Biopesticide Registration Improvement Course

PMRA Risk Assessment and Decision-Making Process for Microbial Pest Control Products

Brian Belliveau, Ph.D.

Head, Microbial & Biochemical Evaluation Section,

Health Effects Division I, Health Evaluation Directorate,

PMRA, Health Canada

Health Canada Santé Canada

On-line Resources

- A Primer on Scientific Risk Assessment at Health Canada
  - http://www.hc-sc.gc.ca/sr-sr/pubs/about-apropos/2010-scientif-ris/index-eng.php
- Health Canada Decision-Making Framework for Identifying, Assessing, and Managing Health Risks
  - http://www.hc-sc.gc.ca/ahc-asc/alt_formats/hpfb-dgpsa/pdf/pubs/risk-risques-eng.pdf
- Science Policy Notice SPN2000-01: *Technical Paper* - A Decision Framework for Risk Assessment and Risk Management in the Pest Management Regulatory Agency
  - http://www.hc-sc.gc.ca/cps-spc/pubs/pest/_pol-guide/spn2000-01/index-eng.php
- Regulatory Directive DIR2006-02, Formulants Policy and Implementation Guidance Document
  - http://www.hc-sc.gc.ca/cps-spc/pubs/pest/_pol-guide/dir2006-02/index-eng.php
- Pest Control Products Act
  - http://laws.justice.gc.ca/en/P-9.01/
- PCPA List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern
  - http://gazette.gc.ca/rp-pr/p2/2008/2008-06-25/html/si-tr67-eng.html
- Federal Toxic Substances Management Policy (TSMP)
  - http://www.ec.gc.ca/toxiques-toxics/default.asp?lang=En&n=2A55771E-1

List of Abbreviations

CEPA	*Canadian Environmental Protection Act*
EP	end-use product
GMO	genetically modified organism
IPM	integrated pest management
LC50	concentration that kills 50% of the population
LC95	concentration that kills 95% of the population
LD50	dose that kills 50% of the population
LT50	time for 50% of the population to die
MPCA	microbial pest control agent
PCPA	*Pest Control Products Act*
SMC	science management committee
SOC	science operations committee

Pest Control Products Act (*PCPA*)

- PMRA's mandate is to administer the *PCPA* which regulates products that are manufactured, or used as a means for directly or indirectly controlling, destroying, attracting/repelling a pest for mitigating or preventing its injurious, noxious or troublesome effects [s. 2(1)]

- Prevent unacceptable risks to people and the environment from the use of pest control products [s. 4(1)]
  - "acceptable": reasonable certainty that no harm to human health, future generations, or the environment will result from exposure to or use of the product, taking into account its conditions or proposed conditions of registration

- Only pest control products that are determined to be of acceptable value are approved for use in Canada [s. 4(2)(d)]
  - Value is further defined as including efficacy; effect on host organisms (e.g., crop tolerance); and health, safety and environmental benefits and social and economic impact [s. 2(1)]

How Does Health Canada Deal with Risk?

The Process Perspective

At a high level, the logic underlying a risk assessment is identical for all contexts, including health and environmental risks. It can be expressed in the following formula:

Risk = Probability of Event × Seriousness of Consequences

Or more simply a function of inherent toxicological hazard and exposure:

Risk = Hazard × Exposure

Decision Steps	Components
Identification of Issue and Context	Initiation of Assessment and Management of Risk Request for Registration Re-evaluation New Monitoring Results
Assessment of Risk and Value	Risk to Health • Hazard Identification • Dose Response Assessment • Exposure Assessment • Risk Characterization Risk to the Environment Value • Efficacy • Economics/ Competitiveness • Sustainability
Management of Risk	Identification and Analysis of Options Selection of a Risk Management Strategy Implementation of the Strategy
Monitoring and Evaluation of Results	Enforcement and Compliance Routine and Special Surveys Maintaining a Modern Supporting Data Base

Hazard Identification: Health

Fate of MPCA in Test Animal

- Passage of intestinal barrier
- Passage of skin barrier
- Passage of lung barrier
- Colonization
- Invasion
- Long residence time/infection

Acute Effects

- Toxicity
- Infectivity
- Pathogenicity
- Skin/Eye Irritation

Higher Tier Tests Triggered ?

- repeat-dose
- reproduction
- mutagenicity
- carcinogenicity

Hazard Identification: Environment

Non-Target Organisms

- Taxonomically related to target host
- Infected by MPCA
- High exposure potential
- Similar physiology
- Susceptible
- Representative indicator species:
  - birds; wild mammals; fish
  - terrestrial/aquatic arthropods
  - non-arthropod invertebrates
  - microorganisms
  - terrestrial/aquatic plants

Acute Effects

- Toxicity
- Infectivity
- Pathogenicity

Higher Tier Tests Triggered?

- Definitive toxicity (LD50/LC50)
- Life-cycle testing
- Small-scale field studies
- Fate/behaviour of MPCA in water, soil

Exposure Assessment

Health

- Identify exposed populations
- Identify all routes of exposure
- Estimate degree of exposure
  - consumption data
  - background levels
  - persistence/survival on crops
  - pre-harvest interval
- Labelled uses
  - rates
  - methods
  - frequencies
  - # applications per season
  - conditions

Environment

Site characteristics

- background levels

- Proliferation/persistence
  - selection
  - ecological fitness
- Dispersal

Value Assessment

Performance Assessment

- Laboratory and growth chamber
  - pest host spectrum
  - LC50, LC95, LT50, etc.
- Field/greenhouse efficacy trials
  - support EP label claims

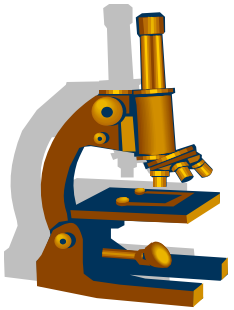
Treatment Effects

- Phytotoxicity/phytopathogenicity
- Compatibility (crop protection and management practices)
  - effects on MPCA performance
  - effects of EP

Crop or Resource Benefits

- Profile of EP
- Nature and economics of pest/disease problem in Canada
- Current crop protection tools and practices
- Contribution to IPM strategies and practices

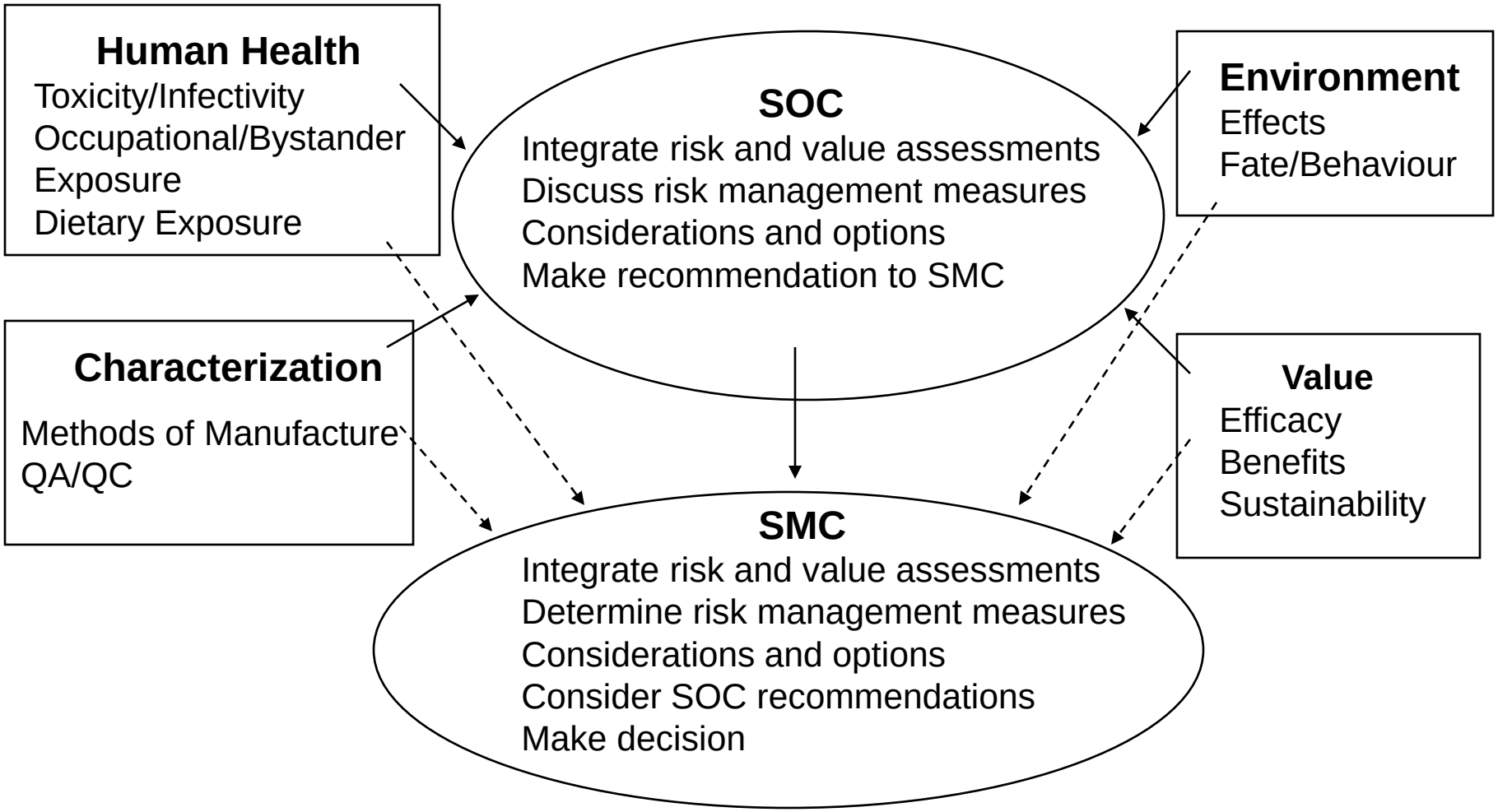
Why are microbial pesticides evaluated differently?



- Microbial and chemical pesticides are regulated to the same scientific standard
- Registration requirements for microbial and chemical pesticides are different

- Potential to replicate in host and environment
- Colonization/invasion/infection of other organisms
- Expression of toxic metabolites and virulence factors can depend on growth conditions
- Natural background population (for non-GMOs)
- Metabolites of concern may be regulated as chemicals

PMRA Decision-Making Process



Other Considerations May Impact Decisions

- Formulants
  - Make an effort to formulate products with List 4A or 4B formulants (inerts)
  - Avoid Toxic Substances Management Policy Track 1 substances (those that are "CEPA-toxic" or equivalent, predominantly anthropogenic, persistent and bio-accumulative)
  - Avoid priority allergens as formulants
- Some MPCAs may produce metabolites of concern (e.g., toxins, antibiotics) or may be closely related to a pathogen
  - Bacteria and fungi can produce an array of secondary metabolites; could trigger food residue studies
  - MPCAs that are, or are phylogenetically close to, primary or opportunistic pathogens will trigger concerns (and more characterization, toxicology data)

Registration

- Decision making:
  - No: health or environmental risks or value unacceptable
  - No: insufficient core test data/information
- Decision making
  - Yes: risks and value acceptable
  - Yes: with conditions (e.g., confirmatory batch analysis data or efficacy testing)
  - Yes: consultation

Transparency Documents

- After a decision to register a pesticide or after re-evaluation, the public is encouraged to review the published evaluation report and decision documents, which explain the risk and value assessments supporting a registration decision and include a summary of the information considered

- 3 types of documents are required by *PCPA*:
  - Consultation Document (full registration)
  - Decision Document (full registration)

  - Evaluation Report (conditional registration)

THANK YOU!