REPORT OF THE OECD/KEMI/EU WORKSHOP ON MICROBIAL PESTICIDES: ASSESSMENT AND MANAGEMENT OF RISKS - ANNEX 6 (PRESENTATIONS - PART 2/3)

Series on Pesticides
No. 76

This document is available only in PDF.
This document contains part 2/3 of the Annex 6 of the REPORT OF THE OECD/KEMI/EU WORKSHOP ON MICROBIAL PESTICIDES: ASSESSMENT AND MANAGEMENT OF RISKS. Annex 6 includes slides of all presentations made during the seminar.

The main part of the seminar report, as well as Annexes 1-5, is published under the reference ENV/JM/MONO(2014)2.
PART 2 OF 3

COMPILATION OF PRESENTATION SLIDES
PRESENTED AT THE
OECD/Kemi/EU WORKSHOP
on Microbial Pesticides:
Assessment and Management of Risks
17-19 June 2013
Vår Gård, Saltsjöbaden, Sweden

Organised jointly by:
OECD (Organisation for Economic Cooperation and Development)
Kemi (Swedish Chemicals Agency)
European Commission
TABLE OF CONTENTS

EFSA’s role in the peer review process within the EU: Experience of concluding for each organism, using the information provided against the EU data requirements, with the existing guidance. By Christopher Lythgo ................................................................. 3
Basic strategies in risk assessment – comparison with chemicals By Kersti Gustafsson ............... 9
Feedback from survey on test guidelines and data requirements By Marloes Busschers .............. 1
Industry/Consultant Views............................................................................................................. 11
Registration of Biocides: Challenges for the Biocontrol Industry By Philip Kessler ............... 11
Experiences with data requirements By Rüdiger Hauschild .......................................................... 20
Experiences with compilation of dossiers etc. where there is a need for more guidance and criteria, obstacles By Mark Whittaker ............................................................................................................. 27
Experiences with compilation of microbial dossiers: relevance of current data requirements By Roma L Gwynn ........................................................................................................................................ 42
The Way Forward – A Vision from IBMA By David Cary ........................................................... 51
EFSA’s role in the peer review process within the EU: Experience of concluding for each organism, using the information provided against the EU data requirements, with the existing guidance.

By Christopher Lythgo
Team Leader, Environmental Exposure, Peer Review, EFSA
ANNEX 6: SLIDES FOR PRESENTATIONS

EFSA’s origins

- Formally set up in January 2002 as an independent source of scientific advice and communication on risks associated with the food chain.


- Created as part of a comprehensive programme to:
  - improve EU food safety
  - help ensure a high level of consumer protection
  - restore and maintain confidence in the EU food supply
  - provide (scientific) evidence based risk assessments

Committed to ensuring that Europe’s food is safe

Scientific advice from farm to fork

Committed to ensuring that Europe’s food is safe
Conclusions on substances including micro-organisms

- Dossier from applicant for limited but representative pesticide uses evaluated by Member State competent authority
- EFSA makes Member State evaluation (DAR) publically available and calls for comments on the DAR
- EFSA arranges peer review of RMS assessment (starting point comments received, arranges discussions with experts from competent authorities)
- EFSA concludes on the risk assessments for these representative uses and publishes its conclusion
- Legal requirements for dossier content; evaluation and peer review process (including responsible parties and deadlines) are prescribed. Eg. currently in play:
  a) Reg. 188/2011 process for first EU evaluation of (older) ‘new substances’
Experience of concluding for each organism, using the information provided against the EU data requirements, with the existing guidance.

Guidance available that should be followed / is accepted:


Guidance available that gives pointers and approaches that can be followed / have been accepted by the peer review in selected cases:

- OECD guidance to the environmental safety evaluation of microbial biocontrol agents Series on pesticides No. 67 ENV/JM/MONO(2012)1 17-Feb-2012
Peer reviewed scientific literature

• Systematic review of the available literature has to be provided for the organism strain and any metabolites that this literature indicates that the strain or species might produce, following the EFSA guidance
• Other peer reviewed scientific literature can be provided on other strains of the same species or related species where the applicant wishes to use this evidence to address individual data requirements
• When evidence from the peer reviewed literature is cited, the paper with the observation or measurement providing the evidence, should be included in the dossier. Quotes and opinions that just originate from authors in their introduction or discussion sections, should not be considered good evidence

Data gaps / issues identified in EFSA conclusions:

• Methods for identity of the strain, best available technology, how to assess if the test procedures presented are appropriate
• Level of evidence to demonstrate relationships to / lack of relationships to known pathogens (EFSA considers evidence of systematic literature review is needed) and how to distinguish from related pathogens
• Information on production of metabolites including other strains of the species, conditions of production, evidence of absence of these from the product
• Insufficient characterisation / evidence / information / measurement that metabolites are not formed at relevant (as described in the data requirements) levels in environmental compartments following application
Data gaps / issues identified in EFSA conclusions:

- Lack of assessment of the potential for transfer of genetic information to other species (primary concern usually plasmids between bacteria species)
- Information not provided on absence of interference of organism on prescribed methods of analysis for pathogens in drinking water
- Insufficient information on competitiveness / multiplication to conclude if the organism will decline to background levels within a year
- Effects studies provided for characterising environmental risk can be too short to conclude lack of pathogenicity or infectivity to non target species. Ensure that information on the biology of the active organism strain / species is considered when designing tests, particularly test duration

Conclusion

- There is a need for guidance, on practice for risk assessment for micro-organisms when used in plant protection products, against the EU regulatory framework (data requirements and uniform principles for product decision making)
- EFSA’s PPR panel could do this, once the relevant EFSA procurements for systematic review of the literature are finalised, to any priority that was agreed by EFSA’s pesticide steering committee (Network of member state competent authorities), subject to resource availability
- Alternatively a member state competent authority (or small group of authorities) could initiate work on a document, that EFSA’s panel might subsequently be mandated to give an opinion on
Basic strategies in risk assessment – comparison with chemicals

By Kersti Gustafsson
Swedish Chemicals Agency

Similarities and differences

• Same/similar regulations
• Same/similar purpose – to kill/to repel harmful organisms
• Same/similar use – the application methods can be quite similar

• Biology is the difference
ANNEX 6: SLIDES FOR PRESENTATIONS

**Basis in risk assessment for pesticides including biocides**

**Micro-organism** *natural occurring, mutant or GMO*
- Identity
- Biological properties including pathogenicity
- Contaminants
- Human health effects and exposure
- Environmental effects and exposure
- Metabolites
- ...

**Chemical** *natural occurring or synthetic*
- Identity
- Physical / chemical properties
- Contaminants
- Human health effects and exposure
- Environmental effects and exposure
- Metabolites
- ...

---

**Risk assessment - same basic outline as for chemicals**

- **Micro-organism**
  - Biological properties
    - Identity
    - Life cycle and nutritional / environmental requirements
    - Mode of action
    - Metabolites

- **Non-target organisms**
  - Effects
    - Lethality
    - Pathogenicity
    - Toxicity

- **Human health**
  - Use / GAP / scenarios
  - Proliferation

- **Ecosystem**
  - User, worker, by-stander, general public

www.kemi.se
ANNEX 6: SLIDES FOR PRESENTATIONS

Naturally occurring micro-organisms ≠ no hazard and no risk

- *Bacillus anthracis*
- *Bacillus thuringiensis israelensis*
- Baculovirus
- *Clostridium botulinum*
- EHEC
- *Escherichia coli*
- *Candida albicans*
- *Saccharomyces cerevisiae*
- ..

*Nature is neither kind nor evil, just is*

What have we done -SE?

- SE as EU MS taken part in development of
  - data requirements;
  - uniform/common principles for product authorisation;
  - guidance documents;
- SE / NL Lead Country EU draft assessment reports for active micro-organisms
- SE microbial ~4% of the total number of pesticide products
  - 21 plant protection products
  - 2 biocidal products
What can we do – EU/OECD?

- Interpretation / improvement of regulations
  - knowledge compilations – Science / Industry
  - guidance documents – Authorities
- Development/improvement of test methods
- Development of decision criteria for active micro-organisms
- Development of exposure scenarios
- Improve general knowledge about biopesticides
- Communication – expert networking
- Facilitate the process – Industry / Authorities

In summary

- As chemicals have been assessed much longer and for many more active substances – take note of valuable experiences
- Interpret/improve the data requirements with detailed guidance and improve the assessment of the biological aspects
- Take special consideration to that micro-organisms are living organisms and improve the exposure assessments based on that
Feedback from survey on test guidelines and data requirements

By Marloes Busschers
CTGB, the Netherlands

BPSG Questionnaire

Test guidelines for microbials, 2013

Marloes Busschers
CTGB, the Netherlands

BPSG meeting June 2012

- To promote harmonisation:
  - table indicating available test guideline per data requirement, interpretation and deficiencies and problems.
  - this will help priority list for development of new test guidelines
  - questionnaire on issues and problems with test guidelines
Questionnaire

- Table with all OECD data requirements for microbials (MPCA and MPCP)

- Indicate deficiencies/problems with test guidelines or any other problems

- E.g. lack of test guideline, different interpretations of guideline or of data point

Questionnaire

Input from:
11 regulatory bodies:
  - 7 EU (Austria, Sweden, Germany, Denmark, United Kingdom, Belgium, Netherlands)
  - Canada
  - USA
  - Japan
  - Australia
IBMA (10 biocontrol companies/consultants)
Main issues MPCA

- Identity (IIM 1)
- Biological properties (IIM 2)
- Further information (IIM 3)
- Analytical methods (IIM 4)
- Toxicology (IIM 5)
- Metabolism and residues (IIM 6)
- Fate and behaviour (IIM 7)
- Ecotoxicology (IIM 8)

Main issues MPCP

- Identity (IIM 1)
- Phys-chem properties (IIM 2)
- Data on application (IIM 3)
- Analytical methods (IIM 5)
- Efficacy (IIM 6)
- Toxicology (IIM 7)
- Residues (IIM 8), see IIM 6
- Fate and behaviour (IIM 9), see IIM 7
- Ecotoxicology (IIM 10), see IIM 8
Main issues: general

- Metabolites
- Data needed on species or strain?
- Strain characterisation
- Impurities, pathogens, quality control data
- Analytical methods
- Fate and behaviour
- Ecotoxicity

Consensus

- **Identity: scientific name**
  - strain level
  - names will change based on modern taxonomy methods
  - no further guideline seems to be needed

(identification methods are however in need of guidance)
Consensus

- **Mamm tox: short term tox testing**
  - no test protocol
  - tier 2 or waiver usually accepted

Problematic

- **Toxins/metabolites**
  - “their presence is suspected”? “known mammalian toxin”?
  - Which metabolites need to be assessed?
  - Theoretical vs practical relevance.
  - How much of concern? How much data needed to assure this fact? Non-presence is difficult to prove
  - Insufficient guidance; highly variable between dossiers. Area frequently ignored by applicants.
Problematic

- **Microbial impurities, human/mammalian pathogens**
  - Insufficient guidance
  - OECD Issue Paper on Microbial Contaminant Limits (ENV/JM/MONO(2011)43)
  - Highly variable between dossiers. Often applicants devise their own quality control testing based on their own experiences.
  - GLP?

Problematic

- **Characterisation: Best available technology**
  - (No) guidance on methods and degree of strain differentiation
  - Genetic techniques for microbial identification are constantly advancing
  - Acceptable molecular identification methods? Different regulatory authorities don’t accept the same data
  - Applicants using outdated methods
Problematic

- **Related to characterisation is Bridging:**
  - Closely related strains and species
  - It is not clear how much information is required
  - Different interpretations about degree of similarity. No clear rules

Divergence

- **Toxins/metabolites**
  - CAN/USA: clear guidance, but frequently ignored by applicants. No/little information/discussion provided for metabolic by-products or toxins.
Divergence

- **Analytical methods**
  - Simple plating techniques:
  - CAN/USA: Standardisation and validation rarely required
  - EU: validation, linearity, accuracy and specificity required. GLP? Criteria needed.

Divergence

- **Sensitisation**
  - CAN: No study, only incidents reporting
  - USA: Study and incidents reporting
  - EU: No study, only incidents reporting. Some countries accept negative study.

  Question: is there an acceptable study for microbials to prove non-sensitiser?
Divergence

- **Tox: Acute tox/infect/path studies**
  - OPPTS most often used
  - However, might need update
  - Is lacking positive control (Bc: human pathogens, but no effects in oral rat study)
  - Necessary if microbe does not grow >30°C?
  - Intratracheal: unspecific effects/mortality?

Divergence

- **Fate and behaviour**
  - EU:
    - tier 1 requirement
    - no guidelines
    - OPPTS not often used, or different interpretation
      - interpretation in relation to background?
  - CAN/USA: Tier 2 data
Divergence

- Ecotoxicity

- CAN: GD EPS1/RM/44 or OPPTS
- USA: OPPTS
- AUS: tailoring data req. by radial taxonomy
- Some OPPTS quite brief, update?

- JP/EU: OECD (=Chemical protocols)
- EU data requirements too strict? (e.g. infectivity/pathogenicity in arthropods)
Industry/Consultant Views

Registration of Biopesticides: Challenges for the Biocontrol Industry

By Philip Kessler
Andermatt Biocontrol AG
The Challenges for the Biocontrol Industry

- How the Biocontrol industry is challenged by regulatory framework
- Experience with OECD guidelines and data requirements
- How the new EU regulation 1107/2009 impacts the Biocontrol Industry
- Lessons learned and future considerations

Registration of Biopesticides

Biopesticides need to be regulated
- ensure safety of the products
- ensure quality of biopesticides (avoid bad reputation, “snake oils”)
- protect R&D investment of the industry

- Registration requirements need to be adapted to special characteristics of micro-organisms
- Registration costs need to be reasonable, especially because most biopesticides have a smaller market potential due to their high specificity to their target organisms (narrow host range)
Registration of Biocides under 91/414

Registration of a biocide in the EU under 91/414/EEC
- Investment in a full OECD compatible data package (data requirements according to Annex II and III part B)
- Existing study guidelines often not appropriate for microorganisms
- Communication possibilities with EFSA and other authorities would improve registration process
- Unpredictable time period for the Annex-1 inclusion and national authorisations
- High registration fees (for RMS, and MS for national registration)
- Efficacy data for each MS

Registration of Baculoviruses under 91/414

<table>
<thead>
<tr>
<th>Active substance product</th>
<th>submitted</th>
<th>Annex-1</th>
<th>status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cydia pomonella granulovirus MADEX</td>
<td>2005</td>
<td>2009</td>
<td>old a.s., list 4 green track, EFSA</td>
</tr>
<tr>
<td>Adoxophyes orana granulovirus CAPEX</td>
<td>2004</td>
<td>2012</td>
<td>Approved in DE after NPA</td>
</tr>
<tr>
<td>Heliothis armigera nucleopolyhedrovirus HELICOVEX</td>
<td>2008</td>
<td>2013</td>
<td>NPA in IT (2010) and GR (2011)</td>
</tr>
<tr>
<td>Spodoptera littoralis nucleopolyhedrovirus LITTOVIR</td>
<td>2007</td>
<td>2013</td>
<td>NPA in IT (2012)</td>
</tr>
<tr>
<td>Spodoptera exigua nucleopolyhedrovirus SPEXIT</td>
<td>2008</td>
<td>2010</td>
<td>SANCO 0263/2008 No MS approval yet! Emergency approval for Andalucia (ES)</td>
</tr>
</tbody>
</table>
Main Hurdles and Challenges

1. Unknown or inappropriate data requirements
2. High and unpredictable costs for data packages
3. Lack of experience of authorities
4. Lack of knowhow within biocontrol industry
5. Unreasonable delays in the evaluation procedure
6. Too high registration fees

High investments and uncertainties are killing factors to register a biopesticide for niche markets

Registration of CAPEX

CAPEX
- Baculovirus product based on *Adoxophyes orana* granulovirus
- Biological control of summer fruit tortrix (*Adoxophyes orana*)

Why to register CAPEX in the EU?
- Fluctuating market for CAPEX
- Estimated annual turnover of 50,000 to 200,000 €
- Registration costs of 650,000 to 750,000 €
- Registration process more than 8 years
- ROI when CAPEX already need to be re-registered?

Consensus Document on information used in the risk assessment of environmental applications involving Baculoviruses

- occur only in arthropods, predominantly in the insect orders
- specific pesticidal agents: host range limited to one or a few species of the same genus.
- Effects on non-target species can be excluded
- not infective for mammals and no replication in mammalian cells.
- Not pathogenic, genotoxic, mutagenic, or carcinogenic
- produce no metabolites or toxins


REBECA ➔ SANCO 0253/2008

- Assessment of new isolates of baculovirus species already included in Annex I of 91/414/EEC
- New isolates for Cydia pomonella granulovirus (CpGV) quickly authorised, after Annex I inclusion of reference isolate (CpGV-M)
- Make new CpGV products available to bring solutions against CpGV-M resistance

- However....!

<table>
<thead>
<tr>
<th>Country (OECD)</th>
<th>Request for additional studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Italy</td>
<td>non-target studies on honey bees, <em>Typhlodromus pyri</em> and <em>Aphidius mpopulosphi</em></td>
</tr>
<tr>
<td>EFSA</td>
<td>non-target studies on earthworms</td>
</tr>
<tr>
<td>Australia</td>
<td>non-target studies on caddiesflies (Trichoptera)</td>
</tr>
<tr>
<td>USA</td>
<td>Human toxicology: cell culture study</td>
</tr>
</tbody>
</table>

OECD Guidance Document Nr. 65 (2011)

OECD issue paper on microbial contaminant limits for microbial pest control products

- Guidance on acceptable levels of microbial contaminants
- EU: Thresholds have been accepted by EFSA during evaluation of baculoviruses
- How other OECD countries will implement OECD conclusions (USA, Canada, Australia, ..)?
### 1107/2009: Experience with Biopesticides

#### Adapted data requirements?

<table>
<thead>
<tr>
<th>Pre-Submission meetings</th>
<th>Experience</th>
</tr>
</thead>
<tbody>
<tr>
<td>can help to avoid incomplete or inappropriate data packages at submission</td>
<td>It can be difficult that MS agree to set a date for these meetings</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Draft Registration Report</th>
<th>Experience</th>
</tr>
</thead>
<tbody>
<tr>
<td>should help MS to assess submitted data more efficiently</td>
<td>Template has been just recently developed and accepted for micro-organisms</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Requirements for studies</th>
<th>Experience</th>
</tr>
</thead>
<tbody>
<tr>
<td>No changes in data requirements compared to 91/414 (Annex II and III Part B)</td>
<td>Cost for data packages are actually still at a too high level</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Data requirements for efficacy data</th>
<th>Experience</th>
</tr>
</thead>
<tbody>
<tr>
<td>GEP status and EPPO guidelines</td>
<td>For many biopesticides guidelines are not available or not appropriate, GEP trials are expensive</td>
</tr>
</tbody>
</table>

#### Reduced cost for the application?

<table>
<thead>
<tr>
<th>Draft Registration Report</th>
<th>Experience</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conversion of the AIII data package into dRR format</td>
<td>Additional costs</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Zonal approach</th>
<th>Experience</th>
</tr>
</thead>
<tbody>
<tr>
<td>Should reduces the volume of efficacy trials within a zonal application</td>
<td>1107/2009 zones and EPPO zones are not congruent. Many MS still ask for MS-specific data</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Adapted fees for biopesticides</th>
<th>Experience</th>
</tr>
</thead>
<tbody>
<tr>
<td>Many MS grant special fees for biopesticides, but no harmonisation between MS</td>
<td>Focus on a few preferred, inexpensive MS to be eRMS. In some cases reduced fees are not granted</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mutual Recognition</th>
<th>Experience</th>
</tr>
</thead>
<tbody>
<tr>
<td>No separate national applications necessary anymore</td>
<td>Costs registration through mutual recognition are lower, but are still at too high level for niche markets</td>
</tr>
</tbody>
</table>
### Further Difficulties with Study Requirements and Methodology

- Storage stability studies: Request for new testing of products containing a new baculovirus isolate, but with identical formulation to already approved products.
- GLP studies for quality tests and storage stability studies: Bioassays
- EPPO guidelines for many microorganisms not appropriate

### 1107/2009: Experience with Biopesticides

<table>
<thead>
<tr>
<th>Quicker registration process?</th>
<th>Experience</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strict timelines</td>
<td>Quicker process, help to predict the marketing for new products</td>
</tr>
<tr>
<td>Mutual recognition</td>
<td>Faster authorisation of a PPP within a zone</td>
</tr>
<tr>
<td>Resources in MS</td>
<td>Increased workload in some MS</td>
</tr>
</tbody>
</table>
Lessons learned and Future Considerations

Consideration of the Biocontrol Industry
- The investment of registration of a new biopesticide in the EU may have less priority
- Focus registration for alternative markets (e.g., USA, South America, Asia, South Africa)
- Different focus of R&D investment for biopesticides with markets outside EU

EU growers will lack of new innovative environmental friendly biopesticides in the future, especially in the niche markets.

Lessons learned and Future Considerations

Demand for improved registration process, especially for biopesticides
- Reduce time frame for registration process
- More transparency in the procedure
- Data requirements need to be adapted and predictable
- Increase the experience for assessment of biopesticides
- Reduced fees, especially for products with limited market size

These are not new demands, but we need these improvements NOW.
Experiences with data requirements

By Rüdiger Hauschild
GAB Consulting

Experience with data requirements

Rüdiger Hauschild
GAB Consulting
D-21769 Lamstedt
ruediger.hauschild@gab-consult.de

Experience with data requirements

Data requirements are quite similar in different regulatory systems
Data requirements for use in plant protection or as a biocide are similar
Data requirements are justified to exclude negative effects on humans, non-target organisms or the environment
Experience with data requirements

Differences exist in the interpretation of data requirements

Which requirements need to be addressed by strain-specific studies and which can be covered using published literature?

Experience with data requirements

Most microorganisms used in biological control are scientifically well known

*Bacillus, Pseudomonas*

*Trichoderma, Verticillium, Beauveria*

Baculoviruses

Very little information on negative effects of microorganisms used for biocontrol
**Experience with data requirements**

One Example:
1. Evaluation of microbial metabolites

**Assessment of Microbial Metabolites**

Microorganisms can produce and secrete metabolites in the environment.

Chemical properties differ considerably:
- difference in molecular weight
- biosynthetic pathways
- chemical composition
Assessment of Microbial Metabolites

Possible properties of microbial metabolites:
- inhibitory to fungi
- inhibitory to bacteria
- toxic to insects
- induction of resistance in plants (SAR/ISR)
- toxic to non-target organisms

Metabolites can be involved in the mode of action
- alone
- in combination with other mechanisms

Assessment of Microbial Metabolites

Ecological functions of microbial metabolites:
- facilitation of attachment to surfaces
- inhibition of competitors (fungistasis)
- inactivation of hosts (parasitism)

Production and secretion of metabolites:
- losses in energy and nutrients
- production in nutrient rich media in vitro
- produced during exponential growth
Assessment of Microbial Metabolites

Identification of microbial metabolites:

• Literature information on the species or the genus
  – which metabolites can occur?
  – which of them are potentially harmful to non-target organisms?

• Strain specific data
  – determination and quantification of potentially harmful metabolites in the product
  – analysis of genes encoding potential toxins or enzymes of their biosynthetic pathway

Assessment of Microbial Metabolites

Occurrence of microbial metabolites:

• contained in the product
  – determination and quantification may be possible
  – potential effects can be assessed using safety studies with the product

• synthesized by the microorganism after application of the product
  – identification is not possible
  – quantification is possible for some compounds, difficult in many cases, and may be impossible at all
Assessment of Microbial Metabolites

Synthesis of microbial metabolites after application of the product:

- some metabolites need to be synthesized as they are part of the mode of action
- mainly produced during the interaction of the BCA with its host
- accumulation may occur in infested host insects
- exponential growth rarely occurs under environmental conditions
- accumulation in soil was never demonstrated

Assessment of Microbial Metabolites

Under which conditions do microbial metabolites represent a risk to humans, non-target organisms or the environment?

1. metabolites are toxic
2. metabolites are contained in the product
3. metabolites are produced and accumulated after product application
4. accumulation occurs at sites that are exposed to non-target organisms

Only in case points 1 and (2 or 3+4) are fulfilled, further analysis is required
Experiences with data requirements

Summary

Assessment of Microbial Metabolites
Most microorganisms used in biocontrol are well known
Some metabolites are synthesized as part of the mode of action
Metabolites can be contained in the product
Synthesis occurs often during interaction with the host
Accumulation of microbial metabolites with harmful effects on non-target organisms in the environment is unlikely to occur and was never observed
Evaluation can be based on product data and published literature

Many Thanks!

Rüdiger Hauschild
GAB Consulting
D-21769 Lamstedt
ruediger.hauschild@gab-consult.de
Experiences with compilation of dossiers etc. where there is a need for more guidance and criteria, obstacles

By Mark Whittaker
Biosphere Biopesticide Consulting

ECOTOXICOLOGY AND MICROBIAL BIOPESTICIDES

Dr Mark Whittaker MBPR (Hort)
Managing Director
BIOSPHERE BIOPESTICIDE CONSULTING
Knaresborough Technology Park, Marsoe Lane, Knaresborough, North Yorkshire, HG5 8LF, United Kingdom
Tel: +44 (0)1423 868 694  Mob: +44 (0)7515 900 772  Email: mark@biosphereconsulting.com  Web: www.biosphereconsulting.com

INTRODUCTION
• Biological crop protection industry
  - Consultant Entomologist
  - Research & Regulatory Affairs Manager
  - General Manager (UK)
• EU regulatory affairs consultancy
• BIOSPHERE BIOPESTICIDE CONSULTING

• A GLP lab specialising in microbial biopesticides
• 5-batch analysis
• Phys-chem studies
• Storage stability
• Terrestrial ecotox
• Microbiology for acute tox studies
ECOTOXICOLOGY

• Expertise from some of the best ecotoxicologists in Europe
• High quality, bespoke studies
• Basic limit tests through to field scale studies
• Aquatic ecotox undertaken at local CRO (no vertebrate studies undertaken in-house, hence no fish, and thus no Daphnia & algae)
• Analytical dose verification undertaken for all aquatic studies

Ecotoxicology and microbial pesticides

• For microbial substances, studies are routinely requested on:
  - Aquatic ecotoxicology
  - Avian toxicity
  - Earthworm toxicity
• Waiver arguments may be accepted by RMS, but in many cases the safest approach is to conduct the study
OECD vs OPPTS guidelines

- OECD guidelines poorly adapted to microbial substances
- OPPTS guidelines quite severe in terms of animal usage in vertebrate studies
- A compromise position is often required

**More fundamental issue:**

Are these studies required at all for microbial substances?

Cost vs benefit

- Toxicity studies with microbial substances require a full investigation of pathogenicity, infectivity and clearance
- This adds considerably to the cost of studies, and provides little genuinely useful information

<table>
<thead>
<tr>
<th>Study</th>
<th>Cost (including P, I &amp; C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fish</td>
<td>£10,000 - £15,000</td>
</tr>
<tr>
<td>Daphnia</td>
<td>£6,000 - £10,000</td>
</tr>
<tr>
<td>Algae</td>
<td>£6,000 - £10,000</td>
</tr>
<tr>
<td>Avian toxicity</td>
<td>£15,000 - £25,000</td>
</tr>
<tr>
<td>Earthworm reprotox</td>
<td>£9,000 - £12,000</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>£46,000 - £72,000</strong></td>
</tr>
</tbody>
</table>
AQUATIC ECOTOX

- Aquatic systems are continually exposed to microbial agents through run-off and surface deposition from the air
- Aerobic microorganisms don’t proliferate in water: poor nutrient status, insufficient organic carbon etc
- Where effects are reported they tend to be sub-lethal effects on Daphnia and algae, and are usually attributed to physical rather than toxic effects
### Aquatic ecotox

<table>
<thead>
<tr>
<th>Active Substance</th>
<th>Fish</th>
<th>Daphnia</th>
<th>Algae</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ampelomyces quisqualis</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Aureobasidium pullulans</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Bacillus amyloliquifaciens</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Bacillus firmus</td>
<td>✓</td>
<td>✓</td>
<td>x¹</td>
</tr>
<tr>
<td>Bacillus pumilus</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Bacillus subtilis QST713</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Bacillus thuringiensis Aizawai ABTS1857</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

*Notes*

1. Adverse effect reported on algae due to turbidity in test system.

### Aquatic ecotox

<table>
<thead>
<tr>
<th>Active Substance</th>
<th>Fish</th>
<th>Daphnia</th>
<th>Algae</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacillus thuringiensis Aizawai GC-91</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Bacillus thuringiensis Israelensis AM-6552</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Bacillus thuringiensis Kurstaki ABTS-351</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Bacillus thuringiensis Kurstaki PB-54</td>
<td>✓¹</td>
<td>✓¹</td>
<td>✓¹</td>
</tr>
<tr>
<td>Bacillus thuringiensis Kurstaki SA-11 et al.</td>
<td>✓¹</td>
<td>✓¹</td>
<td>✓¹</td>
</tr>
<tr>
<td>Bacillus thuringiensis Tenebrionis NB-176</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Beauveria bassiana ATCC 74040</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

*Notes*

1. No data submitted. RMS concluded that it posed low risk on basis of evidence provided.
### Aquatic ecotox

<table>
<thead>
<tr>
<th>Active Substance</th>
<th>Fish</th>
<th>Daphnia</th>
<th>Algae</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Beauveria bassiana GHA</strong></td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td><strong>Candida oleophila strain O</strong></td>
<td>✔ 1</td>
<td>✔ 1</td>
<td>✔ 1</td>
</tr>
<tr>
<td><strong>Lecanicillium muscarium Ve6</strong></td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td><strong>Metarhizium anisopliae</strong></td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td><strong>Paecilomyces fumosoroseus</strong></td>
<td>✔ 1</td>
<td>✔ 1</td>
<td>✔ 1</td>
</tr>
<tr>
<td><strong>Paecilomyces lilacinus 251</strong></td>
<td>✔</td>
<td>✔</td>
<td>✗ 2</td>
</tr>
<tr>
<td><strong>Phlebiopsis gigantea</strong></td>
<td>✔ 1</td>
<td>✔ 1</td>
<td>✔ 1</td>
</tr>
</tbody>
</table>

**Notes**

1. No data submitted. RMS concluded that it posed low risk on basis of evidence provided.
2. Slight adverse effect reported on algae due to nutrient competition.

### Aquatic ecotox

<table>
<thead>
<tr>
<th>Active Substance</th>
<th>Fish</th>
<th>Daphnia</th>
<th>Algae</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pseudomonas chlororaphis</strong></td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td><strong>Pseudomonas sp.</strong></td>
<td>✔ 1</td>
<td>✔ 1</td>
<td>✔ 1</td>
</tr>
<tr>
<td><strong>Pythium oligandrum</strong></td>
<td>✔ 1</td>
<td>✔ 1</td>
<td>✔ 1</td>
</tr>
<tr>
<td><strong>Streptomyces lydicus</strong></td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td><strong>Trichoderma asperellum</strong></td>
<td>✔ 1</td>
<td>✔ 1</td>
<td>✔ 1</td>
</tr>
<tr>
<td><strong>Trichoderma atroviride IMI-206040</strong></td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td><strong>Trichoderma atroviride I-1237</strong></td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
</tbody>
</table>

**Notes**

1. No data submitted. RMS concluded that it posed low risk on basis of evidence provided.
Aquatic ecotox

<table>
<thead>
<tr>
<th>Active Substance</th>
<th>Fish</th>
<th>Daphnia</th>
<th>Algae</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trichoderma harzianum Rifai</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Trichoderma polysporum IMI-206039</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Trichoderma viride ICC-080</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Verticillium albo-atrum WCS-850</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
</tr>
</tbody>
</table>

Notes
1. No data submitted. RMS concluded that it posed low risk on basis of evidence provided.
### DAR risk assessment conclusions

#### Avian toxicity

<table>
<thead>
<tr>
<th>Active Substance</th>
<th>Birds</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Ampelomyces quisqualis</em></td>
<td>✓</td>
</tr>
<tr>
<td><em>Aureobasidium pullulans</em></td>
<td>✓</td>
</tr>
<tr>
<td><em>Bacillus amyloliquefaciens</em></td>
<td>✓</td>
</tr>
<tr>
<td><em>Bacillus firmus</em></td>
<td>✓</td>
</tr>
<tr>
<td><em>Bacillus pumilus</em></td>
<td>✓</td>
</tr>
<tr>
<td><em>Bacillus subtilis</em> QST713</td>
<td>✓</td>
</tr>
<tr>
<td><em>Bacillus thuringiensis Aizawai</em> ABTS1857</td>
<td>✓</td>
</tr>
</tbody>
</table>

Notes:

1. No data submitted. RMS concluded that it posed low risk on basis of evidence provided.
### Avian toxicity

<table>
<thead>
<tr>
<th>Active Substance</th>
<th>Birds</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Beauveria bassiana</em> GHA</td>
<td>✓</td>
</tr>
<tr>
<td><em>Candida oleophila</em> strain O</td>
<td>✓ 1</td>
</tr>
<tr>
<td><em>Lecanicillium muscarium</em> Ve6</td>
<td>✓</td>
</tr>
<tr>
<td><em>Metarhizium anisopliae</em></td>
<td>✓</td>
</tr>
<tr>
<td><em>Paecilomyces fumosoroseus</em></td>
<td>✓ 1</td>
</tr>
<tr>
<td><em>Paecilomyces lilacinus</em> 251</td>
<td>✓ 1</td>
</tr>
<tr>
<td><em>Phlebiopsis gigantea</em></td>
<td>✓ 1</td>
</tr>
</tbody>
</table>

**Notes**

1. No data submitted. RMS concluded that it posed low risk on basis of evidence provided.
### DAR risk assessment conclusions

#### Avian toxicity

<table>
<thead>
<tr>
<th>Active Substance</th>
<th>Birds</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Trichoderma harzianum</em> Rifai</td>
<td>✓</td>
</tr>
<tr>
<td><em>Trichoderma polysporum</em> IMI-206039</td>
<td>✓</td>
</tr>
<tr>
<td><em>Trichoderma viride</em> ICC-080</td>
<td>✓(^1)</td>
</tr>
<tr>
<td><em>Verticillium albo-atrum</em> WCS-850</td>
<td>✓(^1)</td>
</tr>
</tbody>
</table>

**Notes**

1. No data submitted. RMS concluded that it posed low risk on basis of evidence provided.
Earthworm toxicity

- There are no reported pathogens of earthworms
- When one is found, it has a ready market in the amenity sector
- Worms live in constant contact with soil and have highly efficient immune systems
- Earthworms are used in vermistabilisation – removing dangerous pathogens from contaminated waste
- Where pathogenic effects have been reported they were either induced at rates greatly in excess of field application rates, or were due to something other than the toxicity of the MBCA

### DAR risk assessment conclusions

#### Earthworm toxicity

<table>
<thead>
<tr>
<th>Active Substance</th>
<th>Earthworms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ampelomyces quisqualis</td>
<td>No data¹</td>
</tr>
<tr>
<td>Aureobasidium pullulans</td>
<td>✓</td>
</tr>
<tr>
<td>Bacillus amyloiquefaciens</td>
<td>✓</td>
</tr>
<tr>
<td>Bacillus firmus</td>
<td>✓</td>
</tr>
<tr>
<td>Bacillus pumilus</td>
<td>✓</td>
</tr>
<tr>
<td>Bacillus subtilis QST713</td>
<td>No data¹</td>
</tr>
<tr>
<td>Bacillus thuringiensis Aizawai ABTS1857</td>
<td>✓</td>
</tr>
</tbody>
</table>

**Notes**

¹. Acute study with full histopathological investigation requested by RMS
### Earthworm toxicity

<table>
<thead>
<tr>
<th>Active Substance</th>
<th>Earthworms</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Bacillus thuringiensis</em> Aizawai GC-91</td>
<td>✔</td>
</tr>
<tr>
<td><em>Bacillus thuringiensis</em> Israelensis AM-6552</td>
<td>✔</td>
</tr>
<tr>
<td><em>Bacillus thuringiensis</em> Kurstaki ABTS-351</td>
<td>✔</td>
</tr>
<tr>
<td><em>Bacillus thuringiensis</em> Kurstaki PB-54</td>
<td>✔¹</td>
</tr>
<tr>
<td><em>Bacillus thuringiensis</em> Kurstaki SA-11 <em>et al.</em></td>
<td>✔¹</td>
</tr>
<tr>
<td><em>Bacillus thuringiensis</em> Tenebrionis NB-176</td>
<td>×²</td>
</tr>
<tr>
<td><em>Beauveria bassiana</em> ATCC 74040</td>
<td>✔</td>
</tr>
</tbody>
</table>

**Notes**

1. No data submitted. RMS concluded that it posed low risk on basis of evidence provided.
2. Lowest test concentration was 4 orders of magnitude greater than highest field concentration.

---

### Earthworm toxicity

<table>
<thead>
<tr>
<th>Active Substance</th>
<th>Earthworms</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Beauveria bassiana</em> GHA</td>
<td>✔</td>
</tr>
<tr>
<td><em>Candida oleophila</em> strain O</td>
<td>✔¹</td>
</tr>
<tr>
<td><em>Lecanicillium muscarium</em> Ve6</td>
<td>✔</td>
</tr>
<tr>
<td><em>Metarhizium anisopliae</em></td>
<td>✔</td>
</tr>
<tr>
<td><em>Paecilomyces fumosoroseus</em></td>
<td>✔¹</td>
</tr>
<tr>
<td><em>Paecilomyces lilacinus</em> 251</td>
<td>✔</td>
</tr>
<tr>
<td><em>Phlebiopsis gigantea</em></td>
<td>✔¹</td>
</tr>
</tbody>
</table>

**Notes**

1. No data submitted. RMS concluded that it posed low risk on basis of evidence provided.
### Earthworm toxicity

<table>
<thead>
<tr>
<th>Active Substance</th>
<th>Earthworms</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Pseudomonas chlororaphis</em></td>
<td>✓</td>
</tr>
<tr>
<td><em>Pseudomonas sp.</em></td>
<td>✓</td>
</tr>
<tr>
<td><em>Pythium oligandrum</em></td>
<td>✓</td>
</tr>
<tr>
<td><em>Streptomyces lydicus</em></td>
<td>✓</td>
</tr>
<tr>
<td><em>Trichoderma asperellum</em></td>
<td>✓</td>
</tr>
<tr>
<td><em>Trichoderma atroviride IMI-206040</em></td>
<td>✓</td>
</tr>
<tr>
<td><em>Trichoderma atroviride I-1237</em></td>
<td>✓</td>
</tr>
</tbody>
</table>

**Notes**

1. No data submitted. RMS concluded that it posed low risk on basis of evidence provided.

---

### Earthworm toxicity

<table>
<thead>
<tr>
<th>Active Substance</th>
<th>Earthworms</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Trichoderma harzianum</em> Rifai</td>
<td>✓</td>
</tr>
<tr>
<td><em>Trichoderma polysporum</em> IMI-206039</td>
<td>✓</td>
</tr>
<tr>
<td><em>Trichoderma viride ICC-080</em></td>
<td>✓</td>
</tr>
<tr>
<td><em>Verticillium albo-atrum</em> WCS-850</td>
<td>✓</td>
</tr>
</tbody>
</table>

**Notes**

1. No data submitted. RMS concluded that it posed low risk on basis of evidence provided.
• Aquatic, avian and earthworm studies represent a considerable investment
• Requirement to reduce vertebrate testing
• Effects are rare, and when encountered are usually:
  a) Sub-lethal
  b) Induced at unrealistic rates
  c) Not attributed to the toxicity of the MPCA
• Are these studies required for microbial substances?
Experiences with compilation of microbial dossiers: relevance of current data requirements

By Roma L Gwynn

Rationale

Experiences with compilation of microbial dossiers: Relevance of current data requirements

Roma L Gwynn

Microbial bioinsecticides – MoA

Entomopathogenic fungi
Baculoviruses – MoA

1. Insect feeding on virus-contaminated foliage
2. Close up of occlusion bodies (OBs)
3. Lumen of digestive tract (alkaline conditions)
4. Virus particles being released from OBs and adhering to brush border of gut cells
5. Replication of virus in insect cell

Microbial biofungic Peace – MoA

*Trichoderma* spp.

*Bacillus subtilis*
Microbial Biopesticide production
Microbial production systems

Solid state - mainly fungi
- All fermentation material
- Testing includes +/- metabolites
- Acute test - no end point of concern = no further testing?

Solid state - mainly fungi
- Spores only

Liquid state - mainly bacteria
- All fermentation material
- Testing includes +/- metabolites
- Acute testing relevant? Metabolites = in situ (field) expression
- Acute test - no end point of concern = no further testing?

Liquid state - mainly bacteria
- Spores only

- Production systems often total systems → product
- TGAI or A.S. – often deliberate stop - specifically for sampling
- In product – micro-organisms in quiescent state – no growth
Microbial – metabolites

- **Beauveria** spp. – produced in solid state fermentation – spore product
- Metabolites - in product
  - *in situ* expression post application
- Product:
  - not possible to test for all metabolites
  - from literature possibly 9 metabolites
  - beauvericin most common = representative
  - test for this and x 9 safety factor
  - No beauvericin found in product
- **In situ**
  - *Beauveria* spp. used for example against whitefly in greenhouse
  - Adult whitefly = 40 μg
  - Potential metabolites = max 0.002 μg per adult
  - Very low potential exposure

### Microbials - types

- **Beauveria bassiana**
- New isolate
- **B. subtilis**
- **Bt.**
- **Spinosad**
- **Rhizobium spp.**
- **Coniothyrium sp.**
- **Trichoderma spp.**
- New spp.
Microbial – toxicity, acute studies

- In EU: currently 37 microbialis on Annex I – 28 dossiers
- In EU pending: 12 microbial a.s., 12 dossiers
- Sensitisation – agreement to have standard phrase
  ‘may provoke sensitising reaction’
- For all other acute tests – for cfu no end points of concern
- For metabolites – only 3 cases where metabolites considered significant
  - for each product, reasoned case possible to indicate
    not relevant in field
- No MRL
- Many other areas where study results always negative

Natural microbial infections

Natural declines in cotton aphid, *Aphis gossypii*, caused by the fungus *Neozygites fresenii*, in the southern USA

- Important cotton pest in USA since the 1980s.
- Caused by *A. gossypii* developing pesticide resistance.
Natural microbial infections

- *N. fresenii* started causing epizootics in *A. gossypii* on cotton in Mississippi Delta in 1989.
- Common, begin in July, occur at same time in the same region.
- Prediction service run by Uni. of Arkansas (Steinkraus et al.) - allows farmers to save insecticide sprays.
- Saves money and preserves other natural enemies.

Steinkraus; Arkansas University

Natural microbial infections

Population dynamics

- When average prevalence of fungus reaches 15%, the aphid population will soon begin to decline.

- When this starts, the aphid population falls by 80% in 3 - 4 days.

- Fungus detectable up to 10 days before the aphid population starts to decline this rapidly.
Biopesticides – efficacy

Microbial – environmental persistence

- Consider application rates compared to background levels
- Product applied to disturbed agro ecosystem not natural ecosystem
- Cultivation more effect on microbial community that short perturbation caused by application of microbial
- Recent work demonstrating that in Denmark in one field – 14 species of Metarizium spp.
- 1 gram of soil, there may be 20,000 to 40,000 species of bacteria

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>3,000,000 to 500,000,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actinomycetes</td>
<td>1,000,000 to 20,000,000</td>
</tr>
<tr>
<td>Fungi</td>
<td>5,000 to 1,000,000</td>
</tr>
<tr>
<td>Yeast</td>
<td>1,000 to 1,000,000</td>
</tr>
<tr>
<td>Protozoa</td>
<td>1,000 to 500,000</td>
</tr>
<tr>
<td>Algae</td>
<td>1,000 to 500,000</td>
</tr>
<tr>
<td>Nematodes</td>
<td>10 to 5,000</td>
</tr>
</tbody>
</table>
Microbials – critical requirements for safety

Questions asked in current system: not specifically designed to assess safety of a microorganism – are they right Q’s?

1. Identity: taxonomic position = biology, ecology and specificity
2. More differences between isolates than between spp.
3. Ability to persist and spread – potential to disturb natural ecosystem
4. Efficacy
5. Test only product
6. ?

Thank you for your attention
The Way Forward – A Vision from IBMA

By David Cary
Executive Director, IBMA

Values and Perception of Value?
OECD International Regulatory Co-operation
– Addressing Global Challenges – April, 2013

“The world is becoming increasingly global. This raises important challenges for regulatory processes which still largely emanate from domestic jurisdictions. In order to eliminate unnecessary regulatory divergences and to address global challenges pertaining to systemic risks, the environment, and human health and safety, governments increasingly seek to better articulate regulations across borders and to ensure greater enforcement of rules and their application across jurisdictions.”

OECD Policy

– IRC – International Regulatory Co-operation
  ◦ Growing regulatory co-operation
  ◦ Layering of co-operation
  ◦ Shift from complete harmonisation to more flexible regulatory co-operation mechanisms
    ◦ Such as mutual recognition
  ◦ Multiplication of state & non-state actors
  ◦ Rise of soft law
    ◦ Codes of conduct, guidelines & guidance
  ◦ Increase in using intergovernmental organisations
    ◦ OECD, FAO, etc..
  ◦ Utilise formal regulatory partnerships where established
    ◦ NAFTA, ECOWAS, CILWAS, etc..

May 2013
What have we got with biopesticides?

- A system designed for substances presenting different risks to environment & health
- Lack of a system in many OECD & non-OECD Member States
- Restricted expertise in regulatory bodies
- Rapid global expansion in the industry
- Expansion of fraud and false practice
- Expansion & lack of clear boundaries with related industries
- Policy support for expanded use
- Support from Growers, NGOs, PMOs and Consumers
- Wide range & experience of actors

Recommendation of the Council on Regulatory Policy and Governance – OECD 2012

How to proceed

- Clearly define all bio industries & propose proportionate legislation for all based on risk to human health & the environment
- Apply soft law
  - Guidance
- Recognise, Foster and Utilise formal regulatory partnerships or umbrellas
  - Use established groups and co-operations where possible
- Recognise and utilise the strengths and benefits of Intergovernmental Organisations – OECD & FAO

Current tool categories available from the Biocontrol industry

- **Microbials**: Viruses, Bacteria & Fungal Pathogens
- **Macrobials**: Predatory mites & insects, nematodes
- **Semiochemicals**: Pheromones, Plant volatiles
- **Natural Products**: Plant extracts, Seaweed products & Basic substances
A new global regulatory approach utilising FAO / OECD / Regional areas of expertise

**OECD Guidance & Definitions**
- Regional representation
- BRC participation
- EU involvement
- EPA & PMRA expertise utilised

**Global evaluations**
- EU centres of excellence
- Regional representation from LATAM, AF, Asia & Pacific
- Utilise US EPA expertise

**FAO Global Regulatory Toolbox**
- Adopt existing NAFTA / EU registrations into toolbox
- Available for cross adoption on a global basis
- Progressively incorporate new global reviews

---

**Regulation of Biopesticides**

**OECD Definitions & Guidance for information requirements and risk assessment**

<table>
<thead>
<tr>
<th>EU / BPSC</th>
<th>NAFTA USA/CA</th>
<th>ALIS</th>
<th>China</th>
<th>Chile</th>
</tr>
</thead>
</table>

**Global Evaluations**

- EU MS Participation

**EU MS Participation**
- Kem SE / DK EPA – Microbials
- Ctgbl NL / DE – Nat Products
- ANSES FR / UK – Samsiochemicals
Regulation of Biocontrol Products

OECD Definitions & Guidance for information requirements and risk assessment

EU / BPSG  NAFTA USA/CA  AUS  China  Chile

Global Evaluations

EU MS  Option B
NAFTA – US EPA / PMRA CA  Asia Pacific - China / APVMA AUS  Africa - Cits  LATAM – BRA, ARG / CL

Using Pan EU MS Leads


May 2013

How to future proof any regulation

Promote & Promote True Innovation

Protection against fraud

Facilitating & Documenting

OECID & FAO Support

Well Defined with Solid Progression

Global Scientific Peer Reviews

Proportionate to risk

Biological Chemistry based

May 2013
Conclusion

- Forward thinking to incorporate and not hinder future innovation
- Harmonised OECD and non-OECD global regulatory frameworks
- Information requirements proportionate to risk to human health & environment
- “Innocence until proven guilty principle” or “Green Track principle”

Innovative products need innovative regulatory frameworks