Biopesticide Registration Improvement Course

Environmental Assessment of Microbial Pest Control Products:

PMRA Approach

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Resources

- Regulatory Directive DIR2001-02 *Guidelines for the Registration of Microbial Pest Control Agents and Products*:
  - http://www.hc-sc.gc.ca/cps-spc/pubs/pest/_pol-guide/dir2001-02/index-eng.php

- Data Evaluation Record (DER) templates for non-target organism studies can be can be requested electronically by following the instructions at:
  - http://www.hc-sc.gc.ca/cps-spc/pest/registrant-titulaire/prod/templates-modeles-eng.php

List of Abbreviations

CFU	colony forming unit
CR	conditionally required
DACO	data code
DAR	draft assessment report (EU)
DER	data evaluation record (EPA)
EP	end-use product
EPA	United States Environmental Protection Agency
EU	European Union
MPCA	microbial pest control agent
MSDS	material safety data sheet
NTO	non-target organism
OCSPP	Office of Chemical Substances and Pollution Prevention (EPA)
PAI	pure form of the active ingredient
TGAI	technical grade active ingredient
R	required

Overview of Approach to Testing

Data requirements aimed at assessing impact of MPCAs on non-target organisms and fate/expression in the environment are divided into 4 tiers, with progression dependent on results of lower tier testing

Addressing Requirements

- PMRA strongly recommends presubmission consultations for microbials to identify required and conditionally required data as well as non-required data elements
  - PMRA prepares a customized data requirement (DACO) table (valid for 2 years)
- Test data/information requirements identified during presubmission consultation denoted by "R" or "CR"

Addressing Requirements

- "R" means data/information are required:
  - Data on the test organism
  - Published scientific literature
  - Surrogate information or bridging data to another strain/species, if both belong to a well-known (familiar) taxon
  - A rationale to waive the requirement on the MPCA because it is unnecessary or impractical
- "CR" means data are conditionally required if specified conditions are met or could be triggered

Data Requirements are Tiered

Tier I

- Maximum hazard/challenge approach to testing on non-target organisms

Tier II

- Potential exposure to the MPCA estimated by means of terrestrial, freshwater and marine or estuarine environmental expression testing (application rate, fate, population dynamics) plus additional acute testing

Tier III

- If Expression tests show significant exposure potential to Tier I susceptible species, additional studies required on these species to examine chronic, reproduction, life cycle and population effects

Tier IV

- Simulated or actual environmental field tests designed on a case-by-case basis to evaluate any specific problem that cannot be resolved by lower tier testing

Selection of NTO's in Tier I

- Selection of non-target species and routes of administration are usually determined during the presubmission consultation process, but in general the following criteria are followed:
  - Taxonomically related to the target pest
  - May be infected by the MPCA
  - High exposure potential
  - Similar physiology to target pest
  - Susceptible to pathogens related to the MPCA
  - Representative species from 7 broad taxonomic groups

Environmental Toxicology Tier I

Test	Test Material	Type of Test
Avian oral	TGAI or EP	Maximum Challenge Concentration
Avian pulmonary, inhalation or injection		
Wild mammals		
Fish: Freshwater		
Fish: Estuarine or marine		
Arthropods: Terrestrial		
Arthropods: Aquatic		
Non-arthropod invertebrates: Terrestrial		
Non-arthropod invertebrates: Aquatic		
Microorganisms		
Plants: Terrestrial		
Plants: Aquatic		

Test Guidelines

- Environment Canada's "Guidance Document for Testing the Pathogenicity and Toxicity of New Microbial Substances to Aquatic and Terrestrial Organisms"
  - http://www.ec.gc.ca/Publications/default.asp?lang=En&xml=F9BF9993-4BAC-4215-BD3E-9B0962980915
- Studies conducted using EPA OCSPP (formerly OPPTS) Harmonized Test Guidelines Series 885 are also accepted
  - Identify protocol used for study design
  - Identify and provide rationales for deviations from protocol

Areas for Improvement: Data Issues

- Test substance not clearly identified in study report
- Inappropriate test material (PAI, TGAI, EP) and test concentrations selected
- Not enough raw data to allow for independent analysis by PMRA evaluators
- Multiple papers addressing a single data requirement not accompanied by a critical review demonstrating how each one addresses the requirement

Areas for Improvement: Test Concentrations

Maximum Challenge Concentration/Dosing

- Tier I testing must use a dose or concentration that gives the highest degree of challenge to the test organism – negative results from such tests provide high degree of confidence that no unreasonable/unacceptable adverse effects will likely occur from actual use of MPCAs

- Formulas for calculating doses/concentrations can be found in test guidelines (PMRA Regulatory Directive DIR2001-02)

- For pathogenicity testing, CFUs (or activity units) should be measured at time of testing versus using nominal measurements

Areas for Improvement: Scientific Rationales for Data Omission (Data Waivers)

- Data requirements may be “waived” in response to written requests where:
  - It is not possible to generate test data on the MPCA to be registered
  - Data not useful in risk evaluation
- Rationales must be based on sound scientific reasoning and address the underlying concern behind the requirement with information other than actual test data (e.g., studies on a related strain/species)

Areas for Improvement: Scientific Rationales for Data Omission (Data Waivers)

- Early discussion on the preparation of scientific rationales is encouraged to ensure PMRA acceptance of intended approach

- When multiple papers are submitted to address a requirement, a critical review of the papers should also be submitted, summarizing and explaining how each one addresses the data requirement

Scientific Rationales: Supporting Information

- Surrogate data
  - Data on a related strain or species
  - Describe relationship of tested strain to the MPCA
  - Address potential for production of toxins/metabolites
- Discussion of MPCA's mode of action, known pest/host range, temperature growth range, natural occurrence, ecological niche(s) and natural routes of exposure to the NTO
- Information on the effects of formulation ingredients/impurities
  - Material Safety Data Sheets (MSDS)
  - Published literature

Data Waivers: Supporting Information

- Literature search results in relevant databases
  - BIOSIS, PubMed, Biological Abstracts, AGRICOLA, TOXLINE, etc.
  - Include key search words
- Published scientific literature
  - Legible copies must be submitted
  - Certified translations in either English or French, if applicable

Parting Advice

- For public transparency reasons, ensure proper use of e-Index Builder and submit all studies and supporting literature separately rather than in files containing multiple papers, waiver rationales, forms, etc.
  - Each element must be assigned its own PMRA ID Number in e-Index Builder

- Help facilitate the PMRA review process and submit foreign study reviews and monographs if active ingredient and product are registered elsewhere (e.g., EPA DERs, EU DARs)

THANK YOU!