reports	CR***	—
12.5		**Foreign Reviews**		
12.5.2	NX	Foreign Reviews of Chemistry Requirements for TGAIs or Integrated System Products	CR***	—
12.5.3	NX	Foreign Reviews of Chemistry Requirements for MAs and EPs formulated from registered TGAIs or ISPs	CR***	—
12.5.4	NX	Foreign Reviews of Toxicology	CR***	—
12.5.5	NX	Foreign Reviews of Exposure (Occupational and/or Bystander)	CR***	—
12.5.6	NX	Foreign Reviews of Metabolism/Toxicokinetics Studies	CR***	—
12.5.7	NX	Foreign Reviews of Food, Feed and Tobacco Residue Studies	CR***	—
12.5.8	NX	Foreign Reviews of Environmental Chemistry and Fate	CR***	—
12.5.9	NX	Foreign Reviews of Environmental Toxicology	CR***	—
12.5.10	NX	Foreign Reviews of Value	CR***	—
12.7	**NX**	**Comprehensive Data Summaries**	R***	—

[1] DACOS marked with NX are not required for seed treatment products used on seed for export only.

* For information tracking and data organization, the PMRA's DACO system provides DACO numbers for the identification of product, manufacturing site and applicant. Similar information is also required by the EPA although not assigned a guideline reference number.

** The PMRA requires that DACO items listed as "R" (requirement) or "CR" (conditional requirement) are addressed either by the provision of data or a waiver request rationale.

*** For information tracking and data organization, the PMRA's DACO system provides DACO numbers for summaries of submitted data, other studies, and foreign reviews which are submitted to support waiver requests or in lieu of Canadian data.