Guidance for Developing Datasets for Conventional Pest Control Product Applications:

Data Codes for Parts 1, 2, 3, 4, 5, 6, 7 & 10 (updated guidance for DACO Parts 8 & 9 will be communicated when available)

20 August 2018

Canada

Purpose

This document is an update to the Health Canada Pest Management Regulatory Agency's (PMRA) Guidance for Developing a Database for Conventional Pest Control Products, which was first made available to registrants and applicants of pesticides and other pest control products in July 2013, and subsequently in September 2015. An applicant applying to register a pesticide in Canada can use this information to better understand the data required for completing their application. This guidance must be used along with the Data Code (DACO) Tables and use-site category information available on the Pesticides section of Canada.ca. The DACO tables outline the required data elements for a specific use-site category and this guidance document will clarify the conditions for each required data element. Note that this document contains guidance and conditions for DACO Parts 1 through 10, excluding Parts 8 and 9, which are being developed separately (refer to PRO2016-01-Regulatory Proposal: Revised Environemtal Data Requirements).

Document History

Update:	Update/Rationale:
July 2018: Acute Dermal Toxicity DACO 4.2.2 and DACO 4.6.2	To reflect the results of the retrospective analyses outlined in SPN2017-03.
July 2018: Acute Studies: DACO 4.2 and DACO 4.6	To reflect expanded set of considerations for data waivers outlined in OECD guidance document.
March 2016: Short-Term Oral Toxicity: DACO 4.3.2	To reflect changes to the requirement for a 1-year dog toxicity study.
September 2015: Part 2.3 Chemistry, Part 10 Value	Amendments to guidance for certain Chemistry and Value data requirements.

List of Acronyms:

a.i.	Active Ingredient
CAS	Chemical Abstracts Service
cm^2	centimeters squared
DACO	Data Code
DER	Date Evaluation Record
F_1	First generation
Ha	hectare
ISP	Integrated System Product
kg	Kilogram
L	Litre
LOD	Limit of Detection
LOQ	Limit of Quantitation
MA	Manufacturing Concentrates
Mg	Milligram
M/L/A	Mixer/Loader/Applicator
MRL	Maximum Residue Limit
N	Nominal Concentration of Ingredient
NAFTA	North American Free Trade Agreement
OECD	Organisation for Economic Co-operation and Development
PAI	Pure Active Ingredient
ppm	parts per million
PMRA	Pest Management Regulatory Agency
SPSF	Statement of Product Specifications Form
µg	Microgram
USEPA	United States Environmental Protection Agency
UV	Ultraviolet

Label DACO Part 1 (Technical Grade Active Ingredient and End-Use Product)

Data Code	Title	Conditions/Guidance
1	Label	Use directions should be clear and well-organized. Information pertaining to the pest, crop, application rate, application interval, and application timing should be included. Other instructions and use restrictions, where appropriate should also be included.

Chemistry Data Requirements: DACO Part 2 (Technical Grade Active Ingredient)

Data Code	Title	Conditions/Guidance (Updated from DIR98-04)
2	**Chemistry requirements for the registration of a technical grade of active ingredient or an integrated system product (ISP)**	
2.1	Applicant's Name and Office Address	The *applicant* identifies the company that has the ultimate responsibility for certifying the information found on the PMRA Statement of Product Specification Form (SPSF), as distinct from the *manufacturing plant*, which is addressed under DACO 2.2 below.
2.2	Manufacturer's Name and Office Address and Manufacturing Plant's Name and Address	The actual *manufacturer* would typically form part of the same company identified under DACO 2.1, but it could also reflect the use of a toll manufacturer. The *manufacturing plant* identifies the specific location at which the material is produced.
2.3	Product Trade Name	
2.3.1	Other Names	Include any company development code as well as any equivalent foreign name to which data found in the submission may refer.
2.4	Common Name	Include the International Organization for Standardization common name of each active ingredient or, if not yet established, the proposed name.
2.5	Chemical Name	Both the International Union of Pure and Applied Chemistry and Chemical Abstracts Service names of each active ingredient are to be provided. If applicable, each stereoisomer listed as an active ingredient must be individually identified and have a corresponding structure depicted under DACO 2.7 showing the stereochemical designation(s).
2.6	Chemical Abstracts Registry Number	Identify for each active ingredient or each isomer and/or group of isomers, if established.
2.7	Structural Formula	Provide for each active ingredient including, if applicable, each stereoisomer identified as an active ingredient.

Data Code	Title	Conditions/Guidance (Updated from DIR98-04)
2.8	Molecular Formula	
2.9	Molecular Weight	
2.11	**Manufacturing Methods for the Technical Grade Active Ingredient**	Information may be based upon pilot plant production or initial commercial production but must be updated to reflect current commercial production whenever applicable (see corresponding batch data requirement under DACO 2.13.3).
2.11.1	Manufacturing Summary	Provide a brief overview of the manufacturing process outlining the major steps and reactants, summarizing the more comprehensive description required under DACO 2.11.3. This is to include a general characterization of the process, for example, batch or continuous, and the typical quantity of product produced per batch (or per unit time, if continuous).
2.11.2	Description of Starting Materials	The following information is to be provided for each starting material used to produce the active ingredient: (i) each brand name, trade name, common name, chemical name, Chemical Abstracts Service Registry number, or other commercial designation; (ii) the name and address of the companies that produce the starting materials or, if that information is not known to the applicant, the name and address of the companies that supply the starting materials; and (iii) all information concerning the composition of each starting material, including a copy of all specifications or other documents describing it. It should be emphasized that an applicant is not required to perform chemical analysis of starting materials to meet the above criteria, but only provide information to which the applicant has, or should have, access. The information required for formulants, if applicable to an ISP, is consistent with the three requirements identified above for starting materials. If multiple suppliers are used for starting materials/formulants, specifications for all suppliers should be provided. Changes in suppliers once a product is registered are subject to the requirements of Regulatory Directive DIR2013-02, *Notification/Non-Notification*, or subsequent revisions.
2.11.3	Detailed Production Process Description	An applicant must submit information on the manufacturing process used to produce the technical grade active ingredient or ISP at each stage of production resulting in a separately isolated substance, as follows: (i) a flow chart of the chemical reactions, including structures, at each step of the process and of the major unit operations, including separation steps; (ii) the identities of the reactants, solvents and catalysts used to produce the product, their quantities and the order in which they are added; (iii) a description of the equipment used that may influence the composition of the substance produced; (iv) a description of the conditions–for example, reaction time, temperature, pressure, pH, humidity–that are controlled during each step of the process to affect the composition of the substance produced, and the corresponding limits that are maintained; (v) a description of the purification steps, including those used to recover or recycle starting materials, intermediates or the substance produced; and

Data Code	Title	Conditions/Guidance (Updated from DIR98-04)
		(vi) a description of the procedures used to assure consistent composition of the substance produced, for example, calibration of equipment, sampling regimens and other quality control measures such as tests used to monitor reaction completion. Additional requirements are applicable to the manufacturing of stereoisomeric active ingredients. Three types of products may form during the manufacturing of such actives: (i) a racemic mixture; (ii) a single stereoisomer (enantiomer or diastereomer that, by definition, includes geometric [cis/trans or Z/E] isomers); or (iii) a stereoselectively enhanced isomeric mixture. For (ii) and (iii), a full description of the stereoselective manufacturing process is to be provided. Stereospecific identity and purity is to be identified for starting materials.
2.11.4	Discussion of Formation of Impurities	The applicant must provide a discussion of the impurities that may be found in the product and why they may be present. The discussion should be based on established chemical theory and on what the applicant knows about the starting materials and the production process. The thoroughness of the theoretical discussion can be evaluated in parallel with the preliminary analysis data under DACO 2.13, to assess whether potential impurities would be comprehensively identified by the methods used. If the applicant has reason to believe that an impurity the PMRA would consider to be toxicologically significant may be present, the discussion must include an expanded description of the possible formation of the impurity and the amounts in which it might be present. The following potential sources of impurity formation must be discussed, as applicable: (i) each impurity that was found to be present in any analysis of samples produced according to the process identified under DACO 2.11.3 conducted by or for the applicant; and (ii) each other impurity that the applicant has reason to believe *may be present* in a product at any time before use at a level $\geq$ 0.1% by weight, based upon what is known about: a) the composition (or composition range) of each starting material used to produce the product; b) the impurities that are known to be present (or believed likely to be present) in the starting materials, and the known or presumed level (or range of levels) of these impurities; c) the intended reactions and side reactions that may occur in the production of the product, and the relative amounts of byproduct impurities produced by such reactions; d) the possible degradation of the ingredients in the product after its production but prior to its use; e) the potential post-production reactions between the ingredients in the product; f) the possible migration of components of packaging materials into the pest control product; g) the potential carryover of contaminants from use of production equipment previously used to manufacture other products or substances; and h) the process control, purification and quality control measures used to produce the product that may preclude the presence of potential impurities. On a case-by-case basis, the PMRA may require an expanded discussion of potential impurity formation resulting from other potential chemical reactions, involving other ingredients, or at additional points in the production process.

Data Code	Title	Conditions/Guidance (Updated from DIR98-04)
2.12	Specifications	The nominal concentration and corresponding certified limits must be provided for each product component, as per *Guidance for Completing the Statement of Product Specification Form,* which is available on request. The nominal concentration is defined as the typical amount of an ingredient present in a pest control product at the time of its production. Both the active ingredient nominal concentration and a corresponding nominal equivalence statement, if applicable (for example, acid salts), are to be provided. The product guarantee, identified on the SPSF and appearing on the draft product label, is synonymous with the active ingredient(s) nominal concentration. This number most accurately identifies the amount of active ingredient found in the technical grade active ingredient or ISP and is subsequently used to establish corresponding enforceable certified limits, as further discussed under DACO 2.12.1. Precise identification of impurities present in products at or above 0.1% by weight in one or more of the analyzed batches is required while components of toxicological concern must be identified at any concentration. The appropriate level is dictated by the limit of quantitation (LOQ) of the toxic impurity analytical method, which is sample/chemical dependent, and must also be below any applicable regulatory limit. For all types of stereoisomer mixtures, specified limits are required for each active component as well as individual stereoisomeric impurities, as supported by preliminary batch analysis as described under DACO 2.13.3. Specification data are to be submitted on a SPSF that includes a signed and dated *Declaration of Applicant* certifying that the information is true and complete. For full instructions on the proper completion of the form the applicant should refer to *Guidance for Completing the Statement of Product Specification Form,* which is available on request. The SPSF is to be submitted under DACO 0.1.6003 in the e-index builder.
2.12.1	Establishing Certified Limits	Standard certified limits based upon nominal concentration are required for active ingredients and formulants, unless an applicant proposes, and justifies, alternate limits which are deemed acceptable by the PMRA. Standard limits are defined as follows: **Nominal Concentration (N) of Ingredient** **20.0% < N ≤ 100.0% (Upper Limit N+3% N; Lower Limit N–3% N)** **1.0% < N ≤ 20.0% (Upper Limit N+5% N; Lower Limit N–5% N)** **N ≤ 1.0% (Upper Limit N+10% N; Lower Limit N–10% N)** An applicant may propose a certified limit for an active ingredient or formulant that differs from the standard limits, but must include an explanation of the basis for the proposed limits, including how they were established, for example, sample analysis or a quantitative estimate based upon the production process. For impurities, the applicant must propose upper certified limits as standard certified limits may not be used for such components. As a guideline, three standard deviations plus the mean value from the five batch data should be used to set the upper certified limits for the impurities. Proposed limits should not greatly exceed those actually occurring in the product. All certified limits must: (i) be based on a consideration of the variability of the concentration of the ingredient in the product when good manufacturing

Data Code	Title	Conditions/Guidance (Updated from DIR98-04)
		practices and normal quality control procedures are used; (ii) allow for all sources of variability likely to be encountered in the production process; and (iii) take into account the stability of the ingredient in the product and the possible formation of impurities between production and sale or distribution. If the PMRA finds any certified limit unacceptable (either standard or applicant proposed), the PMRA will inform the applicant of its determination and will provide supporting reasons. The PMRA may also require, on a case-by-case basis, any or all of the following: (i) more precise limits; (ii) a more thorough explanation of how the certified limits were determined; or (iii) a narrower range between the upper and lower certified limits than that proposed.
2.13	**Preliminary Analysis**	
2.13.1	Methodology/Validation[1]	Methods for specifically identifying and quantifying the active ingredient(s) and impurities present in products at or above 0.1% by weight, or those of toxicological significance at any concentration, are to be provided. For the latter, the appropriate level is dictated by the LOQ of the toxic impurity analytical method, which is sample/chemical dependent, and must also be below any established applicable regulatory limit. A more thorough discussion of impurities of toxicological significance is provided under DACO 2.13.4; however, all corresponding analytical methods are to be reported under this DACO number. A method capable of separating stereoisomers, when applicable, as identified under DACO 2.12, is also required and may result in the need for two methods for the active ingredient(s); one for total stereoisomeric content and a second to confirm any specified ratio. The recommended reporting format for analytical methods is outlined in Appendix I. All methods must have sufficient precision, accuracy and sensitivity to determine whether the amount of the ingredient found in any sample of the product is within its certified limits.
2.13.2	Confirmation of Identity	The identity of the active ingredient and each specified impurity must be supported by relevant chromatograms and/or spectra. Ideally, full spectral characterization by mass spectrometry of each isolated impurity (or on-line determination using gas chromatography/mass spectrometry or liquid chromatography/mass spectrometry) and comparison to the spectrum of a corresponding analytical standard is required. If commercial reference materials are not available, unambiguous characterization of the isolated component should be accomplished by mass spectrometry and nuclear magnetic resonance.
2.13.3	Batch Data[1]	The composition of a minimum of five batches of the product manufactured at the site proposed for registration, determined using the methods described under DACO 2.13.1, must be provided to support the specifications. Date of manufacture and site of production for each batch must be included. Corresponding raw data to be submitted include representative quantitative chromatograms of: (1) standards; (2) blanks, and (3) the five batches of the technical grade active ingredient or ISP that were used to support each specified active ingredient and impurity. Chromatograms must be clearly labelled to identify all analytical parameters and peaks, including those that may represent compounds quantitated by other methods included in the submission. These batches may initially represent pilot plant production from the proposed site; however, once commercial production commences (either at the same location or at a different facility), data from an additional five batches that correspond to the commercial-scale location/process will be required under a separate application to support the specifications. If multiple manufacturing sites are proposed at once, batch data are required for each site.
2.13.4	Impurities of Toxicological	Analysis for these impurities is required when there is a potential for their presence in starting materials or their formation during the manufacture of the technical active ingredient.

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	Concern (Impurities of Human Health and Environmental Concern)[1]	For example, nitrosamine analysis is required when appropriate amines and an identifiable nitrosating agent (including nitrites and nitrates) are present due to the raw materials or manufacturing process utilized. The primary focus is upon smaller molecular weight volatile and nonvolatile nitrosamines, such as N-dimethylnitrosamine and N-nitrosodipropylamine respectively. It should be noted that inherent contamination would be expected from products whose chemical structure features both amine functionality and nitrosating potential, such as dinitroanilines. These analyses, when required, should reflect the lowest practical LOQ, which will vary according to the sample and chemical, but must at least be below any corresponding applicable regulatory level. Upper certified limits are required for impurities of toxicological significance present above the LOQ. Any waiver request for not providing such data must be supported by a scientific rationale as to why the presence of such impurities can be excluded and will be assessed based upon the nature of the raw materials, chemistry of the active ingredient and the specific manufacturing process. Impurities and classes of impurities of toxicological concern include, but are not limited to: • 2,3,7,8-tetrachloroazobenzene and 2,3,7,8-tetrachloroazoxybenzene • Anilines and substituted anilines • Dichloro-diphenyl-trichloroethane and other chlorinated diphenyl ethanes and ethylenes, such as analogs and isomers of Dichloro-diphenyl-trichloroethane, Dichloro-Diphenyl-Dichloroethane, Dichloro-Diphenyl-Ethane and Extrachloro-Dichloro-Diphenyl-Trichloroethane • Ethylene thiourea • Halogenated dibenzodioxins/halogenated dibenzofurans • Hexachlorobenzene, pentachlorobenzene and tetrachlorobenzenes • Hydrazines • Nitrosamines • Oxygen analogs of organophosphates • Polynuclear aromatics also referred to as polynuclear aromatic hydrocarbons • Polychlorinated biphenyls • Sulfoxides and sulfones of organophosphates and carbamates • Tetraethyl thiodiphosphate (Sulfotep) or tetraethyl pyrophosphate • Metals such as antimony, arsenic, cadmium, chromium, cobalt, nickel, lead and mercury • Aflatoxins • Dimethyl sulfate • Ethyl methanesulfate • Formaldehyde • Hydrogen cyanide • Isobutyl methanesulfonate • Pentachlorobenzonitrile

Data Code	Title	Conditions/Guidance (Updated from DIR98-04)
		• Sodium cyanide • Toluene Impurities having characteristics of potential toxicological significance may include: (i) any impurity that is a structurally related analog of the parent compound of toxicological significance; (ii) any impurity that is also an active ingredient; or (iii) any impurity that is identified in standard toxicology data bases, such as Toxline or the Registry of Toxic Effects of Chemical Substances, as being oncogenic, neurotoxic, genotoxic, a developmental toxicant, endocrine disrupter, etc. If a product has been analyzed for any of these compounds, methods, validation data including recovery and limit of detection (LOD)/LOQ for expected contaminant(s), or reasonable surrogates if appropriate, and batch data as per DACO 2.13.3, are to be provided. Where it is deemed essential for evaluation, such data from pest control products or potential precursors will be requested. Since detection and quantitation limits may vary from case to case, consultation with the PMRA is recommended. Applicants should contact the PMRA if there is a question about the status of any specific impurity not listed.
2.14	**Chemical and Physical Properties**	*Requirement:* To provide methods and observations/values for the properties identified in DACO 2.14.1 to 2.14.14. *Purpose:* Property data are requested for a number of reasons. The requirements include properties that (i) are used directly in risk assessment as they represent one of a number of factors that influence concentration and exposure. Certain properties are indicators of the behaviour of a pesticide in the environment with respect to mobility and accumulation; (ii) are needed as basic or supportive evidence in initiating or evaluating studies required by other disciplines. For example, the octanol/water partition coefficient is used as a criterion in determining whether certain bio-accumulation/bioconcentration studies must be conducted and UV/visible absorption identifies wavelengths of light at which compounds may be susceptible to phototransformation; (iii) confirm or provide supportive information on the identity of ingredients and products; (iv) provide information that is useful in reviewing the manufacturing process used to produce the pest control product as well as the methodologies used for its analysis; and/or (v) permit response to emergency requests for identification of unlabelled pest control products potentially involved in accidents, spills, or medical emergencies such as poisonings. *Guidance:* Protocols for developing the data requirements identified in this section are not included in this document. Applicants should consult protocols developed and published by various agencies. Methods must be thoroughly described or a copy of the scientific publication describing the protocol must be included with the submission. A reference to internationally established protocols is sufficient, if followed without deviation, and the specific procedure used is clearly identified for those protocols providing multiple options. Study reports should include a complete presentation of the data, sample calculations and an interpretation of the results. In addition, basic physio-chemical information on individual stereoisomers is to be provided, if applicable; typically, this may include information on melting point, optical rotation, and stability towards inversion. A pure active ingredient (PAI) is equivalent to the analytical standard of active ingredient described in Appendix II. Care should be exercised in the selection of appropriate test materials for properties that provide a technical grade active ingredient or PAI option to ensure data relevance. Typically, as these properties are characteristic of the active principle, the PAI should be used whenever available. This is most important for properties that may be significantly affected by impurities, such as water solubility, particularly in the presence of residual solvents. Conversely, it may be appropriate to use the technical grade active ingredient if

Data Code	Title	Conditions/Guidance (Updated from DIR98-04)
		impurities do not significantly impact upon the outcome of the test and if the corresponding detection principle is selective for the PAI. For example, certain vapour pressure protocols may be conducted on either the technical grade active ingredient or PAI. Regardless of the material used, the purity of the test substance must always be clearly identified in the study report. Note: (i) Several of the identified tests require the use of distilled water. Although double distilled water is preferred, deionized water with a resistivity greater than 10 megohms/cm and a total organic content below 0.01% is also acceptable. (ii) If data are not required for a specific property of a product, as per the notes, include this information in the corresponding section of the submission.
2.14.1	Colour[1]	USEPA (United States Environmental Protection Agency) test guideline 830.6302 Test substance must be technical grade active ingredient
2.14.2	Physical State[1]	USEPA test guideline 830.6303 Test substance must be technical grade active ingredient
2.14.3	Odour[1]	USEPA test guideline 830.6304 Test substance must be technical grade active ingredient
2.14.4	Melting Point/Melting Range[1]	USEPA test guideline 830.7200, OECD (Organisation for Economic Cooperation and Development) guideline 102 Test substance must be technical grade active ingredient or PAI Required when the test substance is a solid at room temperature
2.14.5	Boiling Point/Boiling Range[1]	USEPA test guideline 830.7220, OECD guideline 103 Test substance must be technical grade active ingredient or PAI Required when the test substance is a liquid at room temperature.
2.14.6	Density or Specific Gravity[1]	USEPA test guideline 830.7300, OECD guideline 109 Test substance must be technical grade active ingredient Bulk density must be defined for solids. True density or specific gravity is applicable to other test substances.
2.14.7	Water Solubility[1] (mg/L)	USEPA test guidelines 830.7840 and 830.7860, OECD guideline 105 Test substance must be technical grade active ingredient or PAI Solubility in water may be a function of pH if the compound ionizes in an aqueous solution. In such situations, it may be necessary to determine solubility at more than a single pH (see USEPA 830.7860, *Effect of pH on solubility*).
2.14.8	Solvent Solubility[1] (mg/L)	USEPA test guideline 830.1000 Test substance must be technical grade active ingredient or PAI Required in representative polar and non-polar solvents at 20° ± 5°C.
2.14.9	Vapour Pressure[1]	USEPA test guideline 830.7950, OECD guideline 104 Test substance must be technical grade active ingredient or PAI Required unless the substance is a salt. For methodologies requiring the use of elevated temperatures, the vapour pressure should not be extrapolated over a phase change unless log p (pressure) versus 1/T (temperature) linearity is maintained.

Data Code	Title	Conditions/Guidance (Updated from DIR98-04)
2.14.10	Dissociation Constant[1]	USEPA test guideline 830.7370, OECD guideline 112 Test substance must be technical grade active ingredient or PAI Required when the test substance contains an acid or base functionality. For products that are salts, data are required for the corresponding acid/base.
2.14.11	Octanol/Water Partition Coefficient[1]	USEPA test guidelines 830.7550, 830.7560 and 830.7570, OECD guidelines 107 and 117 Test substance must be technical grade active ingredient or PAI Determined at pH 5, 7 and 9 for all organic chemicals unless they hydrolyse in water or are soluble in water in all proportions.
2.14.12	UV/Visible Absorption Spectra[1]	USEPA test guideline 830.7050, OECD guideline 101 Test substance must be technical grade active ingredient or PAI Not required in the absence of a UV chromophore. Absorption at wavelengths between 300 and 900 nm is of particular interest in assessing the potential for photodegradation. Where it is not possible to obtain sufficient concentrations in aqueous media, a suitable organic solvent should be used, with methanol preferred. Further guidance in the performance of the test is found in USEPA and OECD guidance documents.
2.14.13	Stability (Temperature, Metals) [1]	USEPA test guideline 830.6313, OECD guideline 113 (i) Data regarding stability to metal and metal ions is required only if contact with metals during storage or use is likely. (ii) The protocol must include a test to monitor for the stability of optically pure/enhanced active ingredient(s) towards chiral inversion or other isomerization, if applicable, as per DACO 2.12. (iii) The temperature stability requirements for a technical grade active ingredient, as per the referenced guidance documents, reflect Collaborative International Pesticides Analytical Council MT 46 method, i.e., 14 days at 54°C. Methods for the analysis of the active ingredient(s) would typically be consistent with that provided in DACO 2.13.1; however, if the method differs, it must be fully described as per Data Code 2.14.
2.14.14	Storage Stability Data[1]	USEPA test guideline 830.6317 Test substance must be ISP Storage stability data must adhere to the following requirements: (i) Samples of the material must be stored for at least one year at a constant ambient temperature or under warehouse conditions that reflect the expected storage conditions of the commercial product. (ii) The study shall be conducted with the product in its commercial package or in smaller packages of the same construction and materials. If the package is permeable, a relative humidity of at least 50% must be maintained throughout the study. (iii) The study should be carried out with sufficient replicates and sufficient sampling frequency to establish the actual shelf-life if degradation occurs within one year. If a product has a shelf-life of less than one year, an expiration date may be required on the product container. The protocol must include a test to monitor for the stability of optically pure/enhanced active ingredient(s) towards chiral inversion or other isomerization, if applicable, as per DACO 2.12. Note that the storage stability requirement for end-use products and manufacturing concentrates has been amended under DACO 3.5.10, but has not been changed for technical grade active ingredients/ISPs.

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2.14.15	pH[1]	USEPA test guideline 830.7000 Required for 1% solution/suspension
2.14.16	Nanomaterial Characteristics[1]	The following physical properties may also be required for products that may contain nanomaterial (requirements still under development and subject to change): - Agglomeration/aggregation - Physical form/basic morphology - Particle and mass concentration/distribution - Specific surface area - Surface chemistry - Surface charge
2.15	Sample(s) of Analytical Standards and ROC	Required for active ingredient if new to Canada; otherwise, if requested.
2.16	Other Studies/ Data/Reports	If available and relevant to the current submission.
12.5.2	Foreign Reviews	If available, or if unavailable for submission, please indicate if another regulatory authority has completed specific data reviews.
12.7.2	Applicant Generated Study Reviews (Technical Grade Active Ingredient)	Study reviews prepared by applicants using standard review templates. a) For Canada-only applications (i.e., not Joint Review applications), NAFTA (North American Free Trade Agreement) study profile templates are requested [although use of OECD format is also acceptable]. NAFTA study profile templates are available upon request. (These templates are also available on the USEPA) b) For Joint Review applications of conventional (traditional) chemicals - OECD format is required, to include both Document M for non-confidential information and Document J for confidential information. Note that actual study reports should be submitted separately from Documents M and J. Documents M and J are intended to be Word-format summaries of the results obtained. c) For Joint Review applications of biopesticides, either NAFTA or OECD format is acceptable.

[1] Studies requiring Good Laboratory Practice compliance

Chemistry Data Requirements: DACO Part 3 End-Use Product

Data Code	Title	Conditions/Guidance (Updated from DIR98-03)
3	**Chemistry Requirements for the Registration of Manufacturing Concentrates (MA) and End-Use Products Formulated from Registered technical grade of active ingredients or integrated system products**	
3.1	**Product Identification**	
3.1.1	Applicant's Name and Office Address	
3.1.2	Formulating Plant's Name and Address	
3.1.3	Trade Name	
3.1.4	Other Names	Include any company development code name/number as well as any equivalent foreign name to which data found in the submission may be referenced.
3.2	Formulation Process	Together, the descriptions of the materials used to formulate the product and the formulation process itself identify the major factors affecting the composition of a (Manufacturing Concentrates) MA or an end-use product. The PMRA reviews this information, along with the end-use product analytical data requirements showing the absence of formulation interferences, to determine whether the applicant's product will contain the stated ingredients at the certified limits listed on the Statement of Product Specification Form (SPSF).
3.2.1	Description of Starting Materials	The following information is to be provided for each active ingredient present in the MA or end-use product: (i) the name and guarantee of the PMRA-registered product; and (ii) the PMRA registration number of that product. The following information is to be provided for each formulant present in the MA or end-use product: (i) chemical name(s), if it is a specific discrete chemical substance(s); (ii) brand name, trade name, common name, Chemical Abstracts Service Registry number, and other commercial designation of the ingredient; (iii) all information that the applicant knows (or that is reasonably available) concerning the composition of the ingredient, including a copy of specifications or other documents describing the ingredient; and (iv) the name and address of the producer of the ingredient or, if that information is not known to the applicant, the name and address of its supplier. It should be emphasized that an applicant is not required to perform chemical analysis of starting materials to meet the above criteria, but only provide information to which the applicant has, or should have, access. If multiple suppliers are used for starting materials, specifications for all suppliers should be provided. Changes in suppliers once a product is registered are subject to the requirements of Regulatory Directive DIR2013-02, *Notification/Non-Notification,* or subsequent revisions.

Data Code	Title	Conditions/Guidance (Updated from DIR98-03)
3.2.2	Description of the Formulation Process	The following information must be provided: (i) a general characterization of the process, for example, whether it is batch or continuous, and the quantity of product produced per batch (or per unit time, if continuous); (ii) the identities of the reactants, solvents, and catalysts used, as applicable, to formulate the product, including their quantities and the order in which they are added; (iii) a description of the equipment used that may influence the composition of the MA or end-use product; (iv) a description of the conditions, for example, mixing time, temperature, pressure, pH, humidity, that are controlled during each step of the process to affect the composition of the substance produced, and the limits that are maintained; and (v) a description of the procedures used to assure consistent composition of the substance produced, for example, calibration of equipment, sampling regimens and other quality control measures such as tests used to monitor reaction completion.
3.2.3	Discussion of the Formation of Impurities of Toxicological Concern	If applicable: The level of detail required for MAs or end-use products is typically less stringent than for the registered sources of their active ingredients since the impurities associated with an active ingredient in an MA or end-use product will almost exclusively reflect those present in the registered material from which they are prepared. Impurities or side reactions rarely occur as a result of the basic blending process typically employed. However, if the applicant has reason to believe that an impurity the PMRA would consider toxicologically significant may be *introduced* or *enhanced* due to the formulation process, the discussion must include an expanded description of the potential formation of the impurity and the amounts at which it might be present. Analytical methods applicable to such components are to be provided as per DACO 3.4.2. In this context, the following potential sources of impurity formation must be considered and identified: (i) possible reactions occurring during the formulation of the product between any of its active ingredients, between the active and formulants, or between the active ingredient and the production equipment; (ii) post-production reactions between any of the MA or end-use product active ingredients and any other component of the product or its packaging; (iii) the possible migration of packaging materials into the product; and (iv) the potential carryover of contaminants from earlier use of production equipment to formulate other products. See Part 2 DACO 2.13.4 (for technical grade active ingredient) for a more detailed discussion of impurities of toxicological significance. The required level of determination is dictated by the LOQ of the corresponding analytical method, which is sample/chemical dependent, and must also be below any applicable regulatory limit.
3.3	**Specifications**	The nominal concentration and corresponding certified limits must be provided for each MA or end-use product component. The nominal concentration is defined as the typical amount of an ingredient present in a pest control product at the time of its production. Both the active ingredient nominal concentration and a corresponding nominal equivalence statement, if applicable (for example, acid salts), are to be provided. The PMRA requires a nominal approach to active guarantee expression for new technical products and associated end-use products. However, currently registered technicals may have minimum active content guarantees and end-use products formulated from such

Data Code	Title	Conditions/Guidance (Updated from DIR98-03)
		products must also express their active ingredient level in terms of a minimum guarantee. Registrants/applicants who have products registered with minimum guarantees are encouraged to convert to nominal guarantees. The product guarantee, identified on the SPSF and appearing on the draft product label, is synonymous with the active ingredient(s) nominal concentration. This number most accurately identifies the amount of each active ingredient typically found in the end-use product or MA and is based upon the nominal concentration of the active ingredient in the registered technical grade active ingredient, ISP, or MA from which it is formulated. End-use product or MA active ingredient nominal concentrations are subsequently used to establish corresponding enforceable certified limits, as further discussed under DACO 3.3.1. Specification data are to be submitted on a SPSF that includes a signed and dated Declaration of Applicant certifying that the information is true and complete. For full instructions on the proper completion of the form the applicant should refer to *Guidance for Completing the Statement of Product Specification Form*. The SPSF is to be submitted under DACO 0.1.6003 in the e-index builder.
3.3.1	Establishing Certified Limits	Standard certified limits for active ingredients and formulants are based upon nominal concentration, unless the applicant proposes alternate limits which are deemed acceptable by the PMRA. **Standard limits are defined as follows:** **Nominal Concentration (N) of Ingredient** **20.0% < N ≤ 100.0% (Upper Limit N + 3% N; Lower Limit N – 3% N)** **1.0% <N ≤ 20.0% (Upper Limit N + 5% N; Lower Limit N – 5% N)** **N ≤ 1.0% (Upper Limit N + 10% N; Lower Limit N – 10% N)** An applicant may propose a certified limit for an active ingredient or formulant that differs from the standard limits, but must include an explanation of the basis of the proposed limits, including how they were established, for example, sample analysis or quantitative estimate based upon the formulation process. Where warranted by DACO 3.3, the applicant must propose upper certified limits for impurities of toxicological significance as standard certified limits may not be used for such product components.Proposed limits should not greatly exceed those actually occurring in the product. All certified limits must: (i) be based on a consideration of the variability of the concentration of the ingredient in the product when good manufacturing practices and normal quality control procedures are used; (ii) allow for all sources of variability likely to be encountered in the formulation process; and (iii) take into account the stability of the ingredient in the product between production and sale or distribution. If the PMRA finds any certified limit (either standard or applicant proposed) unacceptable, the PMRA will inform the applicant of its determination and will provide supporting reasons. The PMRA may also require, on a case-by-case basis, any or all of the following: (i) more precise limits;

Data Code	Title	Conditions/Guidance (Updated from DIR98-03)
		(ii) a more thorough explanation of how the certified limits were determined; or (iii) a narrower range between the upper and lower certified limits than that proposed.
3.4	**Product Analysis**	
3.4.1	Enforcement Analytical Method[1]	An analytical method suitable for enforcement purposes must be provided for each active ingredient in an end-use product or MA. This method should reflect that routinely used by the applicant to ensure that batch-to-batch variability does not result in product being released for use that does not meet the criteria identified on the SPSF. A method capable of separating stereoisomers, when applicable, is also required and may result in the need for two methods for the active ingredient(s), one for total isomeric content and a second to confirm any specified ratio. The recommended reporting format for analytical methods is outlined in Appendix I. All methods must have sufficient precision and accuracy to determine whether the amount of the ingredient found in any sample of the product is within its certified limits. In addition to validation data including linear range, accuracy and precision; the applicant must provide labelled chromatograms of the end-use product, the active ingredient analytical standard, the internal standard (if used) and the corresponding blank formulation (containing all formulants without the active) to demonstrate the absence of analytical interference. If the formulation contains two or more active ingredients, chromatograms of the blank formulation individually spiked with each active and another spiked with the internal standard, if used, are to be provided. Methods may be validated by the PMRA laboratory at the time the product chemistry data are reviewed. Methods should use commonly available equipment, be written to include all steps performed even when the author believes that certain steps are *normally* performed in all laboratories, and not be claimed confidential.
3.4.2	Impurities of Toxicological Concern (Impurities of Human Health and Environmental Concern)	If potential exists for the formulants/formulating process to create or enhance the presence of an impurity of toxicological concern, methods, validation data, including spiked sample recovery at the LOQ for expected contaminant(s) or reasonable surrogates, as appropriate, and representative data from the analysis of five batches of the MA or end-use product are required. For example, data would be required if there exists a potential for N-nitrosamine contamination above that found in the corresponding source of registered material, due to the introduction of a nitrosating agent in the formulation process. Since detection and quantitation limits may vary on a case-by-case basis, consultation with the PMRA is recommended. The required level of determination is dictated by the LOQ of the corresponding analytical method, which is sample/chemical dependent, and must also be below any applicable regulatory limit. If identified, and there is a potential for increased levels over time, the analysis of impurities of toxicological significance must be included in the storage stability study required by DACO 3.5.10.
3.5	**Chemical and Physical Properties**	Protocols for developing property data are not included in this guidance document. Applicants should consult protocols developed and published by various agencies, including those referenced for each property below. Methods must be thoroughly described or a copy of the scientific publication describing the protocol must be included with the submission. A reference to internationally established protocols is sufficient, if followed without deviation, and the specific procedure used is clearly identified for those protocols providing multiple options. Study reports should include a complete presentation of the data, sample calculations and an interpretation of the results.

Data Code	Title	Conditions/Guidance (Updated from DIR98-03)
3.5.1	Colour[1]	USEPA test guideline 830.6302 Required for all MAs. Only required for end-use products if the property is expected to affect product efficacy.
3.5.2	Physical State[1]	USEPA test guideline 830.6303
3.5.3	Odour[1]	USEPA test guideline 830.6304 Required for all MAs. Only required for end-use products if the property is expected to affect product efficacy.
3.5.4	Formulation Type	
3.5.5	Container Material and Description	
3.5.6	Density or Specific Gravity[1]	USEPA test guideline 830.7300, OECD guideline 109 Bulk density must be defined for solid products. True density or specific gravity is applicable to other test substances.
3.5.7	pH[1]	USEPA test guideline 830.7000 Required for, (i) 1% solution/suspension as per Collaborative International Pesticides Analytical Council MT 75 for end-use products applied as aqueous dilutions and, (ii) liquid products as packaged.
3.5.8	Oxidizing or Reducing Action[1] (Chemical Incompatibility)	USEPA test guideline 830.6314 Requirements include an assessment of hazardous reactions that may result from contact with common oxidizing and reducing agents. See the referenced USEPA guidance document for a complete description.
3.5.9	Viscosity[1]	USEPA test guideline 830.7100, OECD guideline 114 Required when the product is a liquid.
3.5.10	Storage Stability Data[1]	USEPA test guideline 830.6317 Storage stability data must adhere to the following requirements: (**i**) A storage stability study shall be conducted under at least one of the following regimes: (a) at least one year's duration at a constant ambient temperature of 20 or 25°C and, if the package is permeable, at a relative humidity of 50%, with quantitative analysis for the active ingredient(s) at study commencement and following storage periods of 3, 6 and 12 months; or (b) at least one year's duration under warehouse conditions that reflect the expected storage conditions of the commercial product (this may include the need for freeze-thaw studies). Where possible, the storage environment should approximate any extremes of temperature or climate expected to occur under actual storage conditions. Quantitative analysis for the active ingredient(s) is required at study commencement and following storage periods of 3, 6 and 12 months; or (c) of 14 days' duration under accelerated conditions at a constant temperature of 54°C, with quantitative analysis for the active ingredient(s) at study commencement and after 14 days. (**ii**) The study shall be conducted with the product in its commercial package or in smaller packages of the same construction and

Data Code	Title	Conditions/Guidance (Updated from DIR98-03)
		materials. (**iii**) For long-term ambient studies, the study should be carried out with sufficient replicates and sufficient sampling frequency to establish the actual shelf-life if significant degradation occurs within one year (i.e. the level of active is no longer within the certified limits). If significant degradation is observed under accelerated conditions, a one-year study as described above may be required to determine the shelf-life. If a product has a shelf-life of less than one year, an expiration date may be required on the product container. (**iv**) The analysis is to be conducted using a specific validated method. For end-use products, the same method used to determine the level of the active ingredient for establishing certified limits would typically be employed. However, if the methodology differs from that provided under DACO 3.4.1, it must be fully described as per Data Code 3.5. (**v**) The storage stability report submitted in support of registration shall include the following information: (a) a description of test procedures and conditions, for example, study duration, humidity and temperature (b) a description of any physical changes, for example, phase separation or clumping, in the product and any changes to the integrity of the packaging material during the test period, and also the consequences, if any, of such changes for safe handling and use of the product; and (c) quantitative analytical data for the active ingredient at study commencement and all storage periods. If product degradation or packaging deterioration is expected to cause the formation or increase in content of impurities of human health or environmental concern, such impurities (as identified in DACO 2.13.4) must also be monitored at each time point. (**vi**) A surrogate study of a similar formulation may be acceptable in lieu of the storage stability study. The formulation used for the surrogate study must be fully described to allow the acceptability of the study to be determined. (**vii**) The stability protocol must contain a test to monitor for the stability of optically pure/enhanced active ingredient(s) towards chiral inversion or other isomerization, if applicable.
3.5.11	Flammability[1]	USEPA test guideline 830.6315 The flash point shall be determined for combustible liquid products. For aerosols, the flame extension test method should be conducted. See the referenced USEPA guidance document for a complete description.
3.5.12	Explodability[1]	USEPA test guideline 830.6316 Required when the product is potentially explosive.
3.5.13	Miscibility[1]	USEPA test guideline 830.6316 Required when the product is an emulsifiable liquid and is to be diluted with petroleum solvents.
3.5.14	Corrosion Characteristics[1]	USEPA test guideline 830.6320 Required unless a reasonable explanation of a lack of corrosivity is provided, for example, lack of extreme pH, lack of reaction with container material. This study may be performed in combination with the storage stability requirements described under DACO 3.5.10.

Data Code	Title	Conditions/Guidance (Updated from DIR98-03)
3.5.15	Dielectric Breakdown Voltage[1]	USEPA test guideline 830.6321 Required when the end-use product is a nonconductant liquid and is to be used around electrical equipment.
3.5.16	Nanomaterial Characteristics[1]	The following physical properties may also be required for products that may contain nanomaterial (requirements still under development and subject to change), - Agglomeration/aggregation - Physical form/basic morphology - Particle and mass concentration/distribution - Specific surface area - Surface chemistry - Surface charge
3.6	Other Studies/Data/Reports	If available and relevant to the current submission.
12.5.3	Foreign Reviews	If available, or if unavailable for submission, please indicate if another regulatory authority has completed specific data reviews.
12.7.3	Applicant Generated Study Reviews	Study reviews prepared by applicants using standard review templates. a) For Canada-only applications (i.e., not Joint Review applications), NAFTA study profile templates are requested [although use of OECD format is also acceptable]. NAFTA study profile templates are available upon request. These templates are also available on the USEPA website. b) For Joint Review applications of conventional (traditional) chemicals - OECD format is required, to include both Document M for non-confidential information and Document J for confidential information. Note that actual study reports should be submitted separately from Documents M and J. Documents M and J are intended to be Word-format summaries of the results obtained. c) For Joint Review applications of biopesticides, either NAFTA or OECD format is acceptable.

[1] Studies requiring Good Laboratory Practice compliance

Toxicology Data Requirements: DACO Part 4 (Technical Grade Active Ingredient)

Data Code	Title	Conditions/Guidance (Updated from DIR2005-01)
4	**Toxicology**	
4.1	Summaries	**This section is an overview of supporting information. All studies, rationales, foreign reviews, Data Evaluation Records (DERs), should be submitted under the appropriate DACO.** Summarize background information that provides context to/purpose of the submission. For example: · Highlight changes/additions requested to any current registration (if relevant). · Explain how the submitted data support the proposed uses/request. List any data on-hand, but not provided to the PMRA. Explain why those data are not being submitted. · Include any bridging rationales and/or data waiver requests to justify the acceptability of the data. Also, include references to any previously submitted data (with submission number and PMRA number, or other identification, if available) that support the current request(s). · Explain any unusual test protocols and why the standard protocols were not appropriate. · Cross-reference any information provided in another DACO Part that is relevant to the assessment of the Part 4 Toxicology data (for example, a document in Part 6 that includes a discussion of the toxicological equivalence of a metabolite). · Confirmation that the test material used in the toxicity studies is identical in composition to the active for which registration is being sought. If not identical, provide specifications of the test material used in the studies and a rationale indicating why the submitted studies can be used to support the active. The rationale should include any code names used for the test material or the active. · A summary of study-specific batch data is helpful. Please identify the location (for example, study title and page number) of the certificates of analyses for each batch of product tested in the submitted studies. Provide a summary of **all** corresponding synonyms of the active, whether used in the present submission or not. · If the end-use product builds on a precedent product(s), provide a list of precedent pest control product registration numbers and product names for comparison purposes, as well as the detailed formulation of the originally registered product (i.e., the one for which toxicity studies were submitted) for products that may not have an associated SPSF. • Please explain any ownership changes relating to the toxicity studies or active ingredient. • Cross-reference any foreign reviews of the newly submitted data, if available (for example, USEPA, DERs).
4.2	**Acute Studies - Technical Grade Active Ingredient**	Acute toxicity studies on active ingredients are necessary to determine the potential hazards from acute exposures. Acute data are used for classification purposes and for the development of appropriate precautionary statements for product labels. Acute studies identify relative acute toxicities by different routes of exposure as well as the potential to produce irritation and sensitization. It should be noted that the PMRA does not endorse irritation testing that seriously compromises animal welfare. Waivers should be requested if the test material is known to be severely irritating or corrosive, or if irritation potential can be estimated from other reliable information. For more detail on potential waivers for acute toxicity studies, consult OECD Series on Testing and Assessment No. 237 Guidance Document on Considerations for Waiving and Bridging of Mammalian Acute Toxicity Tests (2016).

Data Code	Title	Conditions/Guidance (Updated from DIR2005-01)
4.2.1	Acute Oral	The preferred species is the rat. Not required if the test substance is a gas or highly volatile liquid.
4.2.2	Acute Dermal	The preferred species is the rat or the rabbit. Not required if the test substance is a gas or highly volatile liquid. Not required if the test substance is corrosive to skin or has a pH lower than 2 or greater than 11.5. As per SPN2017-03, this study is only required in exceptional cases. Refer to SPN2017-03 for more details.
4.2.3	Acute Inhalation	The preferred species is the rat. Required if the test substance consists of, or under conditions of use will result in, a respirable material (for example, gas, vapour, aerosol or particulate).
4.2.4	Primary Eye Irritation	The preferred species is the rabbit. Not required if the test substance is corrosive to skin or has a pH lower than 2 or greater than 11.5.
4.2.5	Primary Dermal Irritation	The preferred species is the rabbit. Not required if the test substance is a gas or highly volatile liquid. Not required if the test substance is corrosive to skin or has a pH lower than 2 or greater than 11.5.
4.2.6	Dermal Sensitization	Preferred species is guinea pig (maximization and Buehler assays) or mouse (local lymph node assay). Not required if the test substance is corrosive to skin or has a pH lower than 2 or greater than 11.5; however, diluted end-use product testing may be required if the end-use product is diluted under conditions of use.
4.2.7	Potentiation/Interaction	If available.
4.2.8	Antidote	If available.
4.2.9	Other Acute Studies	If available and relevant to the current submission – includes studies that elaborate on the toxicity profile of a test substance.
4.3	**Short-Term Studies - Technical Grade Active Ingredient**	These studies provide information on the toxic potential of the pest control product through daily repeated exposure. A short-term study has been defined as having a duration lasting up to 10% of the animal's lifespan. The data obtained from these short-term studies are useful in determining possible cumulative or delayed toxicity and variability in species sensitivity, as well as in identifying effects in organs or systems that are vulnerable to the chemical insult. They also provide guidance for selecting dosages for long-term studies. Post-treatment recovery phases assist in detecting reversibility or persistence of adverse effects. The use pattern and physical properties of the product as well as toxicokinetic considerations will assist in determining the appropriate route of exposure and duration of study.

Data Code	Title	Conditions/Guidance (Updated from DIR2005-01)
4.3.1	Short-Term Oral (90-day rodent)	The preferred species is the rat. Consideration should be given to incorporating a post-treatment recovery phase.
4.3.2	Short-Term Oral (90-day dog)	Required when the product is to be used on food or likely to come in contact with food. Refer to specific use-site category. In exceptional cases only, when a dog has been demonstrated to be the most sensitive laboratory animal and there is evidence for the potential of cumulative or delayed toxicity in the database, a dog study of 12 months duration may be required. The PMRA may also require the appropriate metabolism and pharmacokinetic studies to evaluate more precisely bioavailability, half-life, and steady state in making this determination. Note: In cases where a 12-month study has already been conducted, it is acceptable to submit this in lieu of a 90-day study to avoid duplicative animal testing.
4.3.3	Short-Term Oral (28-day rodent)	If available – submit studies of shorter duration including range-finding studies that elaborate on the toxicity profile of a test substance.
4.3.4	Short-Term Dermal (90-day)	Required for certain use patterns. Refer to specific use-site category.
4.3.5	Short-Term Dermal (21/28-day)	Required for certain use patterns. Refer to specific use-site category. Not required if an acceptable 90-day dermal toxicity study (DACO 4.3.4) is performed and submitted.
4.3.6	Short-Term Inhalation (90-day)	Required if there is the likelihood of significant repeated inhalation exposure to the product as a gas, vapor or aerosol. Based on estimates of the magnitude and duration of human exposure, studies of shorter duration, (for example, 21 or 28 days) may be sufficient to satisfy this requirement. Registrants should consult with the PMRA to determine whether studies of shorter duration would meet this requirement.
4.3.7	Short-Term Inhalation (21/28-day)	If available – submit studies of shorter duration including range-finding studies that elaborate on the toxicity profile of a test substance.
4.3.8	Other Short-Term Studies	If available and relevant to the current submission – includes studies that elaborate on the toxicity profile of a test substance.
4.4	**Long-Term Studies - Technical Grade Active Ingredient**	Long-term daily repeated exposure studies are generally designed to investigate the chronic toxicity and oncogenic potential of the pest control product when administered to test animals over the major portion of their lifespan. Ideally, the data thus generated should identify dose-response relationships and possible effects of cumulative toxicity as well as permit assessment of the potential for neoplastic development.
4.4.1	Chronic (rodent)	4.4.1 and 4.4.2 could be submitted as a combined study under 4.4.4. The preferred species is the rat. The oral route is recommended when the product is to be used on food or likely to come in contact with food. Minimum study duration for the rat is 24 months.

Data Code	Title	Conditions/Guidance (Updated from DIR2005-01)
4.4.2	Oncogenicity (rodent species 1)	4.4.1 and 4.4.2 could be submitted as a combined study under 4.4.4. The preferred species is the rat. The oral route is recommended when the product is to be used on food or likely to come in contact with food. Minimum study duration for the rat is 24 months.
4.4.3	Oncogenicity (rodent species 2)	The preferred species is the mouse. The oral route is recommended when the product is to be used on food or likely to come in contact with food. Minimum study duration for the mouse is 18 months.
4.4.4	Combined Chronic/Oncogenicity (rodent)	4.4.1 and 4.4.2 could be submitted as a combined study under 4.4.4. The preferred species is the rat. The oral route is recommended when the product is to be used on food or likely to come in contact with food.
4.4.5	Other Long-Term Studies	If available and including mode of action data that elaborate on the toxicity profile of a test substance.
4.5	**Special Studies - Technical Grade Active Ingredient**	
4.5.1	Multigeneration/ Extended One-Generation Reproduction (rodent)	These studies provide information on the potential of the pest control product to influence the reproductive performance and function of the male and female parental animals, through assessment of effects on gonadal function, estrus cycles, mating behaviour, conception, parturition, lactation and weaning. Observation of progeny from conception through lactation and weaning may enable the detection of possible adverse effects on survival, viability, development and behaviour. These studies have a pivotal role in determining the potential sensitivity of the young animal. The preferred species is the rat. The oral route is recommended when the product is to be used on food or likely to come in contact with food. For the multigeneration study, a second **litter** per generation should be considered if: • any effect on routinely evaluated reproductive parameters required elucidation, particularly at dose levels below those causing minimal adverse effects in repeated exposure studies in the same species; • the observed effects in the first litters were induced postimplantation; or • the test substance is known or likely to be bio-accumulative, and where blood and tissue levels had not stabilized or attained plateau levels prior to mating.

Data Code	Title	Conditions/Guidance (Updated from DIR2005-01)
		For the Extended One Generation Study, a second **generation** should be considered if the following is observed (See OECD test guidelines 443 & Guidance Document 117): • an adverse effect on fertility or fecundity of the parental generation, • indications of abnormal sexual development of the F_1 pups, • adverse effects on F_1 litter parameters and developmental landmarks, • death or evidence of toxicity to the F_1 pups pre-weaning, and • equivocal effects on F_1 parameters or unusual control data compared to historical background.
	Developmental Toxicity	These studies, referred to in the past as teratogenicity studies, permit assessment of the potential of the pest control product to induce adverse effects on the developing embryo and fetus when administered to the pregnant female test animal during critical periods of organogenesis. Studies are generally conducted in a rodent and a non-rodent species. The teratogenic potential of the pest control product may be measured by the increased incidence or induction of congenital malformations. These studies also have a pivotal role in determining the potential sensitivity of the young animal.
4.5.2	Prenatal Developmental Toxicity (rodent)	The preferred species is the rat. Unless the chemical or physical properties of the test substance or the pattern of human exposure suggest a more appropriate route of exposure, the oral route, by oral intubation, is preferred. Additional testing by other routes may be required if the test substance is determined to be a prenatal developmental toxicant after oral dosing.
4.5.3	Prenatal Developmental Toxicity (non-rodent)	The preferred species is the rabbit. Unless the chemical or physical properties of the test substance or the pattern of human exposure suggest a more appropriate route of exposure, the oral route, by oral intubation, is preferred. Additional testing by other routes may be required if the test substance is determined to be a prenatal developmental toxicant after oral dosing.

Data Code	Title	Conditions/Guidance (Updated from DIR2005-01)
	Genotoxicity	Tests for genetic damage are designed to assess both gene mutations and chromosomal changes as well as the competency of DNA repair mechanisms. The basic criteria considered when evaluating the genotoxic activity of a pest control product are as follows: 1. determine whether the pest control product is genotoxic in some biological system by means of sensitive in vitro short-term tests; 2. through the prudent use of in vivo tests in mammalian somatic cells, establish whether the pest control product is a mammalian genotoxic agent; and 3. ascertain if the genotoxic activity of the pest control product is expressed as an adverse health effect. With respect to the latter, it is necessary to determine if cancer or heritable mutations are induced by evaluating the data from the appropriate bioassays for carcinogenicity and the induction of heritable mutations. Genotoxicity tests typically preferred for pest control products are listed below. There are, however, some pest control products for which another test could be justified scientifically as a substitute. In these instances, it would be necessary to substitute a valid alternative test for the same endpoint, i.e., gene mutation or chromosome aberration.
4.5.4	Genotoxicity – Bacterial Reverse Mutation Assay	
4.5.5	Genotoxicity – in vitro Mammalian Cell Assay	Choice of assay using any of the following: i. mouse lymphoma L5178Y cells, thymidine kinase gene locus, maximizing assay conditions for small colony expression and detection (also addresses DACO 4.5.6); ii. Chinese hamster ovary or Chinese hamster lung fibroblast (V79) cells, hypoxanthine-guanine phosphoribosyl transferase gene locus (needs appropriate in vitro study submitted under DACO 4.5.6); iii. Chinese hamster ovary cell strain AS52, xanthine guanine phosphoribosyl transferase gene locus (needs appropriate *in* vitro study submitted under DACO 4.5.6).
4.5.6	Genotoxicity – in vitro Mammalian Cell Clastogenicity	Required if not addressed in in DACO 4.5.5.
4.5.7	Genotoxicity – in vivo Cytogenetics	Assays using rodent bone marrow, using either metaphase analysis (aberrations) or a micronucleus assay, are preferred.
4.5.8	Other Genotoxicity Assays	If available.

Data Code	Title	Conditions/Guidance (Updated from DIR2005-01)
4.5.9	Metabolism/Toxicokinetics in Mammals (laboratory animals)	Toxicokinetic studies provide data on the absorption, distribution, metabolism and excretion of the pest control product. This information may be valuable in interpreting toxic effects, or lack thereof, and may assist in the extrapolation of animal toxicity data to humans. A good understanding of the toxicokinetics of the pest control product may also enable more judicious selection of appropriate routes of administration and dose levels in long-term studies. Studies should be conducted in the most appropriate animal model(s). The variability of test material absorption by different routes of exposure should be considered. In general, toxicokinetic studies should be performed using the same route of administration as that used in the majority of studies. Although dermal absorption studies are not included as part of the current toxicology data requirements, they often play a pivotal role in the risk assessment. These studies are included under the data requirements for occupational and/or residential/bystander exposure (DACO Part 5).
	Neurotoxicity	The neurotoxic potential of the pest control product may be assessed on the basis of behaviour, neurophysiology, neurochemistry and neuropathology. Neurotoxicity screening tests may be incorporated into several of the standard protocols for acute toxicity as well as short- and long-term repeated exposure toxicity studies. This may be accomplished through expanded histopathological examination of the brain, spinal cord and peripheral nervous system, a functional observational battery of tests for general behaviour and neurology as well as autonomic and sensory assessment. Appropriate tests may also be incorporated into the standard protocol for reproduction studies for the purpose of assessing the neurotoxic potential of the pest control product in the progeny. Further testing may be appropriate for pest control products known or suspected to be neurotoxicants. For pest control products requiring an assessment of delayed neurotoxicity, studies are performed in the most susceptible animal species, the adult hen.
4.5.10	Acute Delayed Neurotoxicity (hen)	Required if the test substance is an organophosphorus substance or is structurally related to other substances that may cause delayed neurotoxicity. Organophosphorus substances include the following: • uncharged organophosphorus esters, thioesters or anhydrides of organophosphoric, organophosphonic or organophosphoramidic acids; and • uncharged organophosphorus esters, thioesters or anhydrides of related phosphorothioic, phosphonothioic or phosphorothiamidic acids.
4.5.11	28-day Delayed Neurotoxicity (hen)	Required if results of acute delayed neurotoxicity study indicates effects, or if other available data indicate the potential for this type of delayed neurotoxicity.
4.5.12	Acute Neurotoxicity (rat)	Required if there is neurotoxic potential. Additional measurements such as cholinesterase activity determinations for certain test substances (for example, organophosphates and carbamates) will also be required. The route of exposure must correspond to the primary route of human exposure.

Data Code	Title	Conditions/Guidance (Updated from DIR2005-01)
4.5.13	90-day Neurotoxicity (rat)	Required if there is neurotoxic potential. Additional measurements such as cholinesterase activity determinations for certain test substances (for example, organophosphates and carbamates) will also be required. The route of exposure must correspond to the primary route of human exposure. All 90-day short-term studies in rats can be designed to simultaneously fulfill the requirements of the 90-day neurotoxicity study using separate groups of animals for testing. Although the short-term guidelines include the measurement of neurological endpoints, they do not meet the requirement of the 90-day neurotoxicity study.
4.5.14	Developmental Neurotoxicity	Required if neurological effects are observed in other studies. Should be considered if test substance: i) causes neuropathology or neurotoxicity in adults; ii) is hormonally active in vivo; or iii) causes other types of nervous system involvement at a developmental stage. May be combined with DACO 4.5.1.
4.5.15	Immunotoxicity	The potential of the pest control product to affect the immune system may be discerned from hematology, blood chemistry, organ weights and histopathology, routinely investigated in short-term repeated exposure studies. The assessment of potential immuno-modulating effects of the pest control product may be supplemented by immuno-toxicological assessments such as a host resistance assay. If deemed appropriate, specific aspects of the immune response or elucidation of immunomodulation mechanisms may be investigated through additional assays to help predict a chemically induced functional effect on the immune system. These assays may be considered to further investigate lymphocyte subsets, humoral antibody mediated immunity as well as cell-mediated and non-specific immunity.
4.8	Other Studies/Data/ Reports	If available and relevant to the current submission. Ancillary studies designed to elucidate specific mechanisms of action in the test animal may be key in interpreting the toxicological properties of the pest control product. Such information may permit a more comprehensive assessment of potential health hazards and risks to humans.
12.5.4	Foreign Reviews	If available, or if unavailable for submission, please indicate if another regulatory authority has completed specific data reviews.
12.7.4	Applicant Generated Study Reviews	Study reviews of DACO Part 4 data prepared by applicants using standard review templates. a) For Canada-only applications (i.e., not Joint Review applications), NAFTA study profile templates are requested [although use of OECD format is also acceptable]. NAFTA study profile templates are available upon request. These templates are also available on the USEPA website. b) For Joint Review applications of conventional (traditional) chemicals - OECD format is required.

Toxicology Data Requirements: DACO Part 4 – End-Use Product

Data Code	Title	Conditions/Guidance (Updated from DIR2005-01)
4	**Toxicology**	
4.1	Summaries	**This section is an overview of supporting information. All studies, rationales, foreign reviews, DERs, should be submitted under the appropriate DACO.** Summarize background information that provides context to/purpose of the submission. For example: · Highlight changes/additions requested to any current registration, including a comparative table of the proposed formulation changes (if relevant). · Explain how the submitted data support the proposed uses/request. List any data on-hand, but not provided to the PMRA. Explain why those data are not being submitted. · Include any bridging rationales and/or data waiver requests to justify the acceptability of the data. Also, include references to any previously submitted data (with submission number and PMRA number, or other identification, if available) that support the current request(s). · Explain any unusual test protocols and why the standard protocols were not appropriate. · Cross-reference any information provided in another DACO Part that is relevant to the assessment of the Part 4 Toxicology data. · Confirmation that the test material used in the toxicity studies is identical in composition to the product for which registration is being sought. If not identical, provide specifications of the test material used in the studies and a rationale indicating why the submitted studies can be used to support the proposed product. The rationale should include any code names used for the test material or the end-use product. · A summary of study-specific batch data is helpful. Please identify the location (for example, study title and page number) of the certificates of analyses for each batch of product tested in the submitted studies. Provide a summary of **all** corresponding synonyms of the active, whether used in the present submission or not. · If the end-use product builds on a precedent product(s), provide a list of precedent pest control product registration numbers and product names for comparison purposes, as well as the detailed formulation of the originally registered product (i.e., the one for which toxicity studies were submitted) for products that may not have an associated SPSF. • Please explain any ownership changes relating to the toxicity studies or active ingredient. • Cross-reference any foreign reviews of the newly submitted data, if available (for example, USEPA, DERs).

Data Code	Title	Conditions/Guidance (Updated from DIR2005-01)
4.6	**Acute Studies – End-Use Products**	Acute toxicity studies on end-use products are necessary to determine the potential hazards from acute exposures. Acute data are used for classification purposes and for the development of appropriate precautionary statements for product labels. Acute studies identify relative acute toxicities by different routes of exposure as well as the potential to produce irritation and sensitization. It should be noted that the PMRA does not endorse irritation testing that seriously compromises animal welfare. Waivers should be requested if the test material is known to be severely irritating or corrosive, or if irritation potential can be estimated from other reliable information. For more detail on potential waivers for acute toxicity studies, consult OECD Series on Testing and Assessment No. 237 Guidance Document on Considerations for Waiving and Bridging of Mammalian Acute Toxicity Tests (2016). For end-use formulations in which more than one active ingredient is present, a full complement of acute studies is necessary to identify acute hazards and assist in determining acceptable labelling statements. In addition, where the combination of active ingredients is suspected to be of greater than additive toxicity based on known information (for example, acute testing results, mode of action, quantitative structure-activity relationships or other), additional information such as a short-term toxicity study may be required.
4.6.1	Acute Oral	The preferred species is the rat. Not required if the test substance is a gas or highly volatile liquid.
4.6.2	Acute Dermal	The preferred species is the rat or the rabbit. Not required if the test substance is a gas or highly volatile liquid. Not required if the test substance is corrosive to skin or has a pH lower than 2 or greater than 11.5. As per SPN2017-03, this study is only required in exceptional cases. Refer to SPN2017-03 for more details.
4.6.3	Acute Inhalation	The preferred species is the rat. Required if the test substance consists of, or under conditions of use will result in, a respirable material (for example, gas, vapour, aerosol or particulate).
4.6.4	Primary Eye Irritation	The preferred species is the rabbit. Not required if the test substance is corrosive to skin or has a pH lower than 2 or greater than 11.5.
4.6.5	Primary Dermal Irritation	The preferred species is the rabbit. Not required if the test substance is a gas or highly volatile liquid. Not required if the test substance is corrosive to skin or has a pH lower than 2 or greater than 11.5.
4.6.6	Dermal Sensitization	Preferred species is guinea pig (maximization and Buehler assays) or mouse (local lymph node assay). Not required if the test substance is corrosive to skin or has a pH lower than 2 or greater than 11.5; however, diluted end-use product testing may be required if the end-use product is diluted under conditions of use.

Data Code	Title	Conditions/Guidance (Updated from DIR2005-01)
4.6.7	Potentiation/ Interaction	If available.
4.6.8	Other Acute Studies	If available - include studies that elaborate on the toxicity profile of a test substance.
4.6.9	Safety to Treated Animals	May be required if the product's use will result domestic animals being exposed through, but not limited to, direct application or consumption of treated feed. Refer to DACO requirement for specific use-site category.
4.7	**Short-Term Studies – End-Use Products**	If available. Route-specific short-term toxicity data on the EP may be required if the potential toxicity of the end-use product is greater relative to the technical grade active ingredient, and depending on the use pattern and increases toxic or pharmacologic effects.
4.8	Other Studies / Data/Reports	If available – includes data that elaborate on the toxicity profile of the end-use product.

Occupational/Residential Exposure Data Requirements: DACO Part 5 – End-Use Product

Data Code	Title	Conditions/Guidance
5	**Exposure (Occupational and/or Residential/Bystander)**	
5.1	Summaries	**This section is an overview of supporting information. All studies, rationales, foreign reviews, DERs, should be submitted under the appropriate DACO.** Summarise occupational and residential exposure data and include cross-reference to any data submitted under a different submission number that also pertains to the current submission. If the application relies on a precedent product or proprietary data belonging to another registrant, please cite the relevant information and provide a Letter of Access.
5.2	Use Description/ Scenario (Application and Postapplication)	Demonstrate access to Residential Joint Venture, if applicable. This includes information that fully describes the use of the product and human activity associated with its use. Qualitative information that will help characterize the exposure should be included here and can be divided into mixer/loader/applicator (M/L/A) and postapplication categories. The sources of the information should be cited (for example, label, grower groups, surveys, custom applicators, agricultural experts and associations, databases, etc.). Specific information should be provided for different product users where relevant (for example, farmers vs. custom applicators; homeowner vs. pest control operator). All numerical values should be reported as fully as possible (for example, min, max, mean). Also see Appendix III for additional information that should be included under DACO 5.2.
5.3	Pesticide Handlers Exposure Database	**One of DACO 5.3, 5.4 or 5.5 is required.**

Data Code	Title	Conditions/Guidance
	Assessment; Agricultural Handlers Exposure Task Force Database; Outdoor Residential Exposure Task Force Database (or other database)	**Applicant-Generated Risk Assessments using Databases and/or Surrogate Studies:** Submit the occupational/residential risk assessments for M/L/A exposure. Describe inputs and reference any default values and database/Task Force or surrogate data used. Explain how the surrogate data are representative of the exposure scenarios assessed. (Refer to DACO 5.6 for postapplication assessments) Please submit the actual studies under the appropriate DACO (i.e., data used in the risk assessment need only be referenced under DACO 5.3). Access to Task Force or surrogate data used in the risk assessment must be provided. Please reference all sources of inputs or assumptions for the risk assessment (for example, area treated per day, etc.). Additional guidance for specific products is described below: **Agricultural Uses (except seed treatment products)** Submit M/L/A exposure assessment using version 1.1 of the Pesticide Handlers' Exposure Database unless access to the Agricultural Handlers Exposure Task Force Database can be demonstrated, if appropriate scenarios/data are available. If the Pesticide Handlers' Exposure Database or Agricultural Handlers Exposure Task Force exposure scenarios/data are not applicable to the proposed product, provide exposure data under DACO 5.4/5.5, or demonstrate access to other surrogate data used in the risk assessment. **Seed treatment products** Submit risk assessments for the various exposure scenarios (on-farm treatment, commercial seed treatment, and planting), worker tasks (mixer/loader, treater, bagger, etc.), and seed types. Submit the exposure data used in the risk assessment under DACO 5.4/5.5/5.6/5.7, or demonstrate access to Seed Tropex Task Force data and/or other surrogate data used in the risk assessment. **Residential Uses:** Submit M/L/A risk assessments for the potential exposure scenarios (i.e. for commercial applicators or homeowners). Provide the exposure data used in the risk assessment under DACO 5.4/5.5, or demonstrate access to the data supporting the 2012 USEPA Residential standard operating procedures, and/or other surrogate data used in the risk assessment. Antimicrobial Uses Submit chemical handler exposure assessments using submitted DACO 5.4/5.5 exposure data, or using the Chemical Manufacturers Association Antimicrobial Assessment Study and/or other surrogate data. Please demonstrate access to the Antimicrobial Exposure Assessment Task Force and provide a scientific rationale bridging the proposed use to an occupational scenario assessed from the

Data Code	Title	Conditions/Guidance
		study used. Demonstrate access to other surrogate data used in the risk assessment. Wood preservative Uses Submit mixer/loader/applicator risk assessments using submitted DACO 5.4/5.5 exposure data, or using the Sapstain Industry Group study for antisapstain products, the American Chemistry Council exposure data for heavy duty wood treatment products, or other surrogate data, if applicable. If the Sapstain Industry Group study, American Chemistry Council study, or other surrogate data are used in the risk assessment, demonstrate access to these data.
5.4	M/L/A: Passive Dosimetry Data	
5.5	M/L/A: Biological Monitoring Data	
5.6	Agricultural Re-entry Task Force (or other database)	DACO 5.6 and/or 5.7 may be required if there is potential for postapplication exposure. Other databases include the Non-Dietary Exposure Task Force database. For residential indoor uses on surfaces, risk assessment is required only when there is potential for postapplication exposure. Postapplication passive dosimetry data may be required to refine risk assessments. **Applicant-Generated Risk Assessment using Databases and/or Surrogate Studies:** Demonstrate access to the Agricultural Re-entry Task Force data or other Task Force data, if applicable. Agricultural Uses: For postapplication exposure, submit the risk assessment using default agricultural transfer coefficients from USEPA Policy 3.0, unless DACO 5.6/5.7/5.9 data are provided, or access to the Agricultural Reentry Task Force (ARTF) Database and/or other surrogate data used in the risk assessment is demonstrated. Residential Uses: Submit risk assessments for the potential postapplication exposure scenarios (for example, from treated turf, insect repellents, treated surfaces, items, or pets, etc.). Provide the exposure data used in the risk assessment under DACO 5.6/5.7/5.9, or demonstrate access to the 2012 USEPA Residential standard operating procedures and/or other surrogate data used in the risk assessment. Antimicrobial Uses: Submit a postapplication risk assessment that characterizes the potential exposure of industrial workers in each facility when handling finished products and of consumers contacting finished products which were manufactured using the treated material. Provide exposure data used in the risk assessment under DACO 5.6/5.7 or demonstrate access to surrogate data used in the risk assessment.

Data Code	Title	Conditions/Guidance
		Wood Preservative Uses: For heavy duty wood preservatives, submit postapplication risk assessments using submitted exposure data (DACO 5.9).
5.7	Postapplication: Biological Monitoring Data	See DACO 5.6. One of DACO 5.7 or 5.8 may be required for products that are directly applied to human skin. Required in the absence of Dermal Absorption data (see DACO 5.8), or for refining risk assessments for swimming pool use.
	Dermal Absorption Data	See DACO 5.7. Required for refining risk assessments. If no data are submitted, a default of 100% dermal absorption is used to assess exposure. To refine the dermal absorption value, DACO 5.8A and 5.8B may be submitted. Applicants wishing to submit in vitro data should contact the PMRA regarding appropriate strategies and study designs. In the absence of Dermal Absorption studies, the applicant may provide a scientifically-based rationale using a weight-of-evidence approach based on the *OECD Guidance Notes on Dermal Absorption (Series on Testing and Assessment No. 156)* to refine the dermal absorption value down to 50%.
5.8A	Dermal Absorption (in vivo)	An in vivo study, typically conducted with rodents, from which estimates of dermal absorption can be derived. Refer to the USEPA's *Office of Prevention, Pesticide and Toxic Substances Test Guidelines Series 870, Health Effects Test Guidelines* (formerly Subdivision F), OECD Guidance Document for the Conduct of Skin Absorption Studies: OECD Testing and Assessment Number 28, and OECD Guideline for Skin Absorption: In vivo Method No. 427, for guidance on conducting in vivo dermal absorption studies on rodents. If performing in vivo studies involving human volunteers or monkeys, refer to the following references: • Feldmann, R.J., Maibach, H.I. (1974). Percutaneous penetration of some pesticides and herbicides in man. *Toxico Appl. Pharmacol.* **28:** 126–132. • Wester, R.C., Maibach, H.I. (1985). In vivo percutaneous absorption and decontamination of pesticides in humans. *J. Toxicol. Environ. Health* **16:** 25–37.
5.8B	Dermal Absorption (in vitro)	In vitro studies alone are insufficient for determining the dermal absorption pattern of a given pesticide. However, in vitro data may be useful when combined with other information in a weight-of-evidence approach for predicting dermal absorption. When in vitro data is submitted to the agency, the NAFTA group recommends submission of a data set consisting of a "Triple Pack" of in vitro human and animal studies and an in vivo animal study. If performing in vitro studies, refer to the following references: • NAFTA (2008) NAFTA Dermal Absorption Group Position Paper on the Use of in vitro Dermal Absorption Data in Risk Assessment. Unpublished. • USEPA (1998) Office of Prevention, Pesticide and Toxic Substances Human Effects Test Guidelines for Dermal Penetration (Office of Prevention, Pesticide and Toxic Substances 870.7600). • OECD (2004) OECD Environmental Health and Safety Publications Series on Testing and Assessment No. 28, Guidance Document for the Conduct of Skin Absorption Studies Environment Directorate. Organisation for the Economic Co-operation and Development. • OECD (2004) OECD Guideline for Skin Absorption: in vitro Method No. 428.
		A study that estimates the amount of residue that can be dislodged or transferred from a surface may be submitted to refine dislodgeable/transferable residue values used in postapplication risk assessment (i.e., in lieu of applying default values – see below).

Data Code	Title	Conditions/Guidance
	Dislodgeable Residue Data	Media of interest include foliage (DACO 5.9A,B,C), soil (DACO 5.9A,B,C), turf (DACO 5.9B), indoor surfaces such as hard surfaces, carpets (DACO 5.9C), the fur of companion animals (DACO 5.9C), or treated articles (DACO 5.9D). Studies representative of dislodgeable/transferable residues may be required for specific use sites (for example, greenhouse, field, or high tunnel scenarios), as well as on different types of crops. This data, in conjunction with transfer coefficients, may be suitable for estimating postapplication exposure. Refer to the *Office of Prevention, Pesticide and Toxic Substances Test Guideline Series 875, Occupational and Residential Exposure Test Guidelines: Group B, Post Application Monitoring Guidelines* (formerly Subdivision K) for guidance on conducting these types of studies.
5.9A	Dislodgeable Residues (Foliar, Soil, Surface) - Agricultural	In the absence of chemical-specific dislodgeable/transferable residue data, default values will be used: • For foliar use on agricultural/ornamental crops: 25% of the application rate is the default dislodgeability value on the day of application, with 10% daily dissipation for outdoor scenarios, and 0% dissipation for greenhouse scenarios • For turf: 1% of the application rate is the default transferable residue on the day of application, with 10% daily dissipation • For residential scenarios: default values are specified in the 2012 USEPA Residential standard operating procedures. For heavy duty wood preservative products, a wipe study for treated wood is required (R). For other scenarios, dislodgeable/transferable residue data is conditionally required (CR).
5.9B	Dislodgeable Residues (Foliar, Soil, Surface) - Turf	
5.9C	Dislodgeable Residues (Foliar, Soil, Surface) – Indoor Surface	
5.9D	Dislodgeable Residues (Surface) – Treated Articles	
5.10	Ambient Air Samples (Indoor – Outdoor)	Ambient air samples and dissipation data are required if there is potential for postapplication or bystander inhalation exposure. Products with potential postapplication or bystander inhalation exposure include fumgiants, preservatives used to treat materials that produce dust during postapplication activities, etc. Ambient air samples are to be taken in areas of potential exposure to estimate inhalation exposure, where such exposure may occur, or to establish appropriate re-entry intervals. Breathing zone samples are preferable for estimating inhalation exposure. Refer to the *Health Canada Regulatory Proposal PRO98-04 Postapplication Exposure Monitoring Test Guidelines* for guidance on conducting air sampling. Information about the threshold limit value of the active ingredient, if applicable, is also helpful.
5.11	Glove/Clothing Penetration Data	
5.12	Epidemiology	
5.13	Package Integrity Study	

Data Code	Title	Conditions/Guidance
5.14	Other Studies/ Data/Reports	
5.15	Dust-Off Studies (or other bridging study)	May be required if surrogate chemical and seed studies are used in the risk assessment Dust-off studies may be required to bridge submitted surrogate dosimetry studies to the proposed crops. Acceptable dust off data comparing the relative dustiness of seeds treated with the proposed formulation, to the dustiness of the seeds used in the surrogate passive dosimetry studies submitted, may be required. The basic requirement is that the dust-off study compares the seed and product in the seed treatment study (surrogate seed type and product) to the proposed seed and product that is being evaluated. It is recommended that the seed be treated exactly as it is intended to be treated, including any additives such as stickers or polymers that reduce dust generation. The dust measurements are not used quantitatively, but are simply used to help demonstrate whether the dust generated by the proposed crop and formulation/product, is either less than or greater than that generated by the surrogate seed and formulation/product (i.e. relative dustiness). If the relative dustiness is found to be less than that expected from the surrogate seed type, then the surrogate data is determined to be adequately representative of the scenario. It is important to note that there is currently no standardized protocol for dust-off studies. Applicants wishing to submit dust-off studies for the purpose of bridging surrogate data should contact the Health Evaluation Directorate regarding appropriate strategies and study designs.
12.5.5	Foreign Reviews	If available, or if unavailable for submission, please indicate if another regulatory authority has completed specific data reviews.
12.7.5	Applicant Generated Study Reviews	Study reviews of DACO Part 5 data prepared by applicants using standard review templates. a) For Canada-only applications (i.e., not Joint Review applications), NAFTA study profile templates are requested [although use of OECD format is also acceptable]. NAFTA study profile templates are available upon request. These templates are also available on the USEPA website b) For Joint Review applications of conventional (traditional) chemicals - OECD format is required .

Agricultural Uses: Food Residue Chemistry Data Requirements: DACO Parts 6 (Technical Grade Active Ingredient & End-Use Product) and 7 End-Use Product[1]

Data Code	Title	Conditions/Guidance
6	**Metabolism/Toxicokinetics Studies (Technical Grade Active Ingredient or End-Use Product)**	
6.1	Summaries	**This section is an overview of the supporting data. All studies, rationales, foreign reviews, DERs, should be submitted under the appropriate DACO Part.** Summarize background information that provides context to/purpose of the submission. • Highlight changes/additions requested to any current registration. • Explain how the submitted metabolism data support the proposed uses and/or MRL request (including imported commodities). • Include any rationales and/or data waiver requests to justify the acceptability of the data. Also, include any previously submitted data (with references, submission number and PMRA number, if available) that are required in the context of the current request(s). • If the application relies on a precedent product or proprietary data belonging to another registrant, please cite the relevant information and provide a Letter of Access. Please cross-reference any foreign reviews of the newly submitted metabolism data, if available (for example, USEPA, DERs).
6.2	Livestock	Animals produced in an aquatic environment for human consumption. Fish/Shellfish: When fish/shellfish may be exposed to the pesticide or its degradation products, a fish/shellfish metabolism study is required.
		As per DIR98-02, animal metabolism studies are required whenever a pesticide is applied to crops or crop parts used for feed.
		As per DIR98-02, animal metabolism studies are required whenever a pesticide is applied directly to livestock or to crops or crop parts used for feed, or when animal premises are to be treated. In general, separate metabolism studies should be conducted for ruminants and poultry. Non-ruminant (swine) metabolism studies may be necessary if the rat metabolism is significantly different from the ruminant or poultry metabolism. **Note**: If samples are stored frozen for more than four to six months during the livestock metabolism study, evidence demonstrating that the identity of residues did not change during the storage period from collection to final analysis must be provided.
		No feed items associated with greenhouse uses.
6.3	Plants	Plants produced in an aquatic environment for human consumption. When the plant (produced in the aquatic environment) may be exposed to the pesticide or its degradation products, an aquatic plant metabolism study is required.
		As per DIR98-02, plant metabolism studies are required for a minimum of three diverse crops unless the pesticide is to be used on only one or two crops. If the metabolism in three diverse crops, i.e., crops whose agronomic characteristics are different, is similar (metabolic pathways and major metabolites), then the metabolism in other crops is assumed to be similar.

Data Code	Title	Conditions/Guidance
		A plant metabolism study should be submitted for each type of crop group for which use is proposed. Metabolism studies reflecting each of the intended use pattern such as foliar, soil/seed, or post-harvest treatments should be provided. According to OECD, crops can be considered to belong to one of five categories for crop metabolism studies: root vegetables, leafy crops, fruits, pulses and oilseeds and cereals (refer to OECD Test guideline 501 for details). One crop from a group will cover the entire group for purposes of metabolism in those crops within the group. In order to extrapolate metabolism of a pesticide to all crop groupings, metabolism studies on a minimum of three representative crops (from the five different crop categories) should be conducted. **Note**: If samples are stored frozen for more than four to six months during the plant metabolism study, evidence demonstrating that the identity of residues did not change during the storage period from collection to final analysis must be provided.
6.4	Other Studies/ Data/Reports	If available and relevant to the current submission.
12.5.6	Foreign Reviews - Plant/Livestock Metabolism	If available. It is highly recommended to include the foreign reviews (for example, USEPA, DERs) of newly submitted studies, when available, to facilitate the review process, or if unavailable for submission, please indicate if another regulatory authority has completed specific data reviews.
12.7.6	Applicant Generated Study Reviews	Study reviews of Plant and Livestock Metabolism Data prepared by applicants using standard review templates. a) For Canada-only applications (i.e., not Joint Review applications), NAFTA study profile templates are requested [although use of OECD format is also acceptable]. NAFTA study profile templates are available upon request. These templates are also available on the USEPA website b) For Joint Review applications of conventional (traditional) chemicals – OECD format is required
7	**Food and/or Feed Residue Studies (End-Use Product)**	
7.1	Summaries	**This section is an overview of the supporting data. All studies, rationales, foreign reviews, DERs, should be submitted under the appropriate DACO Part**. Summarize background information that provides context to/purpose of the submission. • Highlight changes/additions requested to any current registration. • Explain how the submitted residue data supports the proposed uses, amendments to the use pattern and/or MRL request (including imported commodities). • Include any rationales and/or data waiver requests to justify the acceptability of the data (for example, explain how submitted American data are representative of Canadian requirements, why the residue data are applicable to support a new formulation, why the trials can be considered independent, etc). • Include any previously submitted data (with references, submission number and PMRA number, if available) that are required in the context of the current request(s). • If the application relies on a precedent product or proprietary data belonging to another registrant, please cite the relevant information and provide a Letter of Access. Please cross-reference foreign reviews of the newly submitted residue data, if available (for example, USEPA, DERs), and include the status in the United States with respect to the current request.

Data Code	Title	Conditions/Guidance
7.2	**Analytical Methodology (Plant and/or Animal Commodities)**	
7.2.1	Residue Trial Analytical Methodology (Plant and/or Animal Commodities)	As per DIR98-02, analytical methodologies to determine all components of the residue definition (both for enforcement and risk assessment purposes) are required for the analysis of samples from all the magnitude of residue studies (for example, crop field trials, processing studies and feeding studies).
7.2.2	Enforcement Analytical Methodology (Plant and/or Animal Commodities)	An enforcement method to determine all components of the residue definition (for enforcement purposes) is required. In order to demonstrate the acceptability of the enforcement method, an independent laboratory must successfully validate the method and extraction efficiency of bio-incurred residues (with samples taken from metabolism studies) must be demonstrated. When a use results in no expectation of quantifiable residues in animal commodities (meat, milk and egg) from feeding of treated feed, an enforcement method in animal commodities is required in order to establish MRLs at the LOQ of the enforcement method. Note: • For crops that are only feed items (for example, forage grasses, pasture, etc.), an enforcement method in plant matrices is not required as MRLs are no promulgated in feed crops in Canada.
7.2.3A	Inter-laboratory Analytical Methodology Validation	
7.2.3B	Extraction Efficiency (Radiovalidation)	

Data Code	Title	Conditions/Guidance
7.3	Freezer Storage Stability Tests	Freezer storage stability data are required in conjunction with magnitude of residue studies (for example, crop field trials, processing studies and feeding studies) if samples are stored frozen for more than 30 days between collection and analysis (not extraction of the samples). If the pesticide is known to be volatile or labile, then freezer storage stability data are required. When generating freezer storage stability data, analysis of day-0 samples (spiked samples) must be achieved. As per DIR98-02, if residues are shown to be stable in a given commodity, the residues in other crops of the same crop group would be assumed to be stable for the same time period under the same experimental conditions. At least five diverse crops need to be tested in order to be able to make the assumption that residues are stable in all crops; (1) an oilseed, soybean or nut, (2) a non-oily grain, (3) a leafy vegetable, (4) a root crop, and (5) a fruit or fruiting vegetable. The fruit/fruiting vegetable should be an acidic commodity, such as citrus or tomatoes. Field corn grain is to be considered a non-oily grain as opposed to an oilseed. With respect to processed commodities, if residues are shown to be stable in the three major types of processed fractions derived from oilseeds, grains, fruit/fruiting vegetables, additional storage stability data will generally not be required. With respect to animal commodities, storage stability data are required for muscle from cattle or poultry, liver from cattle or poultry, milk and eggs. If residues are stable in these matrices, analyses of other tissues, such as fat and kidney, will not be required. According to OECD (Test Guideline 506) in the cases involving crop commodities, the principles of extrapolation between commodities within specific commodity categories is recommended and the commodity categories are as follows: commodities with high water content; commodities with high acid content; commodities with high oil content; commodities with high protein content; and commodities with high starch content. It is recognised that some commodities can fit into more than one category. If residues are shown to be stable in all commodities studied, a study on one commodity from each of the five commodity categories is acceptable. In such cases, residues in all other commodities would be assumed to be stable for the same duration of time under the same storage conditions. If there is no observed decline of residues across the range of the five different commodity category, then specific freezer storage stability data for processed foods will not be needed.

Data Code	Title	Conditions/Guidance
7.4	**Crop Residue Data (Food and/or Feed Commodities)**	
7.4.1	Food and/or Feed Crop Residue Trial Study	In lieu of traditional field trial studies, a radiolabeled uptake study (Refer to DIR2003-02; Harmonization of Regulation of Pesticide Seed Treatment in Canada and the United States) can be submitted. As per DIR2003-02: "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 in all plant tissues are less than 5 ppb, no further studies are required. However, the analytical methodology is always required […]. An MRL would then be established based on the analytical method's LOQ, provided that it is sufficiently low from an analytical chemistry standpoint and for risk assessment purposes. If total radioactive residuess 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)."
		Residue data must be generated for all food and feed crop parts according to the proposed use directions (includes Part 7.4.6). Greenhouse uses: As per DIR98-02: Two trials and eight treated samples are sufficient (geographical location irrelevant) For greenhouse residue data generated as of January 2012, refer to DIR2010-05. As per DIR2010-05, four trials are required for greenhouse cucumbers, lettuce, peppers and tomatoes and two trials for mushroom grown in mushroom houses. Post-harvest uses: As per DIR98-02, two trials and eight treated samples are sufficient (geographical location irrelevant) Agricultural field uses: For the number and locations of field trials, refer to DIR98-02. For field trial data generated as of January 2012, refer to DIR2010-05.
		Residue data must be generated as per the proposed use pattern. If the stored crops are intended for processing, a processing study must be generated as per DACO Part 7.4.5.
7.4.2	Residue Decline Study	Greenhouse uses: one of the four trials must be a residue decline trial.
		Agricultural field uses: As per DIR98-02, residue decline studies are often required for many uses on crops needing ≥ 5 trials. Residue decline studies are not required for crops needing ≤ 3 trials, if Preharvest Interval is > 14 days.

Data Code	Title	Conditions/Guidance
		Dependant on the results from 7.4.1. Fumigation uses: For fumigation scenarios, residue data at different time points as a function of the dissipation of residues during/after the aeration protocol are recommended to help mitigate risks of concern when identified.
7.4.3	Confined Crop Rotation Trial Study	As per DIR98-02, studies on confined rotational crops are conditionally required for uses of pesticides on terrestrial food/feed crops and aquatic food crops. A rotational crop use is any field-vegetable crop use, aquatic crop use or any other site use on which it is reasonably foreseeable that any food or feed crop may be produced after the harvest of a treated crop. Rotational crop studies are not required for uses of pesticides on asparagus, avocado, banana, berries, citrus fruits, coconut, cranberry, date, fig, ginseng, globe artichoke, grape, guava, kiwifruit, mango, mushroom, olive, papaya, passion fruit, pineapple, plantain, pome fruits, rhubarb, stone fruits and tree nuts.
7.4.4	Field Crop Rotation Trial Study	A limited field accumulation study is triggered by the results of the confined crop rotation trial study (Part 7.4.3). As per DIR98-02, if the total radioactive residues [or residues that need to be regulated] observed in the confined accumulation study are equal or exceed 0.01 ppm in the rotational crop at the desired rotational interval or at 12 months, then field accumulation trials should be performed.
7.4.5	Processed Food/Feed	As per DIR98-02, whenever there is a possibility of residue levels in processed foods/feeds exceeding the level in the raw agricultural commodity, processing data are required. Processing data are required for apple, sugarbeet, cacao, canola, cereal grains, citrus fruits, coconut, coffee, field corn, cotton, fig, flax, grape, dried herbs, olive, peanut, peppermint/spearmint, pineapple, plum, potato, safflower, sesame, soybean, sugarcane, sunflower, tea and tomato. With the exception of small grains (cereal), PMRA will not normally translate data between crops. In the case of small grains, a processing study on wheat satisfies the requirement for studies on barley, buckwheat, millet, oats and rye if the pesticide is applied to all these crops in a similar manner and comparable residue levels occur in the grains.
7.5	Animal Derived Commodities Residue Data (from feeding of treated crops)	Whenever pesticide residues are observed in feed items, feeding studies are required.
		No feed items associated with greenhouse uses.

Data Code	Title	Conditions/Guidance
7.6	Animal Derived Commodities Residue Data (external application)	Residue studies generated according to the proposed use pattern (external application) are required if the pesticide is to be applied directly to animals or when animal premises are to be treated.
7.8	Other Studies/ Data/Reports	If available and relevant to the current submission.
12.5.7	Foreign Reviews of Food and Feed Residue Studies	If available. It is highly recommended to include the foreign reviews (for example, USEPA, DERs) of newly submitted studies, when available, to facilitate the review process, or if unavailable for submission, please indicate if another regulatory authority has completed specific data reviews.
12.7.7	Applicant Generated Study Reviews	Study reviews of Residue Data prepared by applicants using standard review templates. a) For Canada-only applications (i.e., not Joint Review applications), NAFTA study profile templates are requested [although use of OECD format is also acceptable]. NAFTA study profile templates are available upon request. These templates are also available on the USEPA website. b) For Joint Review applications of conventional chemicals – OECD format is required.

Value Data Requirements: DACO Part 10 – End-Use Product

Data Code	Title	Conditions/Guidance
10	**Value (applicable to each pest/site or host combination)**	
10.1	Value Dossier	A report that summarizes the value information provided to support an application. The report should follow the PMRA value review template.
10.2	**Efficacy**	This requirement may be addressed through trials, use history, published information, or scientific rationales.
10.2.1	Mode of Action (Technical Grade Active Ingredient) and Description of the Product	A description of the formulated product, including its name, active ingredient, mode of action, guarantee, and formulation type. Information on the active ingredient's chemical class, site of action classification, mechanism of selectivity, absorption or translocation in the host should be included.
10.2.2	Description of Pest Problem	For agricultural uses: A description of the importance of the pest (major/minor) and why pest management is required (affects yield, increases chance of secondary infections/infestations, part of complex, decay, etc.). Information regarding the economic or pest threshold for Canadian users should be provided. For non-agricultural uses: A description of the pest problem for the use-site(s) where the proposed product will be used must be provided.

Data Code	Title	Conditions/Guidance
		The information should include the description of organisms causing the contamination/decay/fouling and their possible sources and the consequences of non-treatment.
10.2.3	**Efficacy Trials**	Required if use history is not available or scientific rationales are not appropriate to support proposed use. This specifically addresses the efficacy of the product in relation to a pest claim.
10.2.3.1	Efficacy Summary Table	Required if efficacy trials are being provided. This is a summary of the efficacy trials being submitted in an Excel format following the template provided in the website/efficacy guidelines. Results of statistical analyses should be included, as appropriate. Required if submitting trial data.
10.2.3.2	Efficacy: Laboratory, Growth Chamber Trials	Required if small plot trials are not appropriate or available to support label claims and scientific rationales are not sufficient to support the proposed use. These are individual study reports of laboratory trials to support the application.
10.2.3.3	Efficacy: Small-scale Trials (Field, Greenhouse)	Required if applicable and use history information is not available and scientific rationales are not sufficient to support the proposed use. These are individual trial reports of small plot studies or published information on research trials used to support the application.
10.2.3.4	Efficacy: Operational Trials	Required if applicable and there is a need to demonstrate value of proposed use under typical commercial/operational conditions or to show the performance of the product when used in an Integrated Pest Management system or under commercial operations. These are individual trial reports of studies conducted on a field scale (for example, use of commercial scale farming equipment, incorporation of Integrated Pest Management strategies, materials such as wood tested outdoor, etc.). Appropriate experimental design is key in order to obtain meaningful results.
10.2.4	Use History	Required if little or no efficacy or crop tolerance data is available or if a scientific rationale is not appropriate since there is no basis to form a scientific argument. If the product is registered in a foreign jurisdiction with a comparable pesticide regulatory system, use history information may be submitted to supplement or replace the required efficacy information to support a label claim. This consists of (1) comparison of use patterns, (2) description of the product's effectiveness against the pest and its potential for adverse effects on the crop or use site and (3) a validation statement from a resource person with direct experience with the product. Templates for compiling this information are available upon request.
10.3	**Adverse Effects on Use-Site**	This requirement may be addressed through trials, use history, published information, or scientific rationales.
10.3.1	Summary Table	Required if specific trials on non-safety adverse effects are being provided. A summary of the trials in an Excel format (following the template provided in the website/efficacy guidelines) is required if dedicated phytotoxicity trials were conducted. Otherwise, a statement referring to absence of phytotoxicity may be made under the comments column of the efficacy trials.

Data Code	Title	Conditions/Guidance
10.3.2	Non-Safety Adverse Effects [for example: to crop, site of application (discoloration, corrosion), etc.]	These are individual trial reports, rationales or use history information giving details of the adverse effects of the treatment on the crop or use-site.
10.3.3	Damage to Rotational Crops	Required for all soil applied herbicides and herbicides that are persistent in soil. Effects of fungicides or insecticides on rotational crops may be addressed within the section on efficacy. Information demonstrating the effect of a herbicide application on subsequent crops grown in rotation, conducted under climatic and edaphic conditions representative of the area of use.
10.4	**Social and Economic Impact**	Provide information explaining why the product is needed as well as how and to what extent product registration would benefit Canadian users.
10.5	**Sustainability and Consideration of Benefits**	This section consists of information relating to the benefits of the proposed pesticide use, including its social and economic impact, compatibility with current management practices, its role in resistance management and any potential health, safety or environmental benefits.
10.5.1	Survey of Alternatives (conventional and non-conventional)	This is a list of conventional and non-conventional products that are currently registered for the proposed use. The date when the search was conducted should be reported.
10.5.2	Compatibility with Current Management Practices, Including Integrated Pest Management	Discuss how use of the product contributes to sustainability and how it can be integrated into current pest management practices.
10.5.3	Resistance Management	Where appropriate, an analysis of the proposed use pattern's impact on resistance management is required. The sponsor should indicate whether the use pattern is consistent with current resistance management recommendations. Information on baseline pest sensitivity and reports of laboratory-induced or field resistance should also be provided, when they are available.
10.5.4	Contribution to Risk Reduction	Required if applicable Information explaining the contribution of the product to risk reduction such as if the product is considered to replace or reduce applications of pesticide chemistries with health or environmental concerns.

Data Code	Title	Conditions/Guidance
10.5.5	Health, Safety and Environmental Benefits	Required if applicable. Information regarding the benefits of the proposed use could be described. This is not a summary of the supporting information for the human health or environmental risk assessment. An explanation of specific benefits such as arising from the management of a poisonous or allergenic weed or an invasive alien species or the control of pests that have human health impact could be included, where appropriate.
10.6	Other Studies/Data/Reports	Required if information other than those identified above are needed to assess the value of the proposed use. Other documents that are vital to the value review, such as a certificate of electrical safety.
12.5	**Foreign Reviews**	Reviews relating to the value of the proposed use from the pesticide regulatory organization in foreign countries.
12.5.10	Foreign Reviews Pertaining to Value	If available. Reviews relating to the value of the proposed use from the pesticide regulatory organization in foreign countries should be submitted, or if unavailable for submission, please indicate if another regulatory authority has completed a value review.
12.7.10	Applicant Generated Study Reviews	Study reviews prepared by applicants using standard review templates. *Required if results of research trial results provided to support an application are not included under DACO 10.2.2, 10.2.3, 10.2.4, 10.3.2, or 10.3.3. a) For Canada-only applications (i.e., not Joint Review applications), NAFTA study profile templates are requested [although use of OECD format is also acceptable]. NAFTA study profile templates are available upon request. b) For Joint Review applications of conventional (traditional) chemicals - OECD format is required

Appendix I

Analytical Data Reporting Format

This Appendix is included primarily to address the issue of content and to suggest a consistent format for ease of data review; however, it is the content that is of primary significance and a report need not be rewritten to adapt to the format suggested.

Preliminary pages

Title/cover page

Table of Contents

Introduction and Summary

Scope Identify the analyte(s) for which the method has been validated.

Source of method Include a reference to a published method, such as sources listed below, if applicable.

References for Developing Chemistry Data

Applicants should ensure that they have the latest editions of the following documents.

1. Agriculture Canada, Guidelines for Determining Environmental Chemistry and Fate of Pesticides, Trade Memorandum T-1-255, 1987.

2. American Society for Testing and Materials, Annual Book of ASTM Standards; ASTM, Philadelphia, PA, U.S.

3. Association of Official Analytical Chemists, Official Methods of Analysis of AOAC- International; AOAC-International, Arlington, VA, U.S.

4. Collaborative International Pesticide Analytical Council, CIPAC Handbooks, CIPAC, Hatching Green, Harpenden, Hertfordshire, England, 1970 - 1995.

5. Organisation for Economic Co-operation and Development, Guidelines for Testing of Chemicals, OECD 101 - 117; OECD, Paris, France, 1981 - 1995.

6. United States Environmental Protection Agency, Product Properties Test Guidelines (830 Series); U.S. Government Printing Office, Washington, DC, U.S., 1996.

7. United States Environmental Protection Agency, EPA Manual of Chemical Methods for Pesticides and Devices, 2nd edition; AOAC, Arlington, VA, U.S., 1992.

Analytical principles	Provide a brief description, including the identification of the chemical species determined, the range over which the analyte(s) has/have been analysed and, for impurities, the limits of detection and sensitivity.

Materials and Methods

Equipment	List and describe.
Reagents and standards	List and describe source and preparation.
Analytical procedure	Detail in a stepwise fashion, with special emphasis on reagents or procedural steps requiring special precautions to avoid safety or health hazards, including: (i) preparation of sample; (ii) extraction (if any); (iii) clean-up (if any); (iv) derivatization (if any); and (v) instrumental analysis, including: a) description - make/model, type/specificity of detectors, columns, packing materials, carrier gases, mobile phase, etc.; b) operating conditions - flow rates, detector wavelength, temperatures, voltage, etc.; and c) calibration procedures.
Methods of calculation	Describe in a stepwise fashion.
Other	Identify any and all relevant information the applicant considers appropriate to provide a complete and thorough description of the analytical methodology and the means of calculating the results, i.e., critical control points.

Results and discussion

Describe the established performance criteria for the method.

Accuracy	
Precision	Identify the number of replicates used.
LOD/LOQ	Provide definition used
Selectivity/specificity	Describe tests used to establish the lack of interferences from other product components or from solvents and materials used in the methodology.
Ruggedness testing	If performed.
Limitations	
Linear range	

Tables and figures

These are to be fully referenced to the body of the report and included where appropriate.

References

Appendices

Representative chromatograms, spectra, etc.	As applicable and in accordance with Data Code 2.13.2 and 2.13.3 for technical grade of active ingredients or ISP and Data Code 3.4.1 for Manufacturing Concentrates (MA) and End-Use Products.

Other Any relevant material not fitting into any other sections of this report.

Appendix II

Submittal of Samples

Pursuant to the Pest Control Products Regulations, the Agency may request that product-related samples be provided by applicants. The PMRA's Laboratory Services maintains a central repository of all analytical standards submitted in response to the following requirements.

For new active ingredients and new sources of registered active ingredients, the following samples are required:

(i) a 2.5 g analytical standard of the active ingredient, or if applicable, 1.0 g of each stereoisomer of an active ingredient. This refers to material that:

a) has been purified and analysed extensively to give a certified purity of the active ingredient;

b) typically contains 95% or more of an active ingredient; and

c) may be used as an analytical standard to determine the purity of the same active ingredient in a pest control product or residues of the same active in/on foods or feeds or in the environment.

ii) a 1.0-g analytical standard of any impurity, metabolite or transformation product identified as a Residue of Concern (ROC). If any compounds are difficult or expensive to obtain, 100–200 mg may suffice. Standards are to include all ROCs identified by the applicant in response to data requirements found in Regulatory Directive DIR98-02, *Residue Chemistry Guidelines*, as well as any additional ROCs identified by the PMRA during the review process. The latter scenario is unlikely to occur if the applicant proceeds through the consultation phase as recommended in the *Residue Chemistry Guidelines*. ROC analytical standards refer to material that:

a) has been purified and analysed extensively to give a certified purity of the ROC;

b) contains 95% or more of the ROC; and

c) may be used to determine the levels of the same ROC in pest control products or residues of the same compound in/on foods or feeds or in the environment.

If samples are unstable over a 2-year period, smaller amounts may be sufficient. Replacement samples may be requested after their expiry date.

The following samples may be required by the PMRA:

(i) 10.0 g of the technical grade active ingredient or ISP; and/or

(ii) 1.0-g analytical standard of impurities in the technical grade active ingredient or ISP and/or certain metabolites or degradation products. If any compounds are difficult or expensive to obtain, 100–200 mg may suffice.

Some or all of the above samples may be requested for active ingredients in products currently registered under the *Pest Control Products Act*, for example, for active ingredients under re-evaluation, or as required by the PMRA's Laboratory Services to maintain its inventory.

Samples are to be sent directly to:

Laboratory Services
Health Canada
Pest Management Regulatory Agency
Laboratory Services Building
Central Experimental Farm
Building 22
960 Carling Avenue
Ottawa, Ontario
K1A 0C6

NOTES:

1) Sample packaging must comply with the *Transportation of Dangerous Goods Act* and Regulations. Poorly packed, leaking, or otherwise damaged samples will be destroyed and replacement samples will be requested.

2) Samples must be properly labelled with concentration, weight and common or chemical names, not trade names or company codes.

3) A certificate or statement of purity including a description of the method used to determine purity must be provided with all analytical standards.

4) Storage instructions and information on shelf-life (expiry date) must be provided for analytical standards. Material safety data sheets (MSDSs) must also be provided, if available.

5) Analytical standards of impurities must be labelled to include the common name of their associated technical grade active ingredient or ISP.

6) Samples must be accompanied by correspondence indicating the reason for submission, for example, requested by the PMRA as a requirement of registration, and include a corresponding submission number, for ease of reference.

7) Unless accompanied by an MSDS, the acute oral and dermal toxicity of the sample should be supplied or at least be indicated on the sample label.

8) The shipping/customs invoice accompanying the sample should specify the chemical's name, amount, country of manufacture, value, and the fact that it is a pesticide, and also include reference to the submission number. The cost of shipping is to be borne by the applicant/registrant.

Appendix III

Additional Guidance - DACO 5.2

Use Description/Scenario (Application and Postapplication)
This includes information that fully describes the use of the product and human activity associated with its use. Qualitative information which will help characterize exposure should be included here and can be divided into mixer/loader/applicator (M/L/A) and postapplication categories. The sources of the information should be cited (for example, label, grower groups, surveys, custom applicators, agricultural experts and associations, databases). Specific information should be provided for different product users where relevant (for example, farmers vs. custom applicators; homeowner vs. pest control operator). All numerical values should be reported as fully as possible (for example, min, max, mean).

The information below is not an exhaustive list; other information that could characterize the use will be accepted. Not all items below are relevant for all use-site categories and scenarios.

Occupational Scenarios

Handler (Mixer/Loader/Applicator):

- Type of Registration – Describe the type of registration proposed (i.e. domestic, commercial, restricted, etc.).
- Site of Application – Describe the types of sites to which the pesticide is likely to be applied; for example, crops, growing regions, areas in buildings, etc. (i.e. Use-Site Categories).
- Formulation – Describe the physical and chemical properties of the formulation/active ingredient that may influence exposure (for example vapour pressure, water solubility, ionization constants, octanol-water partition coefficient, and particle size distribution, if applicable).
- Packaging – Describe current and/or proposed sizes and types of packaging.
- Application Method – Describe typical application methods and types of equipment used (for example for agricultural: groundboom, open or closed cab, nozzle size, pressure used, high volume or low volume equipment for greenhouse uses, etc.; for domestic: broadcast using handwand, volume applied per hectare, width of spray swath for residential aerosol sprays, broadcast, crack and crevice spot treatment, etc.). Be as specific as possible.
- Mixing/Loading Method – Describe tasks involved in mixing/loading procedure for each type of equipment (for example open or closed equipment, etc.), duration and frequency of mixing/loading, and number of mix/load cycles per work day.
- Clean-up and Repair Activities – Describe tasks involved in clean-up, maintenance, and repair procedures , duration and frequency of these tasks and who performs these tasks (for example do different people mix/load and apply or perform clean-up, etc.).
- Application Timing – For agricultural products, describe typical and maximum number of applications per season, frequency, timing of applications, and seasonal variation if applicable. Summarize when the product is to be applied relative to standard cultivation practices, crop height at application etc. For non-agricultural products, describe the typical and maximum number of applications per year. Summarize relevant parameters

(for example for a material preservative, the typical and maximum volume of material produced at a facility per day). Where applicable, provide the percentage of the site treated (for example border spray may represent 25% of a field treated; crack and crevice may represent 10% of a broadcast treatment).

- Application Rate – Typical and maximum application in kg a.i./ha or kg a.i./L for agricultural applications. For non-agricultural products such as home and garden products, provide information to characterize the amount handled per day (for example typical and maximum surface areas treated, containers used per day, kg a.i./L, or kg a.i./container, etc.).
- Application Volume – Typical and maximum application volumes in ha/L for agricultural applications.
- Area requiring treatment – For agricultural: typical Canadian hectarage/US acres of crop grown per farm, etc.; for domestic: typical area per room and number of rooms treated, etc.). If relevant indicate regional differences in crop sizes or application technologies (for example typical potato fields range in size depending on the region, also aerial application is used in some areas and not used in others.
- Area Treated per Day – For agricultural: provide area of crop (ha) that can typically be treated in a work day by one applicator, including typical and maximum areas (i.e. how many ha can be treated in a typical day by a farmer and or a custom applicator, etc.). For non-agricultural such as home and garden products, provide typical and maximum number of homes or buildings a pest control applicator can treat in one day, the typical and maximum area a homeowner would treat in one day, area treated using aerosols and paintbrush application in one day etc.
- Quantity of a.i. handled – The amount of a.i. typically handled in a work day by one person is characterized by area treat per day, application rate, area requiring treatment and area treated per day. See the above categories for more details.
- Working Duration – The number of years a farmer or Pest Control Officer would typically work in a lifetime. For cancer risk assessments the numbers of days a farmer or Pest Control Officer would typically work in a year.

Include data for multiple equipment types/use scenarios as applicable (for example hectares/acres treated by a farmer using tractor-groundboom vs. by a custom applicator using a high speed rig). Non-agricultural exposure data may need to be substantiated with user information.

Postapplication Scenarios

For agricultural uses provide:

- Typical Cultivation Practices – How is the crop cultivated, if applicable (for example are the crops staked, what practices are used for weed control etc.).
- Restricted Entry Intervals – Provide current/proposed restricted-entry intervals and if there is no restricted-entry interval, the reason for not establishing one.
- Crop Characteristics during Postapplication Activities – Crop height at time of postapplication activity, leaf development at time of postapplication activities, etc.
- Postapplication Activities – Potential postapplication activities that could result in exposure (for example harvesting, pruning, thinning, children playing on treated lawns, children playing on treated surfaces in homes etc.), together with a description of the

nature of the activity (for example tools used and the intensity of contact with the treated surfaces). Include varietal differences of crops, if applicable.

- Exposure Groups – Description of individuals re-entering treated areas (for example individuals re-entering treated turf may include landscape workers, individuals entering for recreational purposes, etc.; individuals re-entering treated agricultural fields may include farmers, scouts, season contract workers etc.; individuals re-entering treated homes and lawns may include children and adults).
- Repeat Exposure – If the same person conducts the activity at multiple farms (for example a professional scout could scout fields at multiple farms).
- Sources of Exposure – The exposure potential of each activity (for example specify intensity or degree of contact with foliage/treated surface, body areas likely to contact treated surfaces, etc.).
- Timing, Frequency and Duration of Postapplication Activities – For agricultural products: description of when each Postapplication activity is carried out (for example, time of season relative to product application), as well as frequency (for example, how often per day/week/year), and duration of these activities (minutes, hours). This information is important to determine if a calculated restricted-entry intervalis feasible. For non-agricultural products: description of when each Postapplication activity is carried out (for example time a home is re-entered after treatment, or an office building is reoccupied after treatment, etc.), as well as frequency (for example days of exposure per year for residents, number of times an individual or family visits a pick your own facility per year, etc.), and duration of these activities (for example the hours a child is exposed on soft or hard surfaces per day, the number of hours an adult is exposed in a day, duration of pet ownership and treatment for pet treatments, etc.).
- Residue Data – Dislodgeable Foliar Residues /Turf Transferrable Residues, transferable residue and air concentration (indoor and outdoor) data available for use in the risk assessment.
- Dissipation Data – Surface and air dissipation data available for use in the risk assessment.
- Application Rate – Typical and maximum application rates for non-agricultural applications in µg a.i./cm^2 (i.e. domestic products and commercial products applied in residential areas etc.).

Include data for multiple scenarios as applicable (for example range of crop type or varietal differences, indoor and outdoor residential application, etc.). Non-agricultural exposure data may need to be substantiated with user information.