Biopesticide Registration Improvement Course

Human Health and Safety Assessment of Non-Conventional Pest Control Products: PMRA Approach

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Resources

- Regulatory Proposal 2010-06, “Guidelines for the Registration of Non-Conventional Pest Control Products”
  - http://www.hc-sc.gc.ca/cps-spc/pest/part/consultations/_pro2007-02/index-eng.php
- Regulatory Proposal 2002-02, “Guidelines for the Research and Registration of Pest Control Products Containing Pheromones and Other Semiochemicals”
  - http://www.hc-sc.gc.ca/cps-spc/pest/part/consultations/_pro2002-02/index-eng.php
- Regulatory Directive 2006-02: Formulants Policy and Implementation Guidance Document:
  - http://www.hc-sc.gc.ca/cps-spc/pubs/pest/_pol-guide/dir2006-02/index-eng.php

List of Abbreviations

DACO	data code
EP	end-use product
ISP	integrated system product
MRL	maximum residue limit
QSAR	quantitative structure/activity relationship
SCLP	straight-chain lepidopteran pheromone
TGAI	technical grade active ingredient

What is a Non-Conventional Pesticide?

- Characteristics of products eligible for review under this proposal are flexible
- Must have some of the following characteristics:
  - Low inherent toxicity to humans and other non-target organisms
  - Not persistent in the environment
  - Minimal exposure potential
  - Already widely available to the public for other uses with a long history of safe use at equivalent exposure levels
  - Pest control effect is not the result of toxicity to the target organism
  - Unlikely to select for pest resistance

Addressing Requirements

Toxicology Data

- A flexible approach including toxicology studies, public literature and scientific rationales that demonstrate the following:
  - Low acute and chronic toxicity
  - Not genotoxic, carcinogenic, neurotoxic or immunotoxic
  - Doesn't cause reproductive or developmental effects, metabolize into compounds of toxicological concern or be anticipated to bioaccumulate
  - Should not have the potential to cause unintended adverse effects to domestic animals

Addressing Requirements

Information Requirement	Use Patterns		Test Substance	
	Food	Non-food		
Tier I				
Acute Studies				
Acute Oral	R	R	TGAI/ISP	EP
Acute Dermal	R	R	TGAI/ISP	EP
Acute Inhalation	R	R	TGAI/ISP	EP
Primary Eye Irritation	R	R	TGAI/ISP	EP
Primary Dermal Irritation	R	R	TGAI/ISP	EP
Dermal Sensitization	R	R	TGAI/ISP	EP
Other Acute Studies	CR	CR	TGAI/ISP	EP

Addressing Requirements

Information Requirement	Use Patterns		Test Substance	
	Food	Non-food		
Tier I				
Short-term Studies				
Short-term Oral (90 day rodent)	R	CR	TGAI/ISP	EP
Short-term Oral (90 day and/or 12 month dog)	CR	CR	TGAI/ISP	EP
Short-term Dermal (90 day rodent)	CR	CR	TGAI/ISP	EP
Short-term Inhalation (90 day rodent)	CR	CR	TGAI/ISP	EP
Other Short-term Studies	CR	CR	TGAI/ISP	EP

Addressing Requirements

Information Requirement	Use Patterns		Test Substance	
	Food	Non-food		
Tier I				
Special Studies				
Prenatal Developmental Toxicity (rodent)	R	CR	TGAI/ISP	NR
Genotoxicity: Bacterial Reverse Mutation Assay	R	CR	TGAI/ISP	NR
Genotoxicity: In vitro Mammalian Cell Assay	R	CR	TGAI/ISP	NR
Other Studies/Data/ Reports	CR	CR	TGAI/ISP	EP

Addressing Requirements

Exposure

- Occupational and bystander exposure is addressed primarily through the review of the use description which includes the following:
  - A description of typical application practices (amount, site, timing, mixing/loading, application type)
  - Frequency, type and duration of post-application activities
  - Bystander exposure (particularly nearby residential communities, schools or recreational areas)
- Food residue exposure is addressed primarily through an assessment for the requirement of a maximum residue limit (MRL):
  - If a product is to be applied to food or feed it must be shown that any anticipated residues of parent compound or any metabolites will not pose a toxicological concern
  - Residue data may be required when residues of concern exceed natural background levels

Addressing Requirements

Formulants

- If only List 4A formulants are used then acute toxicity data could be waived for the EP
  - Also true for List 4B formulants depending on the use pattern
- Include details on identification and source of formulant so exact identification can be determined
- Use of allergens as formulants should be avoided where application to food is intended; food commodities cannot be labelled. Allergens should also be avoided if there is a potential for repeated exposure via oral, dermal, and/or inhalation routes

Addressing Requirements

SCLP pheromones and other semiochemicals

- Toxicological data are not required for SCLPs
- Harmonized with U.S. EPA data requirements in 40CFR158 Subpart U (biochemicals)
- Exempt from cost-recovery (registration application) fees
- Some regulatory challenges still yet to be resolved and will be addressed, e.g., arthropod traps used for mass trapping
- 12-15 month registration review timeline for Non-SCLPs; 6 months for SCLPs

Areas for Improvement: Scientific Rationales for Data Omission

- PMRA will waive test data requirements on a case-by-case basis in response to written requests that are based on sound scientific reasoning and accompanied by supporting evidence (e.g., published literature)
- Rationales must refer to the supporting evidence and clearly show that further data is not required because either the level of risk is not of concern or the risk can be adequately mitigated (e.g., labelling to minimize exposure)
- Legible copies of all supporting evidence and published literature must be submitted as separate files under the appropriate DACO and properly referenced in the e-Index

Areas for Improvement: Data

- Risk cannot be assessed without a complete understanding of exposure; use description is critical in assessing exposure
  - Typical work day; amount of active ingredient to be handled;
  - Site, timing and method of application; individuals involved;
  - Mixing/loading method; clean-up and repair activities;
  - Personal protective equipment and clothing during mixing, loading, application and during any post-application activities;
  - Crop cultivation practices; proposed restricted-entry intervals;
  - Restricted entry (re-entry) activities; timing, frequency and duration of all re-entry activities
  - Type of field workers; the intensity and the degree of contact and which body parts are anticipated to come on contact with treated surfaces
  - Bystander exposure

Areas for Improvement: Data

- A complete understanding of the hazards and associated risks due to exposure is absolutely required
  - If there is a 'history of safe use' it should be considered in the context of the proposed use
  - Simply because an active is 'natural' does not mean that it can be used without regard
  - The proposed use could result in greater exposure and subsequently risk regardless of route of exposure
  - Describe levels of naturally occurring substance in the environment/use site
  - For complex mixtures, such as essential oils, toxicology of the complex mixture must be considered
  - Contaminants in plant extracts and minerals should be discussed; could vary depending on the source of starting materials

Areas for Improvement: Data

Literature searches

- An extensive search of key databases (e.g. TOXLINE®, Biological Abstracts, CHEMTOX®) should be conducted on the active ingredient and its metabolites to look for any acute, short-term and chronic toxicity data available on humans and/or other mammals
- If no data are available then data on chemically equivalent or similar substances may be considered with a valid rationale
- QSAR data could also be considered on a supplementary basis

THANK YOU!