Biopesticide Registration Improvement Course

Microbial Product Characterization and Analysis: PMRA Approach

Jonas Ptasinski
Senior Evaluator, Microbial & Biochemical Evaluation Section,
Health Effects Division I, Health Evaluation Directorate,
PMRA, Health Canada

Health Canada Santé Canada

Resources

- Regulatory Directive DIR2001-02, *Guidelines for the Registration of Microbial Pest Control Agents and Products* outlines the data requirements by 'Data Code' (DACO). A pdf of this directive can be found at:
  - http://www.hc-sc.gc.ca/cps-spc/pubs/pest/_pol-guide/dir2001-02/index-eng.php

- The Product Characterization and Analysis Data Evaluation Record (DER) template can be used to record data submitted under DACO M.2. An electronic copy of the DER can be requested 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
DACO	data code
DER	data evaluation record
EP	end-use product
MPCA	microbial pest control agent
QA	quality assurance
QC	quality control
SPSF	statement of product specification form
TGAI	technical grade active ingredient

Addressing Requirements

- Detailed information on characteristics and biological properties of a microbial pest control agent (MPCA) significantly influences the nature and extent of data required to assess its safety to human health and the environment

- Origin, derivation and identification of MPCA
  - Taxonomic designation (strain level); alternative, synonymous and superseded names and source; strain numbers, culture collection and company codes; origin of the strain and history of development; preservation and maintenance during development

- Biological properties
  - Natural occurrence; target organisms including pathogenesis; host range; life cycle; description of plasmids or other extra chromosomal genetics; relevant physiological properties; description of unusual characteristics (i.e., if different from classical description); history of use; relationship to known pathogens/dermatophytes; presence of mammalian toxins

Addressing Requirements

- Manufacturing process and quality assurance
  - Preservation and maintenance of production strain
  - Manufacturing process
  - Quality assurance

- Disclosure of ingredients
  - Product specifications
  - Potency estimation and product guarantee
  - Unintentional ingredients

Addressing Requirements

- Analytical data and methodology
  - Active ingredient or MPCA
  - Analysis for microbial contaminants
  - Analysis for other unintentional ingredients
- Storage stability testing
  - EP; TGAI also if appropriate
- Summary of physical and chemical properties
  - Omission of properties that are not applicable is acceptable

Areas for Improvement

Literature searches

- Search for metabolites of interest, adverse effects, related pathogens, and history of use on key databases (e.g., PubMed, AGRICOLA, SCIRUS)
- Include search engines and keywords used
- Submit relevant literature as individual files and reference accordingly when using literature to support specific data requirements

Areas for Improvement

Microbial contamination

- Indicators of microbiological contamination must be routinely monitored in production samples to assess the hygienic state of the production facility and manufacturing process
  - Microbial contaminant analysis must be incorporated into the quality assurance (QA) program for every production batch
- The nature and level of microbiological contamination must be supported by quality control (QC) data from five production batches
- Details and validation of methods used to assay for presence of microbiological contaminants must be submitted

Areas for Improvement

Potency estimation and guarantee

- Guarantee should be related in some valid fashion to product activity or efficacy; most often CFUs
- The analytical methodologies used to determine and verify biological activity must be described in detail, including standardization, sensitivity, reproducibility and statistical validity

Storage stability

- Data are used to determine an appropriate expiry date for most products
- The EP and the TGAI, if stored, should be tested over a suitable period of time in accordance with typical storage and use conditions
- The analytical methodologies used to determine stability must be described in detail

Areas for Improvement

Statement of Product Specification Form (SPSF)

- A complex form for a complex job
- May be ‘corrected’ at any point in the registration review process, prior to the risk management decision; amending SPSFs during the review will not delay or add time to the review
- Critical information includes manufacturing site, guarantee value and units, % composition, identity of formulants

Areas for Improvement

TGAI

	Row: 1	[1]Trade Name: Pestis destrutans strain ABC including fermentation solids	[9] %w/w	10 Purpose: active ingredient		NACT
A ✓		[2]Common Name: Pestis destrutans strain ABC including fermentation solids	100	[11] % LCL: 100	[12] % Nominal: 100	[13] % UCL: 100	LIST
F		[3]Chemical Name: Pestis destrutans strain ABC including fermentation solids		[14A]Label Guarantee: Pestis destrutans strain ABC			ACTIONS
I				[14B]Value: 2.0e9	[14C]Units: CFU/g		
	ACT IN	[4]Name: MPCA Manufacturing Inc. Address Multiple Suppliers? Yes: ☐ Actual Address of Manufacture (same as address above)	[5] Reg #	[14D]LCL: 1.9e9	[14E]UCL: 2.1e9		ACT OUT
			[6] Purity				
			[7] CAS #	15 Other Info			
			[8] List #				

Areas for Improvement

EP

	Row: 1	[1]Trade Name: Pestis destructans Technical Powder		[9] %w/w	[10] Purpose: active ingredient	NACT
A	✓	[2]Common Name: Pestis destructans Technical Powder		50	[11] % LCL: 48 / [12] % Nominal: 50 / [13] % UCL: 52	LIST
F		[3]Chemical Name: Pestis destructans Technical Powder			[14A]Label Guarantee: Pestis destrutans strain ABC	ACTIONS
I					[14B]Value: 1.0e9 / [14C]Units: CFU/g	
					[14D]LCL: 9e8 / [14E]UCL: 1.1e9	ACT OUT
	ACT IN	[4]Name: MPCA Manufacturing Inc.	[5]Reg #: pending		[15] Other Info	
		Address Multiple Suppliers? Yes: ☐ Actual Address of Manufacture of TGAI (may not be same as address above)	[6]Purity			
			[7]CAS #			
			[8]List #			

Areas for Improvement

Formatting and organizing required data

- A data package organized according to the registration guideline directive and/or DER template will present a clear picture of the products proposed for registration and will facilitate the registration review process
- ‘On-hold’ and clarification requests are time consuming and frustrating for both applicant and regulator
- Submitting documents separately allows data to be referenced individually in an open and transparent manner – a legislated requirement

THANK YOU!