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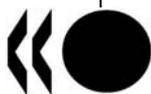
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**ENVIRONMENT DIRECTORATE
JOINT MEETING OF THE CHEMICALS COMMITTEE AND
THE WORKING PARTY ON CHEMICALS, PESTICIDES AND BIOTECHNOLOGY**

**REPORT OF WORKSHOP ON THE REGULATION OF BIOPESTICIDES: REGISTRATION AND
COMMUNICATION ISSUES**

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OECD Environment, Health and Safety Publications

Series on Pesticides

No. 44

**Report of Workshop on the Regulation of Biopesticides:
Registration and Communication Issues**

15 – 17 April 2008, EPA, Arlington, USA

Environment Directorate

ORGANISATION FOR ECONOMIC COOPERATION AND DEVELOPMENT

Paris 2009

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FOREWORD

This document is a report of the OECD *Workshop on the Evaluation of Biopesticides: Registration and Communication*, which took place on 15 – 17 April 2008, in Arlington, US. It was hosted by the US EPA Office of Pesticide Programs.

Forty-seven experts from 12 OECD countries, the European Food Safety Authority (EFSA) and the International Biocontrol Manufacturers Association (IBMA) participated in the workshop, representing government/public authorities, research institutes, academia, and industry. The List of Participants is presented in [Annex 3](#).

The objectives of the workshop were to: (i) resolve sciences issues and harmonise approaches for risk assessment/evaluation associated with the registration of biopesticides; (ii) improve communication and information exchange between regulators and industry; and (iii) consider and identify follow-up activities to some of the conclusions and recommendations of the European REBECA project (Regulation of Biological Control Agents).

The expected benefits of the workshop were to support activities that will result in: (i) the implementation of actions/practical tasks to facilitate work sharing; (ii) the development of 'more harmonised' data sets; (iii) the use of fewer resources for the evaluation of data submission and for peer reviews; and (iv) help regulatory decisions more timely.

The workshop included the following sessions: (a) Overview of regulatory systems; (b) Outcome of REBECA; (c) Qualified Presumption of Safety (QSP); (d) Microbial pesticides overview; (e) Efficacy; (f) Case studies discussed in two breakout groups; (g) Pheromones; and (h) Communication. The Workshop Agenda is presented in [Annex 1](#). Presentations were made at all sessions except for the discussions in the breakout groups. The abstracts of these presentations are presented in [Annex 2](#).

The draft Report of the Workshop was approved by the 23rd Meeting of the Working Group on Pesticides (WGP) that took place on 4-5 November 2008.

The Joint Meeting agreed that it should be made available to the public. This document is published on the responsibility of the Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology of the OECD.

INTRODUCTION

1. The participants were welcomed by *Janet Andersen* (Director of the BioPesticides Division; US-EPA). She emphasised the importance of biopesticides in current agricultural production.

2. The chair, (*Jeroen Meeussen*, CTGB, the Netherlands), expressed his thanks to EPA for hosting this workshop. He expressed, on behalf of *Marie-Chantal Huet* (OECD-secretariat), her sincere apologies for not being able to attend the workshop. The chair introduced the workshop by asking the question: "Are biopesticides a matter of public interest?" As an example, reference was made to an article from the "Science for Environment Policy" newsletter from the European Commission titled: Chemical pesticides on their way out?¹

"Consumer concern about chemical pesticide residues on food is driving the search for alternatives. New research suggests that biocontrol, using beneficial bacteria or fungi to control plant disease and pests, could be developed as an effective alternative. The research focused on developing a way of applying biocontrol agents to seeds before they are planted. This offers an early non-chemical means of reducing or preventing the devastating effects of disease or pest attack on crop production."

3. The goal of the workshop was to make recommendations on how to improve the registration process for Biopesticides worldwide and to resolve the current barriers to joint reviews in light of the OECD "*Vision for the Future*". This includes a statement of the vision for the next ten years, including details of the specific objectives to be achieved and the milestones to be reached along the way:

Building on progress achieved, the OECD has adopted the vision that, by the end of 2014, it will ensure that:

- *The regulatory system for agricultural pesticides will have been harmonised to the extent that country data reviews (monographs) for pesticides prepared in the OECD format on a national or regional basis (e.g. EU or NAFTA) can be used to support independent risk assessments and regulatory decisions made in other regions or countries.*
- *The preparation of data submissions (dossiers) for pesticide active substances and for end-use products is co-ordinated globally by industry (to the extent possible).*
- *Work-sharing arrangements between regulatory authorities in OECD countries take place as a matter of routine.*
- *The generation of a single monograph for each active substance, serving the needs of the regulatory authorities in all OECD countries, has become commonplace, notwithstanding the need for separate independent risk assessments and regulatory decisions in each jurisdiction.*

4. The objectives of the workshop were:

¹ Bennett, A. J. and Whipps, J. M (2008). Dual application of beneficial microorganisms to seed during drum priming. *Applied Soil Ecology* 38 (1): 83-89

- To collect input to resolve science issues and harmonize approaches associated with registering biopesticides (evaluation and risk assessment). Issue papers on different topics will be (further) developed.
- To improve communication and information exchanges between regulators, scientists and/or industry. This can be done by organizing discussions, seminars or workshop on topics related to biopesticides.
- To take forward some of the conclusions and recommendations from REBECA. REBECA (Regulation of Biological Control Agents – BCAs) is an EU policy support action to review the possible risks of biocontrol agents, compare regulations in the EU and the USA and propose alternative regulation procedures.

5. The expected benefits of the workshop are:

- Implement practical tasks to facilitate work sharing e.g. by appointing contact points for biopesticides within each registration authority and to stimulate joint reviews.
- Work to more harmonized data sets by understanding how data requirements are used by other authorities.
- Use fewer resources for the evaluation of data submissions and for peer review. This can be achieved by using the evaluation prepared by a country to support independent risk assessments and regulatory decisions made in other regions or countries.
- Arrive at more timely regulatory decisions. If fewer resources will be used for evaluation as a result the procedure will speed up considerably.

WORKSHOP CONCLUSIONS AND RECOMMENDATIONS

Summary of agreed activities, conclusions, recommendations and future developments

6. The key-word of the workshop was *Communication*. Communication between regulators, scientists, industry, consumer organisations, growers organisations and NGO's should be encouraged. Not only should communication between these groups be improved, but also communication within these groups.

7. Communication implies that all parties understand a common language. If we want to speak a common language we should use the same definitions or at least know what is covered by a definition. If we talk about *biopesticides* or *biological control agents* we have to know if this includes genetically modified organisms (GMO's); if growth regulators are covered by this definition; if products of natural origin fall within the scope of this definition; etc. It is not necessary that everyone uses the same definition, but it should be clear which definition is used and what types of products fall within the scope of the definition.

8. Regarding efficacy, this also applies to the 'label language' used to express the level of performance of the product. Terms such as *control*, *reduction*, *suppression* must be clearly defined.

9. Regarding pheromones, the scope of the definition for straight chain lepidopteran pheromones (SCLP's) should not be stretched.

10. To facilitate information exchange, the registration authorities should consider developing a website for biopesticides and appointing contact points for biopesticides.

11. Pre-submission meetings should be a routine. Clear guidance should be developed on a pre-submission data package. Pre-submission meetings should take place as early as possible in the process, be timed and the purpose of the meetings should be clear. This proposal takes into account, a recommendation from REBECA.

12. A better understanding of the regulatory process will result in earlier decisions.

13. Based on the lessons learned document, the EU and US/Canada can further harmonise their approach to waivers. Changing the data requirements is always a time consuming and lengthy process. A more suitable approach is envisaged in the preparation of guidance documents for the different types of products/product groups. Where possible, a tiered strategy should be considered. This approach also responds to a REBECA's recommendation.

14. Reference was made to the reports of the individual sessions of the breakout groups. Recommendations will be taken forward by the BPSG. Further issue papers will be developed on a number of topics, including:

- Waivers;
- Microbial contamination;
- Evaluation of environmental safety of microbial pest control products (MPCP);
- Fungal metabolites; and
- Pheromones.

15. The use of study report templates for micro-organisms should be taken forward by OECD member countries.

16. Biopesticides should not be treated as 'conventional chemicals'; discussion on this topic should take place in specialised groups. Ideally there should be a separate division dedicated to biopesticides, as it is the case in the US EPA. This issue was also addressed in the REBECA project.

17. Regarding the fee issue, it was emphasised that policy people should be contacted and that reference should be made to countries which have established a reduced fee for biopesticides. This is one of the recommendations from REBECA.

18. The chair thanked all participants for their contributions, patience and discussions. He expressed special thanks to the facilitators of the breakout groups, *Kersti Gustafsson* (Sweden) and *Brian Belliveau* (Canada), the report writers of the breakout groups, *John Dale* (UK) and *Annabel Waggoner* (US), and *Janet Andersen* and *Bill Schneider* (US EPA) for taking care of the workshop arrangements.

SUMMARY OF QUESTIONS AND ANSWERS

Regulatory Overview Summaries

Q: Will biochemicals be considered in this workshop? (*Amy Roberts*, US, Consultant)

A: This is not the intention. Most emphasis in this workshop will be on micro-organisms and pheromones. The scope of the BPSG might be extended to plant extracts, but less emphasis will be put on other biochemicals (*Jeroen, Meeussen*; EU)

Q: What is DT₅₀ and why 60 Days? (*Joel Gagliardi*, US)

A: DT₅₀ represents 50% of substance which is disintegrated within 60 days in the environment. It is not very well defined in the EU why it has been set at 60 days; it comes from the conventional pesticides.

Q: What is the definition of a new substance for microbes? (*Niels Hendriksen*, Denmark)

A: A new microbial strain from a registered source (*Alan Reynolds*, US)

Q: How Europe and the US identify new strains? (*Denise Munday*, Valent Biosciences)

A: In Europe a new strain is differentiated genetically from any other known strain, while the US EPA asks for a registered strain in a cell bank like ATCC (*Alan Reynolds*, US). In addition, strains can be differentiated by the production of metabolites (*Bilgin Karaoglan*, Germany).

Q: What about the fees and fee waivers and what happens if consultants are paid by the US EPA? (*Kersti Gustafsson*, Sweden)

A: Companies pay for consultants, not the EPA

Q: How long a registration is valid? (*Jeroen Meeussen*, Netherlands)

A: In the US, there is no expiration date for registration but a re-assessment every 15 years under FIFRA (*Alan Reynolds*, US)

Q: Are consultants informed of changes of regulations? (*Jeroen Meeussen*, Netherlands)

A: Consultants are aware of changes in regulations (*Alan Reynolds*, US).

Outcome of REBECA

Q: Are there more specific data requirements in REBECA? (*Hans Mensink*, Netherlands)

A: Although the EU member states are in favour of less data requirements, the data requirements as laid down in Council Directive 91/414/EEC will not be changed (at least not in the short-term). A more practical solution will be to develop guidance document on data requirements for the different groups (e.g. pheromones, plant extracts) (*Jeroen Meeussen*, Netherlands).

SUMMARY OF DISCUSSIONS AT BREAKOUT SESSIONS

Science Issues associated with the Registration of Biopesticides

A. Identification / Taxonomy / Extrapolation of Data between Strains

Item for discussion: Identification of micro-organisms and data package

- (a) What methods should be used for identification of micro-organisms?
- (b) This data package – to conclude if strains are similar – can be different for bacteria, fungi and viruses. What should be included in such a data package?

Discussion

- It is a struggle for regulators to determine at what taxonomic level require verification and the types of methods that should be used to identify micro-organisms (this would include viruses).

We all provide guidance to industry to use best available technology (evolving discipline) due to more cost effective molecular technology – probably more common (such as Baculoviruses - DNA sequencing).

- What level of specification is needed for satisfying product identity? In Canada and US, registration is given to the strain level. Canada registers to "strain level", but in practice registers a specific isolate; so one could have the same strain registered by different companies. It is the same situation in the US; it is to make sure that the laboratory does not have microbial contaminants (such as Bt vs. *B. subtilis*); it must ensure purity of the product.
- In EU, industry has to prove their strain is unique and different from all other strains using the best available technique (e.g. DNA sequencing). This can be a challenge and an unreasonable burden (e.g., Bt tends to be clonal); it depends on the micro-organism.
- Taxonomy is important; identifying the micro-organism is first step in risk assessment. Regulators must be more flexible/ reasonable in accepting species/strain designations from registrants with respect to technologies and identification methods to distinguish their strain from other isolates/strains.
- Submittal of samples to a recognized cell culture bank/depository is required by all member countries. This ensures that the specific strain is properly stored and used as the reference strain; useful for compliance/enforcement as well as in cases involving claims of adverse effects. This provides a mechanism to confirm the identity of the specific strain and/or distinguish the strain (if it was not the cause of the hazard) as well as to trace and recall products/food if an adverse effect is confirmed.
- Data requirements include that Industry must have clear manufacturing process, cleaning procedures, and QA measures.
- Consider pharmaceuticals vs. biologicals vs. chemicals: when products are approved, it is important to protect the strain as intellectual property. Therefore, regulators need to closely look at identity (make sure not generic). The unique strain must be proven, but this is difficult when methods, such as gene sequencing, are not readily available or is not a practical or reasonable option.
- Isolate must be characterized; there should be a technique to distinguish it from other isolates (species taxonomy can be changed, but the strain as such will always be the same). Test each strain in relation to strains that do cause concern i.e. QPS approach. Not all organism are up-to-date in terms of genetic identifying.
- In Canada and the US, regulators receive varied identification methods from applicants (gene sequencing or traditional taxonomic methods); it depends on what is available. Some methods are considered out of date, such as serotyping of Bt (where cry gene profiling is favoured).
- Genotyping is done on a comparative basis specifically for Bt. Sometimes industry identifies the strain as a serotype and provides both types of data to regulator. However, some Bt's are indistinguishable according to serotype (thereby, not as useful as traditional/conventional identification methods).

- It is generally recognised that it is difficult to have general guidance; registrants should speak to regulators in pre-submission process/consultation (which is why it is important to regulate these types of products on a case-by-case basis).
- Different strains within one species can produce different metabolites of concern, e.g., aflatoxins produced by *Aspergillus flavus*. However this is not the case for the US EPA registered microbial pesticide *Aspergillus flavus* AF36.

Conclusion

- The best available technology should be used (whether classical or molecular methods) to identify the micro-organism isolate.
- It is important to emphasize that it is the isolate which is registered (there can be products containing the same strain but from different sources).

Follow-up Actions

- EU should consider similar approach to North America's with respect to strain-specific registrations, i.e. not require unequivocal distinction of active substance micro-organism from all other strains of the species; grant authorizations for specific isolates.

Item for discussion: Protoplast fusion

- (a) Is protoplast fusion considered to be a technique of genetic modification and therefore should the fungus *Trichoderma harzianum* T-22 be considered a genetically modified organism (GMO)?
- (b) Protoplast fusion of plant cells is excluded from the Directive 91/414/EEC according to Annex 1B since plant cells are considered capable of exchanging genetic material through traditional breeding methods: Can we agree to this approach?

Discussion

- It was agreed that protoplast fusion could occur naturally in the environment; therefore, this product should not be considered a GMO. For Canada, the term "genetically modified" was not used in their evaluation of this product (since protoplast fusion can occur in a classical sense). In the US, the scope for what qualified as a genetically modified organism is not clearly defined. The US do require notification for small-scale field testing. However, it is difficult to define the distinguishing difference between traditional breeding methods vs. genetic modification. The definition varies in interpretation (for example, would crossing/mating two Bt strains with different plasmid-encoded cry gene profiles result in a new strain that is considered genetically modified?).
- EU has included T-22 on the 4th List programme evaluation which excludes GMOs. The issue of whether this product is considered a GMO was forwarded to EU Commission. Does it fall under pesticide directive or another directive (GM)? Whose jurisdiction would this product fall under? The response is that there is a separate regulation for GMOs in the EU and that T-22 is not considered a GMO; also the Netherlands has authorized it as a plant protection product.
- Inter-genetic transfers according to the U.S. OPPTS, for toxic substances, are difficult to define; this is a very controversial/challenging topic. The US EPA receives pressure regarding the

prohibition of GM techniques and GMO foods in organic agriculture. Organic groups do not want genetically modified biopesticides, however, there is nothing definitive in regulations.

- In the EU 4th List, the submitted dossier contains three or four strains of *T. harzianum*, including T-22; during the process of evaluation, the taxonomy of *T. harzianum* changed; two different species are currently in the dossier for this species.
- Taxonomy: There is a big issue of equivalence; when are they all considered the same species, when different? The US considers separate taxonomy on a case-by-case approach; the most important is to make sure that there are no strains of concern. A change in taxonomic name does not necessarily mean there is a change in the organism's risk profile. If it is still in the same genus, the scientific literature is examined.
- In Canada, current obligations are to keep up-to-date with the latest taxonomic and nomenclature changes, especially for such diverse genera as *Pseudomonas*, *Bacillus*, and *Trichoderma*. The overall issue is a proper identification of the micro-organism and the general knowledge and familiarity associated with that taxon, as well as its phylogenetically close relatives, to aid in the identification of health and/or environmental concerns.

Conclusion

T. harzianum strain T-22 should not be regarded as a GMO since protoplast fusion is a natural process; GMO designation should be reserved for molecular-based nucleic acid technologies (*in vitro*).

Follow-up Actions

No specific recommendation is proposed. Member countries should consider equivalence if taxonomic name/designation of the micro-organism changes; apply the familiarity concept. A change of name does not mean that the micro-organism is novel and must be regulated as such; use body of knowledge (familiarity) of the old name to support authorization.

B. Inclusion of micro-organisms at strain level

Background

It has been concluded that micro-organisms should be included into Annex I at the strain level. In cases where notifiers have submitted dossiers with the intention of Annex I inclusion of more than one strain, and where the notifier argues that the strains are adequately identical to be able to extrapolate data generated on one strain to the other, the Rapporteur Member State (RMS) should request the notifier to submit detailed taxonomic descriptions of the micro-organisms (using best available technology) in order to identify the organisms at the highest possible level of detail. Based on these data, the RMS will decide whether or not extrapolation of data between strains is possible.

Item for discussion: Micro-organisms – EU Annex I

Micro-organisms should be included into Annex I at strain level, however, it is suggested including some micro-organisms at higher (species) level (see item C).

Discussion

- There is an EU proposal for Annex I listing of micro-organisms at the strain level. Keeping in mind similarities/commonalities between strains and species within certain microbe taxa, consideration could be given to annexing at higher epithetic levels (i.e., species or genus level)
- To a question whether in the EU 4th List dossiers involving multiple strains of a species from multiple registrants, registrants have to agree to share the supporting data set, the answer was that in most cases where there was more than one registrant included in a dossier, registrants worked together as a Task Force to allow data sharing.
- In the UK, Task Forces are formed to pull as much data together as possible. Such agreements are not required, but encouraged by the regulator. The UK is moving to transparency. If a waiver is put forth, it will be in evaluation; the evaluation will be published, not all of data waiver rationale. These evaluations are sent to company for comment (any worries about citation of data waiver rationales can be addressed).
- In the UK, if a second developer of a micro-organism came in with not as robust a data package as an existing registrant (i.e., equivalent isolate) then they would be instructed to provide more justifications in their rationale; intellectual effort of the existing registrant is recognized. Literature references must be provided and rights obtained from publisher (i.e., observe copyright laws).
- In Canada, as the regulator you want to have the same data submitted to other jurisdictions for completeness sake. If a waiver rationale is granted based on published literature then that waiver is not protected.
- In US, the biopesticide registration action document (BRAD) is sent to registrant for final review before release (as well as the Proposed Registration Decision document in Canada). In EU, the same process exists with the Draft Assessment Report. In the UK, applicants have referred to the EPA BRAD, but they need the rationale to back up, not just the BRAD. The US publish a concise summary of the full data waiver rationale in the BRAD (therefore, the full justification and how the literature was used to support the data waiver is not available).
- Do other companies/public have access through FOIA (U.S. Freedom of Information Act) to volumes that are not confidential if they cite? We cannot use another company's data for commercial interest/gain unless enter into a data sharing agreement or provide compensation.
- In the EU and US, while published literature is not protected because they are in the public domain, rationales for data omission (waivers) built on published literature are the intellectual effort (property) of the applicant and are treated just like test in terms of protection. It is not considered confidential business information (CBI), though. Only identification, manufacturing methods, and analysis of data are granted CBI status.
- In Europe, an applicant cannot cite Task Force documentation or a White Paper if they have not paid for rights to the publication(s).
- Each authority appears to have in place data protection laws and regulations. In cases where data waivers (justifications for non submission of data) are built mainly on published literature, are the rationales/justifications themselves accorded data protection even though the test data are in the public domain?

Conclusion

Include micro-organisms in the EU Annex I at the strain level; this is consistent with the approach taken by Canada and the U.S.

Follow-up Actions

There is no follow-up action required, though there are uncertainties regarding the protection of waiver rationales that are based on published literature and the extent to which such rationales are protected from other companies wishing to register/authorize equivalent strains.

C. Level of inclusion of Baculoviruses and other groups*Background*

Include Baculoviruses at a higher level than strain/isolate, e. g. on the level of the family Baculoviridae, on genus level (NPV and GV) or on species level. Product components other than the Baculovirus itself resulting from the *in vivo* production process, could be problematic (e. g. microbial contaminants). It is proposed a separate document with generally applicable contamination limits should be developed. It may be necessary in this document to set different contamination levels for bacteria/fungi (which can be grown from sterile cultures) and for Baculoviruses (which must be grown in insect larvae).

Item for discussion: Baculoviruses

Consider specific concerns for inclusion on family level instead of on species level.

Discussion

- A group inclusion of all Baculoviridae in Annex I would remove any incentive to further investigate the properties of such viruses; this would be 'the end of scientific progress in this area'. Experience in the past showed that advancement of science and technology repeatedly created new assessment needs for substances formerly considered as safe. It would be a very big leap of faith to decide that no further information would be required for a whole group of organisms.
- A 'blanket' inclusion of a whole group without any evaluations of the specific species could set precedence also for chemical active substance. Why would it be necessary then for the 15th or 20th pyrethroid or triazole or sulfonyleurea to submit a complete dossier?
- The current evaluations and any new viruses would be rendered futile and interrupted half-way with the first inclusion of a baculovirus. All these dossiers include species, and isolate-specific data to some extent. This is likely to cause difficulties with the data protection (and compensation) for these and subsequent dossiers if the evaluation is only finalised for the first baculovirus.
- Regulatory should be considered not only the scientific possibility of an inclusion at higher taxonomic level but also the practical and legal implications, and then decide on the necessity.
- As long as they are not genetically engineered, baculoviruses represent minimal risk to humans and other animals, and the environment. Including all existing baculoviruses in Annex I either to

the whole family or to genus (e.g., NPV and GV) rather than to species or strain/isolate level would have some advantages. However, what about a new baculovirus?

- In EU there is a guidance document on the assessment of new isolates of baculovirus species already included in Annex I of Council Directive 91/414/EEC. An applicant for a new baculovirus must provide a dossier, but can make lots of reference to the OECD Baculovirus Consensus Document. The EU requires new data for contaminants as well as detailed description of product identity/characterization and methods of manufacture as well as analysis. General waivers for human health and environment testing can be requested by referencing the OECD consensus document.
- What about nontarget organism effects, specifically on insects and particularly those closely related to the targeted host species? Should host range testing be submitted for a new baculovirus (i.e., strain/species/isolate)?
- What does applicant need to provide? It depends on level of familiarity with the strain; there is a need for product specific information as a starting point. However, for human health, Canada is concerned with latent viruses not the baculovirus per se; perhaps focus on mammalian cell culture assays and confirm absence of primary pathogens through an IV and IP injection check in mice. For ecotoxicology, need confirmation on insect host range.
- In US, a hybrid approach is followed. It must adequately identify the baculovirus. Data on host range studies are needed to make sure there are no new hazards. It depends on how similar the baculovirus is to existing registered baculoviruses to bridge to existing database.
- In an EU dossier, each data point (requirement) has to be addressed by either a study or data waiver/justification. All data points must be addressed. Applicants can refer to OECD consensus document for some of the data points, but they need to provide specific data. Applicants cannot refer to data point from another dossier; they must point to specific OECD paragraph as data waiver rationale (cannot just refer to document as a whole).
- What about microbial contaminants for Baculoviruses? Do we have a list of specific microbes of concern to test? (such as *B. cereus*). In US, consideration that production of Baculoviruses as obligate parasite in another organism – this is different compared to cell line cultures which is possible for some baculoviruses, but not for most.
- Some currently registered viruses cannot be produced in laboratory-reared insect colonies. Registrant has to spray forest and collect wild larvae and then purify. Is this approach adequate for other authorities? It presents unique challenges for regulating quality control (particularly contaminants) and batch-to-batch variation in potency. The same issue is with milky spore; applicant must collect Japanese Beetle from the wild; there is concern with the manufacturing process.
- It is to keep original virus established (often named after pest) and produce more through passage in insects. Sometimes this could lead to a mixture of viruses and actual product tested could be a different blend or mixture. Data is required for absence of pathogenicity; for example the Canadian PMRA asks for intraperitoneal study in mice to make sure there are no animal pathogens. This is done on every production batch which may not be considered onerous on the registrant as it may only be produced once or twice a year.

Item for discussion: Phlebiopsis gigantea

A decision on *Phlebiopsis gigantea* can also be taken on species level, based on the very specific application method (mechanised or manual spraying of freshly cut tree stumps) which removes almost all human and environmental exposure. Other types of applications might require strain level decision.

Discussion

- Another example, *Phlebiopsis gigantea* included in Annex I, is a very specific application; it should be considered on species level (not genus level) since many strains are covered in the dossier. It is currently in beginning stage of peer review among EU member states.
- EU-EFSA puts together conclusion based on member state comments.
- What happens if there is a difference of opinion among rapporteur member state, peer review members states and EFSA? Response: (1) At EU there is much discussion and peer review required to resolve issues where there may be differences of opinion. The active ingredients can be included in Annex I. However, while there is consensus, products are regulated by member states; EFSA does evaluate the active ingredient only (risk assessment). (2) EFSA has to go through many active ingredients, trying to streamline process, they tiered their actives according to degree of risk and number of uncertainties. Applicants can withdraw compounds during any stage of the review process. All end-use products are regulated by member countries. EFSA evaluates for member countries "like an umbrella", with the overall safety of active ingredient and one product. They will produce a so-called EFSA-conclusion which will be the basis for the decision of the European Commission (risk management).
- All countries need submittal of samples for cell culture banks, where it is used as reference and in cases of adverse effects or in cases of dispute.

Conclusion

All regulatory jurisdictions have ability to consider registering/authorizing certain micro-organisms at higher epithetic level than strain/isolate, perhaps to species or genus, and in some cases to family. Assessed on a case-by-case basis, but there are minimum data sets (e.g., product manufacture and analysis) that will be needed for every new strain submitted for inclusion. CBI considerations (confidential business industry) could present challenges.

Follow-up Actions

It is proposed to annex Baculoviruses as a group (take similar approach for *Phlebiopsis*). In addition, it may be relevant to have a group list for pheromones (e.g., SCLPs).

D. Efficacy Evaluation*Background*

Compared with conventional chemical substances, many BCAs have a lower level of efficacy. There is some uncertainty as to what levels of efficacy are required for BCAs. In addition, many BCAs have a different mode of action as conventional chemical substances, which may make it necessary to adapt trial protocols. This is particularly the case for semiochemicals, where it is often impossible to use replicated trial designs.

Item for discussion: Efficacy evaluation – REBECA proposals

1. Introduction of efficacy into EU evaluation need to be accompanied by guidance on evaluation criteria.
2. Authorities should accept modified trial protocols, provided that the applicant can justify the modification.
3. Products with minor beneficial effects should be acceptable.
4. There is no efficacy evaluation prior to a 5-year registration period, however, data should be collected over the first five years of market use.

Discussion

- Definitions for efficacy is a moving scale; efficacy can be defined by 95% for control and 80% for suppress. Industry recommended the definition of efficacy as "control above the economical threshold of destruction". However, the definition for "economic threshold" can also vary widely. For some crop diseases, 100% would be required to obtain a control claim on the label.
- At pre-submission meetings, the Canadian PMRA determines what uses can be extrapolated based on proper rationale and crop groupings. It identifies the minimum data set required to get maximum number of uses on the label. Often applicants have 40 – 50 uses proposed on their product labels; from that, PMRA determines how many trials would be needed to support each host/pest combination. With so many uses proposed the cost of generating the required efficacy studies could be prohibitive. Usually applicants are instructed to focus on most important (and profitable) uses and generate efficacy data for those. Once product is on the market, then they can expand label to include other uses. At pre-submission meetings, PMRA provides detailed guidance on how many studies are required to support each proposed use (crop/pest), control groups, as well as how the applicant should summarize their trial data in an Excel spreadsheet.
- In UK, data must be submitted to support label claims. If there is enough crop data, then there is no need for crop destruct. The UK has experimental permitting process, where with supporting toxicity data package there may be no need to destroy crop if passes a dietary risk assessment. Therefore, it is to generate data while making revenue (this is the justification). There is a limitation on area to be treated, no more than 10 hectares. But this can be negotiated for larger scale, depending on product.
- Canada needs crop destruct to make sure that it will not go in food supply unless there is some supporting toxicity data to conduct a dietary risk assessment, and if it passes, then treated commodities can be allowed to enter into normal food marketing channels. It will accept foreign field efficacy trial data, mainly northern US, but will also consider European data if cropping practices, climate and pests are similar (rationale from applicant to have foreign data considered by PMRA must be strong). Greenhouse efficacy studies are accepted from any location.
- Provision should be made to allow growers to evaluate product in experimental trials; this supports registration and gets public support. Growers are under pressure to reduce residues; therefore, they will offer land opportunity to generate supporting efficacy data.
- When a new biological is discovered does industry develop efficacy data or toxicity data first? Industry looks at efficacy very early in product development because companies want to make sure its products are efficacious before investing too many resources in the safety data. Industry is looking for regulatory relief to allow for some (not all) efficacy data, but with full supporting

toxicity and ecotoxicity data. It would like authorities to register and then can allow efficacy data to be generated post-market (more economically feasible for small enterprises).

- Industry proposes granting of conditional registrations pending development of all supporting efficacy data rather than requiring a full efficacy package for pre-market assessment. Efficacy data could be collected over the first five years of market use. It is suggested to rely on human health toxicity and ecotoxicity, i.e. risk rather than risk and value, for initial registration/authorization. It is necessary to know how organism will work; sales data will demonstrate efficacy. This gives a chance for small companies to sell lower risk products.
- There are difference of interpretation among countries with respect to acceptance of foreign efficacy trials (outdoor only). All countries are supportive of accepting greenhouse studies from other parts of the world. The UK will use other countries' data in the cases of glass houses, too. However, country-specific outdoor field data is often needed due to different climatic conditions. Industry is of the opinion that submission of data generated in other countries should be justified with a strong rationale. There may be some work to do to determine global trial sections and cut down the number of trials (each country is only seeing local).
- The UK supports using expert judgement to make a determination whether foreign studies are relevant to each country situation and to know exactly what can be considered with a rationale/justification.
- Industry supports lessening the burden on regulatory authorities if those agree to data sharing and recognised that the developed data can be used in other countries; therefore, there will be more data available to support authorization/registration in each jurisdiction.
- Focus should be on developing a high quality data package.
- Industry gave an example of a company that has two trials in the UK, and the rest from similar climatic regions from US, to submit for efficacy. Industry is concerned that they lose money when they are given advice from authorities to submit a dossier. This is viewed as a gamble since the foreign data may not ultimately be accepted during the review and the company has paid non-refundable regulatory fees.
- There may be a need for having guidelines to exchange data among countries: What we could consider, what general data is applicable, what considerations need to be factored, and when we would accept foreign data? Industry recommends guidelines for efficacy testing for microbials within OECD (keeping in mind that conventional chemical pesticides have different performance standards).
- Canada and the UK prepared an OECD issue paper which covers basis of efficacy testing and provides guidance for developing protocols as well as for assessing data.

Conclusion

- Setting data requirements and assessing product performance of microbial biopesticides require flexibility and an approach to that different from the one for conventional chemicals.
- Separate greenhouse/glass house efficacy studies should not be required for each country/ zone/ region; data generated in one area should be accepted for another.

- Further discussion is needed on phasing-in efficacy data (i.e., pre-market vs. post-market data sets).

Follow-up Actions

It is suggested to consider developing specific OECD guidelines for efficacy testing of microbial biopesticides.

E. Waivers

Background

A 'waiver' document should include and/or take into account the following points: (i) the conclusions from the REBECA project; (ii) the IBMA white paper on the regulation of biologicals; (iii) the recent revision of the US EPA regulation for microbial pesticides data requirements; (iv) Canadian templates for the non-submission of (ecotoxicity) data; and (v) the OECD publications on registration requirements for pheromones (Series on Pesticides, No. 12, 2001) and for microbial pesticides (Series on Pesticides, No. 1, 2003); (vi) a 'Lessons-learned' document prepared in light of the EU review of the fourth list; and (vii) experiences from other OECD member countries in particular from the US EPA.

Item for Discussion: 'Waiver' document – REBECA proposals

- Data requirements on effects on earthworms and soil microbiota should be generally waived because hazards are very unlikely.
- Infectivity studies should be waived when all of the following requirements are met: no clinical reports; not listed in 2001/54 EC; humans and animals are already regularly exposed to the micro-organism; and susceptibility against antibiotics.
- Data requirements regarding the instability of genetic traits affecting the efficacy of the product should be waived or removed because this will be checked by quality assurance.
- Data requirements on fate and behaviour in the environment should be waived for micro-organisms which are already part of the background population.

Discussion

- There was discussion elsewhere in this workshop on what type of justification is needed to support data waiver requests.
- Should a data waiver guideline be developed? There is an existing draft guidance document for dealing with data waivers for ecotoxicity studies which is available on the EPA's website.
- It is important to discuss prospects of obtaining waivers with prospective applicants at pre-submission meetings. Opportunities for waivers to be accepted will be very case-specific and involve level of familiarity with the micro-organism to be registered.
- Waivers may be considered for most requirements, but some bridging data may still be needed to accept rationales if arguments are based on information available on similar strains, species, genus, etc.

- Data requirements for earthworms and soil microbiota ought to be easily waived by authorities because hazards to these non-toxic organisms are very unlikely and difficult to measure; there is no proof of the existence of any earthworm pathogen. The US does not require such studies; Canada sometimes gets data, but substantiates no effects. The EC usually receives waivers: there is no scientific evidence of any problems for these two requirements; there is no allowance for exemption; and it is necessary that the legislative authority ask for data.
- According to an economic analysis survey conducted in the US, it costs \$2000 to industry to prepare a data waiver request. There are more data waivers required in the EU mainly because Europe requires some studies that are at higher tiers in the US and Canada (e.g., repeat dose animal studies, fate data)
- Canada and the US have higher tier for expression/fate levels in the environment (only if triggered from Tier I ecotoxicity tests). At the EU, there is no tiered approach. It may be more expensive for industry because sometimes it is more costly to do a waiver than to do a study.

Item for discussion: Infectivity Studies

Infectivity studies should be waived when all of the following requirements are met: no clinical reports; not listed in 2001/54 EC; humans and animals are already regularly exposed to the micro-organism; and susceptibility against antibiotics.

Discussion

- Canada allows for waivers when infectivity is not expected, but not for all routes of exposure. At least one route is needed (usually pulmonary or injection, rather than oral) that covers infectivity (clearance) to make sure that it is not pathogenic or infective. It will entertain infectivity waiver for other two routes depending on the results of the one toxicity/infectivity study.
- For US, it depends on the biology of the micro-organism and whether it has the potential to affect mammals. Some organisms are common and ubiquitous while others are newly discovered (novel). It depends on level of familiarity. Novel microbes may need all data requirements addressed. If a pattern of clearance can be established and there are no adverse effects (pathogenicity) during the study (intra-peritoneal/intra-venal or pulmonary route), then it is possible to obtain waivers for the clearance (infectivity) portion of the toxicity/pathogenicity studies for the other required actual studies. The EPA generally does not recommend the oral route as the only study to address clearance/infectivity because the acidity of stomach can digest or inactivate the microbe.
- How is clearance defined? Is it absolute elimination from the body or establishment of a distinct pattern of clearance? The answer could have a profound impact on the duration of the study and number of animals involved. It is especially important for spore-formers which generally take longer than non-spore formers to clear the body.
- It may be sufficient to establish a pattern of clearance, not an absolute zero detection of the micro-organism in tissues, fluids, organs, and observe decline in orders of magnitude over several time points to establish clearance pattern.
- The EU does not need to show 100% clearance to zero detected micro-organisms. For spore-formers slow clearance is expected, but one must ask the question about whether this increases

risk. Such a question does not necessarily automatically trigger higher tier toxicity testing or diminish the chances for waiving other test requirements.

Conclusion

- Consider waiver rationales in lieu of actual test data.
- Acceptance of waiver rationales must be done on a case-by-case basis depending on the microorganism and its level of familiarity.

Follow-up Actions

Develop guidance documents or waivers for higher taxons (species, genus, etc.) or well characterized and defined groups of micro-organisms. This approach should be based on solid scientific knowledge, and a number of representative micro-organisms should be known to fulfil the safety criteria (e.g., is non-pathogenic, non-infective). Certain groups (e.g., micro-organisms used in food production like yeasts) could benefit from this general approach. This has been done for baculoviruses (OECD Consensus Document).

F. Contaminants

Background

As a first step the development of manufacturing processes with pure culture and sterile techniques should be encouraged. All involved should benefit from such operational procedures. The quality control would probably be easier by checking the purity, both by traditional methods and molecular biology techniques, as well as absence of growth at 37°C, on a rich medium, rather than by handling unknown maybe pathogenic contaminants. Scaling up a fermentation process might be problematic with regard to contaminants. The quality control is important also to make sure that the production concerns the intended strain and not a contaminant taking over during the fermentation. In some cases, with insecticidal viruses it has been shown to be problematic to grow them in sterile cell-lines. For the virulence it is necessary to cultivate the viruses in larvae.

Item for discussion: Maximum acceptable amount of contaminants

The maximum acceptable amount of contaminants in the technical active organism that will be used to formulate a plant protection product should be given as a threshold value. For this purpose guidance is needed. The threshold value is dependent on the detection limit for respective contaminating organism and also the negative consequences of them in the product.

Discussion

- Different approaches are taken by member countries on what constitutes acceptable types and levels of contamination in microbial products. What is a safe level for microbiological contamination regardless of quality assurance (QA) measures adopted in the manufacturing process?
- In one of the background documents for this workshop there is a proposed standard that products must not contain more than 0.001% microbial contaminants, which means for a product that contains 10^7 CFU/g of active ingredient, the level of contaminants should not exceed 10^2 CFU/g. However, there is no guidance in this document for what type of micro-organisms we are

concerned with. What constitutes acceptability – just the amount of contamination, or that plus types of contaminating micro-organisms (e.g., *E. coli*, *salmonella*, etc.)?

- It is recommended testing on appropriate selective growth media as well as total colony forming units (CFU) counts. Type and levels of contaminants that are accepted depend on product (virus vs. bacteria vs. fungal). It is preferred to see end-product testing data, but usually technical grade active ingredient (TGAI) data are got.
- It was agreed that the first step in the development of manufacturing process should be pure culture and use of sterile techniques.
- The EU examines the active ingredient, but just one product in their evaluation; are there QA measures for other end-use products?
- The US usually receives contaminant data on technical product. The manufacturing process must demonstrate a clean product. It is a given that when you add formulation ingredients, there will be an addition of microbes. In cases of microbial pesticides that are formulated from a liquid to a solid formulation, EPA prefers to see contaminant data on the solid substrate.
- In Canada, there are many products that PMRA reviews have been registered first in other countries/ jurisdictions like the US or EU. It is unclear whether these other jurisdictions require contaminant analysis for only the five representative batches in the dossier/submission or if the registrant is to continue monitoring for contaminants after registration. Canada requires 5- batch analysis data for the pre-market assessment purposes, but requires post-registration monitoring data be maintained by registrants to ensure there are no unacceptable contamination.
- The US also requires five batch analysis for pre-market assessments and post-registration monitoring and analysis of every production batch for microbial contaminants. Industry is of the opinion that it is challenging to do contaminant testing on every production batch.
- The UK receives representative batch data at different stages during the manufacturing process of the MPCA. It sometimes asks for screening data. The UK does not require post-registration monitoring data; the rationale is that companies have their own QA measures as well.
- The UK in conjunction with the EU do post-registration monitoring in the market for relative impurities of concern; there are already requirements for member states to do their own post-market monitoring (which differs from state to state) on products and residues. If there is a product complaint lodged, member states can analyze product off the shelf vs. testing of batches from the company (where there is potential for the analysis to be conducted on the most optimal sample).
- The US also receives independent laboratory validation (ILV) of five batch analysis. In Canada, sometimes ILV data are seen, but they are not required. There is a concern that there is potential for exposure to a pathogen if the laboratory does not have proper containment measures.
- The EU requires testing to be good laboratory practices (GLP) compliant; however, there is no ILV. Industry sometimes has to outsource this type of testing and would subsequently submit ILV data. This is because the independent laboratory is accredited and has the proper containment measures.

Item for discussion: Plant pathogens

One has to bear in mind that it is important to ensure the absence of plant pathogens if the intended use is on plants. Should products be screened for presence of plant pathogens, too?

Discussion

- There are no guidelines for screening plant pathogens. Does the OECD BioPesticide Steering Group (BPSG) want to develop an issue paper on microbial contaminants to cover plant pathogens rather than just animal pathogens?
- There is pathogen screen in product development.
- There is no prescribed method for testing for plant pathogens. Good efficacy studies involve examination of crop for signs of phytotoxicity, so presumably if there were plant pathogens present in the formulation, adverse effects would likely be noted. If guidance is to be developed, it has to be general and consider alternatives and deviations. For impact to be observed in field trials, high levels of contamination would have to be present in the product. It was noted that these considerations are not examined in conventional pesticides.

Conclusion

- Continue BPSG work on harmonizing the approach taken by member countries to assess microbiological contamination in microbial products (e.g., TGAI vs. EP, establish acceptable levels for different contaminant micro-organisms, screening methods, etc.).
- There is no need to establish guidance on testing for presence of plant pathogenic contaminants, as presence of such organisms would likely be noted in efficacy tests on crops.

Follow-up Actions

Consider developing guidance document on when monitoring is necessary for applicants (pre- and post-registration screening).

G. Templates

Summary of discussion

- The workshop asked for feedback from industry on the potential for utilizing data review templates (similar to the OECD summaries) while conducting the study and industry can then submit the data evaluation record (DER) in conjunction with the study report.
- The OECD BPSG has reported that the templates are time-consuming to fill in for regulators; therefore, perhaps industry can fill in. Industry responded that this adds work.
- Should it be the goal or future responsibility for industry to submit the populated DER or studies formatted in the DER template format (i.e. the study summary and data points are already populated by industry)? Canada allows populated DERs to be submitted by applicants/registrants of conventional pesticides.

- In the US, there is a history of controversy due to "cut and paste" claims from activists. Opposition claimed that the use of an industry prepared summary document of the original laboratory study report could lead to a potential for the science reviewer's opinion to become company based.
- A representative of industry noted that OECD summaries represent a summary of the study; however, the conclusion depends on the regulatory evaluator's own expert judgement.
- The following question was posed to industry's representative: can they submit in this format? Perhaps can they even make initiative to start?
- In Canada, the PMRA website posts the DER templates for conventional chemicals (both in WordPerfect and Word formats) for industry to use. If applicant submits a populated DER this provides considerable time savings for the evaluator, as the DER is already populated with the data. Subsequently, the regulatory science reviewer can focus and confirm the findings of the study and make the ultimate conclusion.
- In the US, individual study reports are not submitted in this format. However, EPA is currently advising their science reviewers to put the study report in the DER template format for any new microbial pesticides coming in. In addition, the templates were also provided to the independent contractors who provide the primary review of a study report and then EPA conducts the secondary review.
- It was also noted that in satisfying the EU Member State Reviews, these templates are similar to OECD summary document. Therefore, the DERs serve as guidance for laboratories conducting guideline studies; if industry populates the DER templates, it will save time and become a more efficient system as regulators can better meet their deadlines.
- Canada is the lead country at the OECD in establishing the templates for microbials. However, the templates are still under revision for additional edits, but will be distributed to BPSG members soon (and will be available on PMRA's website).
- In the US, adopting these templates is still in the preliminary phase. The DERs are under revision based on feedback from scientists. The EPA also expects future revisions upon receiving the PMRA's updated templates. Utilizing this type of format for the DERs should also be encouraged for products with global applications.
- DERs are somewhat country specific, but can be readily modified to reflect and suit the reviewing country's needs. DERs are considered living documents as they will be updated to incorporate any new guidance or scientific techniques.

Conclusion

Review (DER) templates for microbials are useful for industry preparing summaries and for regulators conducting primary reviews of dossiers/submissions.

Follow-up Actions

Canada will continue to revise DER templates and these will be distributed to BPSG members once finalized. US EPA also offered to share experiences/comments and existing revised templates to PMRA with revisions or any recommendations.

H. Environmental safety

Background

A proposal for a decision scheme and decision tree for the environmental risk assessment for microbial pesticides has been developed initially by the Netherlands. It was agreed to include them in the Working Document currently in the process of being published. However, because of the complexity of such a decision tree, it was decided to postpone its development and adoption.

Item for discussion:

- Decision tree as developed by the Netherlands (and published in *Biocontrol Science and Technology*, 2007; 17(1): 3_20; *How to evaluate the environmental safety of microbial plant protection products: A proposal*);
- Decision scheme as developed by Germany.

Discussion

- The US is of the opinion that both schemes are acceptable. However, there is no real indication of when we would need to investigate to this level, hence there is a danger of over investigating when not needed.
- Germany indicates that the amount of effect data required for risk assessment is based on whether there is an exposure to non-target organisms. In the German proposal for a decision tree (unpublished handout) the 4th box "effect judgment" aimed at discerning between toxic and pathogenic effects by using attenuated controls. This step might be crucial in order to decide on the route whether a TER-approach for toxic effects or a specific approach for pathogenic effects (based on NOEC/EC₀/LC₀-values) should be used.
- The Netherlands agree that having the scheme is needed only if it is demonstrated that there is a potential problem. For some groups of organisms there is enough information that indicates there is no problem.
- Much information is based on the mode of action, efficacy data, the way the product is used, etc.
- The US indicates that for tier 1 studies (lab) NTA effects, it is the technical that is tested and not the product. The reason is that when products are changed it is not necessary to do a whole re-evaluation. In the US there is a section that looks at inert components. However it is unlikely to have toxic compounds in a formulation with living organisms, as a toxic compound would kill the organism.
- If there is no exposure then we can say that we don't need the toxicity data. But if there is exposure the next step is to consider what is known about that *spp* which the organism comes from. If there are potential issues then it is acceptable to ask for data. If there is no literature on pathogenic behaviour then it is also acceptable not to ask for the data. Probably some or even many assumptions will be made.
- We should always look at exposure and hazard together. The German model says that if it is not quantifiable then it is not acceptable. However, we could have a situation where an organism is so benign that it doesn't matter how much "there is in the environment".

- EPA will provide a three-page paper on the EPA's approach. PMRA's approach is very much a hazard based approach and follows a tiered structure. EPA also has guidance on ecotoxicology waivers that may be useful.

Conclusion

The decision scheme/tree is considered very useful, but also very complex.

Follow-up Actions

The Netherlands and Germany will continue working together to develop guidance.

ANNEX 1

WORKSHOP AGENDA

1st day – 15 April 2008; 8:00 – 16:00

8.00-8.15	1.	<p>Welcome, introductions and objectives</p> <p>Welcome by <i>Janet Andersen</i>, Director of BioPesticides Division; US-EPA Introduction: OECD Secretariat Objectives: Chair <i>Jeroen Meeussen</i>, The Netherlands</p>
8.15-8.30	2.	<p>OECD-BioPesticides Steering Group</p> <p>OECD-BPSG: Short overview of the work achieved, the on-going activities and future developments.</p> <p>Speaker: <i>Jeroen Meeussen</i>, The Netherlands</p>
8.30-10.00	3.	<p>Regulatory Overview Summaries</p> <p>Short overview of the regulatory systems, data requirements and procedures in the different territories.</p> <ul style="list-style-type: none"> • EU biopesticide regulatory system – scope, structure and function • US biopesticide regulatory system – scope, structure and function, incl. new OPP data requirements (40CFR158 Subpart V) • Canada biopesticide regulatory system – scope, structure and function <p>Speakers: <i>Jeroen Meeussen</i>; EU <i>Alan Reynolds</i>; US <i>Brian Belliveau</i>; Canada</p> <p>Background Documents: EU data requirements (Directive 2001/36/EC); EU Uniform Principles (Directive 2005/25/EC).</p>
10.00-10.30		Coffee

10.30-11.15	4.	<p>Outcome of REBECA</p> <p>REBECA (Regulation of Biological Control Agents - BCAs) is an EU policy support action to review possible risks of biocontrol agents, compare regulations in the EU and the USA and to propose alternative, less bureaucratic and more efficient regulation procedures maintaining the same level of safety for human health and the environment but accelerating market access and lowering registration costs. The final report is available (http://www.rebeca-net.de).</p> <p>Speaker: <i>Jeroen Meeussen</i>, The Netherlands</p> <p>Background Documents: REBECA report and deliverables</p>
11.15-12.30		<p>Lunch</p>
12.30-13.00	5.	<p>QPS (Qualified Presumption of Safety)</p> <p><i>Influence of Qualified Presumption of Safety (QPS) approach for the risk assessment of microorganisms.</i></p> <p>Recently EFSA has published the Opinion of the Scientific Committee: “Introduction of a Qualified Presumption of Safety (QPS) approach for assessment of selected microorganisms referred to EFSA”.</p> <p>Also one of the REBECA deliverables is dealing with the QPS approach indicating that if the microbial plant protection products were included in the development of this new concept, it would be a way of defining groups of low risk micro-organisms, and a way of obtaining a faster evaluation and market introduction of microbial plant protection products.</p> <p>Speaker: <i>Coralie Bultel</i>; European Food Safety Authority.</p> <p>Background Documents: REBECA paper; EFSA opinion</p>
13.00-14.30	6.	<p>Microbial Pesticides overview</p> <p>(1) Human Health/Product Analysis, (2) Non-target/Environmental Fate</p> <p>Data requirements: How to use them?</p> <ul style="list-style-type: none"> • How data requirements are actually used, e.g. pre-registration data agreements-data waivers • What data is actually needed for adequate assessment? • Problems with laboratory studies for some taxa. • Review of the data – procedures, problems • How to handle additional subsequent data needs. • Can alternative information be used in lieu of laboratory data? <ul style="list-style-type: none"> - Reliability of taxonomic identification (variable) - Reliability of literature to substitute for laboratory studies - Use of data approved for similar products (data protection)

		<p>Discussion on the Environmental/Ecotoxicology area:</p> <ul style="list-style-type: none"> • Evaluation of the Environmental Safety of Microbial Pest Control Products (summary tables regarding the reliability of provided data; an environmental risk decision tree); • natural occurrence/fate in the environment and persistence. <p>Speakers: <u>Human Health/Product Analysis</u> <i>John Kough</i>; BPPD, US <i>Marloes Busschers</i>; Ctgb, The Netherlands</p> <p><u>Non-target/Environmental Fate</u> <i>Zigfridas Vaituzis</i>; BPPD, US †<i>Hans Mensink</i>; RIVM, The Netherlands</p> <p><i>Templates and electronic submissions</i></p> <ul style="list-style-type: none"> • Electronic submission formatting – including OPP experts • Review Templates – status and experiences using them • Discussion <p>Speakers: <i>Brian Belliveau</i>, ; PMRA, Canada <i>Annabel Waggoner</i>; BPPD, US</p> <p>Background Documents: Survey US-EPA; Publication: How to evaluate the environmental safety of microbial plant protection products: a proposal; EU guideline on the taxonomic level of Annex I inclusion (document Sanco/10754/2005 rev.5); EU Guidance document 4th Stage (document Sanco/10393/2004 – rev.4).</p>
14.30- 15.00		Coffee
15.00-16.00	6.	Microbial Pesticides overview (Cont'd)

2nd day – 16 April 2008; 8.00-16.00

8.00-9.15	7.	<p>Efficacy</p> <p>Discussion on different approaches taken by US/Canada and EU.</p> <p>Efficacy is often mentioned by some sectors of industry as a major difference why there are more actives approved in the US than in the EU.</p> <p>Speaker: <i>Pierre Beauchamps</i>; PMRA, Canada <i>Roma Gwynn</i>; IBMA, UK <i>William Schneider</i>; BPPD, US</p>
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9.15-9.45	8.	A	<p>Breakout session</p> <p>Introduction: Discussion in breakout groups on a number of general issues based on recently carried out reviews by US, Canada and/or EU.</p> <p>Facilitators: <i>Kersti Gustafsson</i> (Sweden) and <i>Brian Belliveau</i> (Canada)</p>
9.45-12.00	8.	B	<p>Breakout session</p> <p>Discussion in breakout groups on a number of general issues based on recently carried out reviews by US, Canada and/or EU.</p> <p>General issues to be discussed:</p> <ul style="list-style-type: none"> o Identity/taxonomy/extrapolation between strains; o Inclusion of micro-organisms on strain level; o Level of inclusion of Baculoviruses and other groups; o Efficacy; o Waivers; o Microbial contaminants; o Fungal metabolites; o Environmental safety. <p>REBECA - proposal – Environmental Risk Indicator</p> <ul style="list-style-type: none"> o REBECA - proposal – Specification of Low Risk Products o Genetic toxicity; o Occupational exposure; o Classification and labelling; o Storage stability; <p>Reference is made to the following documents:</p> <ul style="list-style-type: none"> • Background document for the breakout groups • Working document on the evaluation of microbials for pest control (December 2007) • DRAFT OECD Issue Paper: Discussion on Microbial Contaminant Limits for Microbial Pest Control Products, September 2006 • Guidance developed within the Standing Committee on the Food Chain and Animal Health on the taxonomic level of micro-organisms to be included in Annex I to Directive 91/414/EEC (Sanco/10754/rev. 5) • OECD Consensus Document on information used in the assessment of environmental applications involving Baculoviruses (ENV/JM/MONO (2002)1) • Guidance Document on the assessment of new isolates of baculovirus species already included in Annex I of Council Directive 91/414/EEC SANCO/0253/2008 rev. 2; 12 November 2007 • REBECA (Regulation of Biological Control Agents) Activity Report • REBECA deliverable 10: Proposals for improved regulatory procedures for microbial BCAs • REBECA deliverable 11: List of defining knowledge gaps for microbial BCAs • REBECA deliverable 28: Specification of low risk products

<i>12.00-13.15</i>			Lunch
13.15-15.15	8.	C	Breakout session (Cont'd) Discussion in breakout groups on a number of general issues based on recently carried out reviews by US, Canada and/or EU.
15.15-16.00	8.	D	Breakout session (Cont'd) Report from breakout groups

3rd day – 17 April 2008; 8.00-12.15

8.00-9.30	9.		Pheromones Possibilities of work sharing and harmonization in the field of pheromones. <ul style="list-style-type: none"> • CAN is in the process of harmonizing its regulatory procedures with US; • New OECD-numbering system has to be applied to the pheromone dossier and monograph guidance; • Austria will prepare a 'Lessons learned document' based on the experience with the 4th List; • 'OECD-Guidance Document 12' need to be revised; • Pheromone efficacy guidance is available at the UK website. • (E)-B-farnesene – cotton aphid alarm pheromone Speakers: <i>Alexandra Fischer</i> and <i>Wolfgang Bergermeyer</i> ; AGES, Austria <i>William Schneider</i> ; BPPD, US Background Documents: http://www.pesticides.gov.uk/uploadedfiles/g220.pdf
9.30- 10.00			Coffee
10.00-11.00	10.	A	Communication How to initiate a dialogue between all stakeholders on the regulation of Biological Control Agents (BCAs). <ul style="list-style-type: none"> • Pre-registration meetings The pre-registration meeting is a critical part of the assessment process. In the REBECA framework a proposal for a checklist for pre-consultation meetings has been prepared. For a pre-consultation meeting the following information should be provided: <ul style="list-style-type: none"> o A cover letter requesting a pre-submission meeting (for which a template could be made available).

			<ul style="list-style-type: none"> o A proposed agenda of the issues to be discussed (a template should be made available). o Completeness check tables (document O) containing information about a) which information is included in the pre-submission information package, b) which studies have already been carried out (if any) c) for which data requirements a justification for non-submission of data is submitted in the package. o Proposed use pattern (Table of Good Agricultural Practise), proposed label, international regulatory status. o Characterization of the active substance (for microbials also information on mode of action). o Short summaries of available information regarding manufacturing processes, product specifications, safety to the environment and human health. o Scientific justifications for non-submission of data (waivers). o Proposed study protocols (if available). <p>Speaker: <i>Mike Mendelsohn</i>; BPPD, US <i>Bernard J. Blum</i>; IBMA Global</p> <p>Background Documents: REBECA proposal; Guidance US/CAN</p>
11.00-11.30	10.	B	<p>Communication (Cont'd)</p> <p>How to initiate a dialogue between all stakeholders on the regulation of Biological Control Agents (BCAs).</p> <ul style="list-style-type: none"> • UK Biopesticides scheme <p>The main elements of this approach include: (i) charging lower fees for micro-organisms; (ii) starting a dialogue with IBMA-UK; (iii) having a separate page on the PSD website; (iv) organising a training (one-day) session for industry/applicants; and (v) appointing a contact point ("Champion") within PSD. The feedback from industry is very positive on the approach taken by the PSD.</p> <p>Speaker: <i>John Dale</i> (PSD, UK)</p>
11.30-12.15	11.		<p>Conclusions and recommendations</p> <p>Summary of agreed activities, conclusions, recommendations and future developments.</p>

ANNEX 2

ABSTRACTS OF PRESENTATIONS

Item 2

OECD-BPSG: Short overview of the work achieved, the ongoing activities and future developments

Jeroen J. Meeussen

Ctgb, Wageningen, the Netherlands

(Board for the Authorisation of Plant Protection Products and Biocides)

The OECD work on agricultural pesticides (i.e. chemical and biological pesticides) aims to help member countries improve the efficiency of pesticide control, share the work of pesticide registration and re-registration, minimise non-tariff trade barriers and reduce risks to human health and the environment resulting from their use. In support of these goals, the Pesticides Programme has undertaken work to: (i) identify and overcome obstacles to work-sharing; (ii) harmonise data requirements and test guidelines; and (iii) harmonise hazard/risk assessment approaches.

With the primary goal of facilitating the sharing of national review reports, OECD's work initially focused on ways to harmonise the format/structure of reviews that are exchanged. The OECD dossier and monograph guidance provide a general lay-out and standardised formats for industry reporting (dossier) and government reviews (monographs). They were developed with the aim of facilitating the exchange of reviews among countries.

The BioPesticides Steering Group (BPSG) was established by the WGP in 1999 to help member countries harmonise the biological pesticides assessment and improve the efficiency of control procedures. Biological pesticides involve: microbials, pheromones and other semiochemicals, plant extracts (botanicals) and invertebrates as biological control agents. The BPSG has been chaired by Canada since its inception and by The Netherlands from mid 2005 onward. The first tasks of the BPSG consisted of: (i) reviewing regulatory data requirements for the three categories of biopesticides; and (ii) developing formats for dossiers and monographs for microbials, and pheromones and other semio-chemicals. This was achieved in 2004 and resulted in publications on registration requirements for:

- pheromones (Series on Pesticides, No. 12, 2001);
- microbial pesticides (Series on Pesticides, No. 1, 2003);
- invertebrate biocontrol agents/IBCA's (Series on Pesticides, No. 21, 2004).

The BPSG then decided to concentrate its efforts on *science issues that remain as barriers to harmonisation and work-sharing*. To develop proposals for further work, the BPSG and WGP solicited input from governments and industry on issues creating barriers to harmonised approaches and for areas where work-sharing is needed. This resulted in the preparation of a "working document" which does not provide 'mandatory' guidance but being essentially a set of examples/case studies aimed at helping the

regulatory authorities. The document is titled: *Working Document on the Evaluation of Microbials for Pest Control* and contains the following five chapters:

1. The Taxonomic Identification of Micro-organisms in MPCPs
2. Genetic Toxicity Assessment: Needs and Recommended approaches
3. Occupational, Bystander and Consumer Exposure and Risk Assessments
4. Microbial Metabolite Residues in Treated Food Crops
5. Efficacy Evaluation

The Working Document has been approved by the WGP in February 2008 and will be submitted to the Joint Meeting for declassification.

In the Programme of Work 2009-2012 further activities are foreseen:

5. Resolve sciences issues associated with registering biopesticides and develop a Guidance Document/Working Document with specific chapters on:
 - Waivers;
 - Microbial contamination;
 - Storage stability;
 - Evaluation of environmental safety of MPCP;
 - Fungal metabolites;
 - Classification and labelling;
 - Pheromones.

2. Promote communication and information exchange on Biopesticides. This by means of organising discussions, seminars or workshop on topics related to biopesticides and disseminate results (e.g. via publications) as appropriate. The Annual Biocontrol Industry Meeting (ABIM) which takes place in Lucerne, Switzerland. Can be used as a platform for the exchange of information and the promotion of Biopesticides.

3. Take forward the conclusions and recommendations of REBECA. REBECA (Regulation of Biological Control Agents - BCAs) is an EU policy support action to review possible risks of biocontrol agents, compare regulations in the EU and the USA and to propose alternative, less bureaucratic and more efficient regulation procedures maintaining the same level of safety for human health and the environment but accelerating market access and lowering registration costs. The final report will be available early 2008.

Item 3-1

EU Biopesticide Regulatory System: Scope, Structure and Function

Jeroen J. Meeussen

Ctgb, Wageningen, the Netherlands

(Board for the Authorisation of Plant Protection Products and Biocides)

In the EU biopesticides are regulated by Council Directive 91/414/EEC concerning the placing of plant protection products on the market. It came into force on 26 July 1993. The Directive applies to chemicals as well as biological pesticides.

The main elements of the Directive are as follows:

- To harmonise the overall arrangements for authorisation of plant protection products within the European Union. Product authorisation remains the responsibility of individual Member States;
- The Directive provides for the establishment of a positive list of active substances (Annex I), that have been shown to be without unacceptable risk to people or the environment;
- Member States can only authorise the marketing and use of plant protection products after an active substance is listed in Annex I, except where transitional arrangements apply.

The Directive 91/414/EEC has six Annexes:

- Annex I: Active substances authorized for incorporation in plant protection products;
- Annex II: Requirements for the dossier to be submitted for the inclusion of an active substance in Annex I: Part A - Chemical substances – Part B - Micro-organisms and viruses;
- Annex III: Requirements for the dossier to be submitted for the authorization of a plant protection product: Part A - Chemical preparations – Part B - Preparations of micro-organisms or viruses
- Annex IV: Risk phrases;
- Annex V: Safety phrases;
- Annex VI: Uniform Principles for the evaluation of plant protection products: Part A - Chemical preparations – Part B - Preparations of micro-organisms or viruses

For the purpose of Annex II, Part B, the term “micro-organism” is defined as “a microbiological entity, cellular or non-cellular, capable of replication or of transferring genetic material”. The definition applies to, but is not limited to, bacteria, fungi, protozoa, viruses and viroids. The Directive 91/414/EEC does not apply to Genetically Modified Organisms (GMOs) nor to invertebrate biocontrol agents.

Plant extracts, food additives, pheromones, semiochemicals etc. are covered by Part A of the Annexes II, III and VI of the Directive.

Dossiers have to be presented by industry in OECD-format. Electronic dossiers will only be accepted if they are compiled in accordance with the Format Specification for CADDY Document Interchange Format for Pesticides Registration Applications.

The Rapporteur Member State (RMS) –the Member State that is responsible for the evaluation of the dossier- will prepare a monograph or Draft Assessment Report (DAR) in OECD-format. The peer review (risk assessment) will be carried out by the EFSA (European Food Safety Authority). The decision on Annex I listing (risk management) will be taken by the European Commission (based on a vote of the member states in the Standing Committee on the Food Chain and Animal Health). Decisions on Annex I

listing of active substances are taken by qualified majority. Product (re-)registration will be done at Member State level.

All substances which were on the European market before 26 July 1993 are considered 'old' or 'existing' active substances. The Commission has developed a review programme to take decisions on Annex I listing for the existing active substances. The review programme is organised in 4 stages. Stage 1, 2 and 3 are dealing with conventional chemicals. Stage 4 covers plant extracts, attractants/repellents, pheromones, semiochemicals and micro-organisms. The review programme has to be finalised by December 31st, 2008.

'New' active substances -which were not on the market before 26 July 1993- are dealt with on a case by case basis (depending on the time of submission).

In general the following timelines apply:

- Completeness check: 6 months
- Preparation DAR: 12 months
- Peer review by EFSA: 12 months
- Decision Annex I listing: 6 months

Fees will be set by the individual Member States. A Member States shall establish the amount of the fee in a transparent manner so that it does not exceed the real cost of the examination and administrative treatment of a dossier.

Currently a new Council Regulation concerning the placing of plant protection products on the market is negotiated. Major changes compared to Directive 91/414/EEC are:

- Evaluation of safeners and synergists;
- Division of EU into 3 zones;
- Examination of authorisations by one MS on behalf of the other MS in a zone;
- Introduction of *low risk substances*, *basic substances* and *candidates for substitution*;
- Comparative assessment of plant protection products containing 'candidates for substitution';
- Deadlines in all steps;
- Simplified data protection system.

Item 3-2

US Biopesticide Regulatory System

Alan Reynolds, US EPA

The US biopesticide regulatory system is based on the requirements of the relevant US laws (primarily the Federal Insecticide Fungicide and Rodenticide Act, the Federal Food Drug and Cosmetic Act, and the Pesticide Regulatory Improvement Act). These laws include the EU biocides as well as the agricultural pesticides as pesticides. The US pesticide program has a number of common regulatory actions which include registering pesticides, reviewing experimental use permits, and conducting registration reviews. Our new laws now require payments for regulatory work and set time limits to complete the regulatory actions. We have a separate division dedicated to regulating microbial pesticides and biochemical pesticides (which class includes pheromones). We also work with the various states, some of which also require registration of pesticides and are involved in enforcement activities.

Item 3-3

Canadian Biopesticide Regulatory System – Scope, Structure and Function

Brian Belliveau

Health Evaluation Directorate, PMRA, Health Canada

Health Canada's Pest Management Regulatory Agency (PMRA) is responsible for the federal regulation of pest control products under the authority under the *Pest Control Products Act* (PCPA). The PMRA also develops pest management policies and guidelines, promotes sustainable pest management, enforces compliance with the PCPA, and distributes pest management information to the general public and key stakeholders. The PMRA's mission is to protect human health and the environment by minimizing the risks associated with pest control products in an open and transparent manner, while enabling access to pest management tools and sustainable pest management strategies.

All pesticides are regulated through a program of pre-market scientific assessment, enforcement, and education and information dissemination. These activities are shared among federal, provincial/territorial and municipal governments, and are governed by various acts, regulations, guidelines, directives and bylaws.

All biopesticides granted approval for use in Canada must demonstrate that they pose no unacceptable health or environmental risks and have value (e.g., efficacy; contribution to sustainable pest management).

Biopesticides, which includes microbial and biochemical active ingredients, are considered reduced-risk products and are accelerated through the registration process. Under the reduced-risk program, new biopesticide active ingredients have shortened review timelines and reduced fees compared to conventional chemical pesticides. The PMRA has published a number of regulatory guideline documents detailing data and submission requirements for reduced-risk pesticides, specifically for microbials, pheromones and other semiochemicals as well as for low-risk biochemical and other non-conventional pesticides.

An application for registration of a new pesticide undergoes several review stages from verification to ensure that fees, forms, labels have been provided; screening to ensure that it meets the format, content and fee requirements of the Agency; preliminary review to ensure that all studies/waiver rationales/information are complete and; finally critical review in which studies/waiver rationales/information are subjected to rigorous scientific examination and each science directorate provides a recommendation as to whether the product can be registered and the conditions for doing so. A consultation document summarizing the Agency's scientific review and proposed registration decision is released to the public for a 45-day comment period. Comments received during the consultation period are assessed and the final registration decision is made at the end of the comment period. Once the final bilingual label has been received and approved by the Agency, a registration certificate is issued to the applicant. A registration is normally granted for a term of five years, subject to renewal, but conditional registration may be granted for a shorter period (1-3 years).

Item 4**REBECA: Regulation of biological Control Agents***Jeroen J. Meeussen*

Ctgb, Wageningen, the Netherlands

(Board for the Authorisation of Plant Protection Products and Biocides)

REBECA (Regulation of Biological Control Agents - BCAs) is an EU policy support action to review possible risks of biocontrol agents, compare regulations in the EU and the USA and to propose alternative, less bureaucratic and more efficient regulation procedures maintaining the same level of safety for human health and the environment but accelerating market access and lowering registration costs.

It was noted that "Despite considerable research efforts on BCAs the number of such products on the market in Europe is currently still extremely low compared to USA and Canada. BCAs cannot be treated like synthetic chemicals and need different approaches for registration purposes". REBECA will search for measures to accelerate the registration process.

Biological Control Agents consist of the following groups: microbial pesticides (bacteria, fungi, viruses); plant extracts (botanicals); semiochemicals (pheromones); macrobials (invertebrates).

The REBECA project is organised around a series of workshops and conferences. REBECA is a two-year project that started on 1st January 2006. The project is co-ordinated by Prof. Dr. Ralf-Udo Ehlers from Christian-Albrechts-University, Kiel, Germany. The objectives of REBECA are:

- Review of the current legislation, guidelines and guidance documents at Member State and EU level and compare them with legislation in countries where the market introduction of BCAs has been more successful.
- Review of potential risks of BCAs and proposals on how regulation of BCAs can be balanced according to their potential hazards.
- Costs and benefits analysis.
- Propose alternative regulation strategies with reduced sets of data requirements.
- Bring together stakeholders from industry, science, regulation authorities, policy and environment.
- Provide potential experts, who can assist the EC and member states in the evaluation of risks and regulation of BCAs.
- Identify future research needs to support the development of balanced regulation strategies.
- Characterise and define low risk products, which might be exempted from registration.

Besides specific proposals to improve the registration process for microbials, botanicals, semiochemicals (pheromones) and Invertebrate Biocontrol Agents REBECA has developed some general proposals to improve the current regulation practice of BCAs. Some of the specific proposals for the different groups of biological control agents are:

microbials

- Annex I inclusion of Baculoviruses at a higher taxonomic level;
- Guidance Document on threshold levels for microbial contamination in Baculovirus products.

botanicals

- Identification required for all active substances and plant constituents of concern, but not for other plant constituents.
- Relaxations in efficacy requirements.

Semiochemicals (pheromones)

- Member States to use the OECD Guidance document on data requirements for semiochemicals (No 12);
- Collective listing of SCLPs in Annex I.

Invertebrate Biocontrol Agents

- Produce a standardised Permit application form and accompanying Guidance Document.
- Update of EPPO positive list.

Some general proposals are:

- Pre-submission meetings established as a routine;
- Use of ‘lessons learned’ documents in pre-submission meetings;
- Establish expert groups for BCAs;
- Reduced registration fees;
- Financial support and guidance for registration of new microbials, botanicals and semiochemicals;
- Strict and short timelines for evaluation and risk assessment;
- Regarding efficacy should products with minor beneficial effects be acceptable;
- Centralized registration authority (proposal not supported by REBECA however it may be an option on a longer time frame).

Proposals in the revision of Directive 91/414/EEC highly supported by REBECA:

- Compulsory mutual recognition within a zone;
- Introduction of two new categories: *Low risk substances* and *basic substances*;
- Short timelines for evaluation.

One of the major achievements of the REBECA project was probably an open dialogue between Industry, Regulators and Scientists. Further information and all meeting documents and presentations can be found on the REBECA website: <http://www.rebeca-net.de>

Item 5

Qualified presumption of safety (QSP): the EFSA approach for assessing the safety of microorganisms introduced deliberately in the food chain

Coralie Bultel, Tobin Robinson, Bernard Bottex, Frederique Istace, Christophe N’Guyen-The, Marta Hugas, EFSA

The QPS approach

Experience has shown that there is a need for a tool to set priorities within the risk assessment of those microorganisms used in food/feed production referred to EFSA and consequently the subject of a formal assessment of safety. To meet this need, a simplified tool was proposed for a pre-market safety assessment of selected groups of microorganisms leading to a “Qualified Presumption of Safety (QPS)”. In essence this proposed that a safety assessment of a defined taxonomic group could be made based on four pillars (establishing identity, body of knowledge, possible pathogenicity and end use). If the taxonomic group did not raise safety concerns or, if safety concerns existed, but could be defined and excluded (the qualification) the grouping could be granted QPS status. Microorganisms not considered suitable for QPS would remain subject to a full safety assessment.

QPS and microorganisms used for plant protection

In the framework of the Directive 91/414, different microorganisms have been proposed as plant protection products and should be peer-reviewed in the near future.

The protection offered to plants by microorganisms used for plant protection may depend, in part at least, on their toxicity and/or pathogenicity to the target organism(s). Therefore, the applicability of the QPS approach to these agents may be discussed, as the absence of toxicity is one of the qualifications used in the QPS process.

As part of the initial exercise, EFSA considered the *Bacillus* genus for QPS status and discussed the case of *B. thuringiensis*. The qualification for granting QPS status is the absence of toxic peptides and the absence of enterotoxigenic activity.

According to the opinion of EFSA's Scientific Committee, QPS status could not be granted for *Bacillus* spp. belonging to the *Bacillus cereus sensu lato* group (*B. cereus sensu stricto*, *B. mycoides*, *B. pseudomycoides*, *B. thuringiensis* and *B. weihenstephanensis*), since it is known that a significant number of strains within this group are toxin producers.

The SC decided not to include the filamentous fungi within the QPS system. Although in many cases there has been a history of use, this has been for specific purposes such as the production of citric acid or processing enzymes. The body of knowledge that has developed has, in consequence, been focused on these specific uses. However, many of the filamentous fungi used for production purposes are known to produce substances of potential concern (mycotoxins, *etc*). The strength of QPS lies in the ability to provide a generic system of safety assessment. Its scope can be extended by introducing a limited number of qualifications, allowing the majority of a taxonomic group to be assumed safe while excluding a minority of problematic strains. On examination, while it was possible to identify specific metabolites of filamentous fungi which should be excluded, it was not possible to be sure that these represented the totality of substances of concern capable of being produced by the taxonomic unit. Introducing restricted use as a qualification did not offer a solution since purpose does not offer any reassurance on overall metabolic capacity. The absence of undesirable compounds in one or more selected and well studied production strains does not allow extrapolation to all strains within the selected taxonomic unit.

Future potential developments

The QPS tool was initially intended to set priorities within the risk assessment of those microorganisms used in food/feed production referred to EFSA and consequently the subject of a formal assessment of safety. As a first step, the development of this concept was limited to microorganisms introduced into the food chain or used as producer strains for food/feed additives until the robustness and value of such a system could be tested in practice. Nevertheless, the application of this tool for the plant protection area was also explored. It results that the adequacy of the tool itself for the assessment of microorganisms used for plant protection may be questionable, as it does not take into consideration environmental aspects and operators' potential exposure. It can also be questioned whether it is desirable to adapt this simplified safety assessment approach to this kind of microorganisms, whose interest lies in their toxicity and/or pathogenicity principles to target organisms.

Thus, in its present form, QPS does not offer a generic approach to the safety assessment of microorganisms used as biological control agents. However, the SC has suggested investigating whether the use of robust qualifications would allow a QPS approach in the future for biological control agents.

Item 6-1 and 6-3

Human Health/Product Analysis

John Kough, US EPA

Non-target/Environmental Fate

Zigfridas Vaituzis, US EPA

The EPA Biopesticides data requirements were revised and published in final form October 26, 2007. They reflect our regulatory practices that had evolved over the 23 years since they had previously been published. We try to expedite the regulatory process to encourage the registration of microbial pesticides and ask for only that data needed for an adequate risk assessment. The data requirements are organized into Tiers to better explain what is generally needed for an assessment and we also will waive data submission requirements or accept alternative data from the literature or from other product submissions where justified by the taxonomic identification and the nature of the microorganism. The product characterization is an important step in this process. Different kinds of microorganisms may present different kinds of potential risk. Our assessment is based on the standard risk assessment process of using hazard (toxicity and pathogenicity potential) and exposure to arrive at a risk. Since a full exposure analysis is often difficult to obtain for microorganisms that may replicate in a host or the environment, we prefer to rely initially on a worst-case hazard assessment to rule out the possibility that the microbial pesticide has any potential for hazard, thus allowing us to use only this data for the assessment. The screening high dose used in the Tier I hazard studies (also known as a maximum hazard dose) is analogous to a chemical limit dose but is recorded in terms of Colony-forming-units (CFUs) rather than weight. However if any assessments questions are raised by these tests or by the relationship of a proposed microbial pesticide to similar microorganisms that may have risk concerns, we can require higher tier studies, or even, other unlisted studies on a case-by-case basis. In some cases, particularly for potential environmental effects, if we do not expect the effect actually exists, we can ask for verification data as part of the conditions of registration. This would allow for a more affordable large scale field test to confirm our assessment.

Item 6-2

EU Microbial Pesticide – Data Requirements

Marloes Busschers, Ctgb

(Board for the Authorisation of Plant Protection Products and Biocides), Wageningen, The Netherlands

In the EU biopesticides are regulated by Council Directive 91/414/EEC concerning the placing of plant protection products on the market. The Directive applies to chemicals as well as microbiological pesticides.

The data requirements for microbial pesticides are described in Directive 2001/36/EC, as part of 91/414/EEC. These data requirements are specific for microbials and differ from the data requirements for chemicals. The data requirements are described for micro-organisms in general and are not specified for the different groups, such as fungi, bacteria, (baculo)viruses etc. In principle, each data requirement needs to be addressed: any information such as open literature, statements, and studies can be used to fulfil the data requirement.

In some cases studies on a closely related strain or species can be used to support a request for Annex I inclusion, although it should be convincingly described why the other strain or species is representative for the notified strain. Problems arise as to what level of similarity is needed, and how to handle changes/improvements in taxonomic identification. Other problems are data protection and reliability of literature studies vs. lab studies.

The data requirements in the USA/Canada and Europe do not differ substantially; it's the way in which they are actually used that makes the difference. For example in the USA and Canada pre-registration meetings are held during which the actual data requirements are agreed upon. This is not practical in Europe: no final agreements on the completeness and acceptability of the dossier can be made for each data point at dossier submission, since in the evaluation process 26 other Member States and EFSA will also have to agree on the acceptability of the dossier.

Up till now USA/Canada had much more experience in the evaluation and registration of microbials. However, currently 19 microbial Draft Assessment Reports (DARs) of the so-called 4th list are available to EU Member States or will be in the near future. They will also become available to the general public for commenting via the EFSA site. A decision on Annex I inclusion of these microbials will have to be taken by the end of this year (2008).

The Netherlands is doing a survey on these DARs and eventually a lessons-learned document will be available. These documents can help to harmonise the use of data requirements for microbials in Europe. In the survey we have identified how each data point was addressed in each of the 19 DARs: with literature data, waivers, or studies, on the strain itself, or a related strain. This survey may help in identifying data point that are always addressed by a study, hence the best way to address this point for a new strain is probably a study. On the other hand it can also identify data requirements that are considered not applicable for a specific group of micro-organisms or that are always addressed by a waiver.

The Netherlands have collected all the submitted waivers per data point; from this it might be possible to subtract a more general waiver per data point, probably depending on the group of micro-organism. A document with general waivers can then guide applicants for new strains; these waivers cannot replace the data requirement in 91/414/EEC, but can be a useful tool when addressing the data point.

Item 6-4

Environmental effects and risks of microbial pest control products: science and decision schemes

B.J.W.G. (Hans) Mensink †
RIVM, Bilthoven, The Netherlands.

Science and risk decision schemes should be helpful in facilitating registration procedures for microbial and other non-synthetic crop protection products. This lecture provides notions on this issue and reflects some of the challenges involved. The first part discusses some current desk studies by RIVM on the environmental behaviour and effects of microbial pest control agents (MPCAs). The second part stipulates a proposed environmental risk decision scheme for microbial pest control products (MPCPs). This scheme has been published in *Biocontrol, Science and Technology* 17 (2007), will be used for an OECD working document, and has been presented on meetings (e.g., IOBC, Rebeca, BCPC).

In the EU, the data requirements and the decision criteria, the Uniform Principles, have been laid down in EU Directives. This however does not mean that in practice all aspects of the safety evaluation of MPCAs and their products are clearcut and easy to deal with. Regulatory authorities are confronted with several issues on different levels in this respect that clearly need further attention. These are: (1) general lack of scientific (documented) knowledge on the behaviour and effects of microbiological entities in the environment. (2) registration dossiers which show large differences in quality and quantity (3) lack of scientific guidance for consistent evaluations. (4) difficulties in dealing with waivers: how sure can we be about the lack of adverse effects rather based on general statements than on empirical data.

These issues should be seen against a (slowly) increasing mondial use of MPCPs, increasing experience with efficacious products and a general lack of detrimental environmental effects when products are properly used. Also, the documentation on empirical knowledge on MPCAs is improving (e.g. by Rebeca).

RIVM has started desk studies to fill some of the scientific data gaps often found in registration dossiers. They focus on the environmental behaviour and effects of MPCAs on (non-target) soil microbial systems. Two will be briefly discussed. The first study is on the soil persistence of entomopathogenic fungal MPCAs in relation to natural inoculum levels. The second is on the effects and risks of MPCAs to non-target soil microbial communities and soil functions. The latter includes a comparison of MPCAs with chemical PCAs and a review of the effects on soil disease suppressiveness.

There is consensus that MPCPs with fungi and bacteria always require a proper pre-market safety evaluation. This is not only in view of potential toxicity, infectivity and pathogenicity of the micro-organism, but also because of the possible effects of microbial contaminants and co-formulantia (spreader, sticker). A proper safety evaluation is of particular importance as MPCPs will be increasingly used for sustainable crop protection worldwide. Also, as the efficacy of the current products is not always satisfactorily, there is a trend to improve these products. An improved efficacy may enlarge the potential environmental impact, particularly in case of a broad range of target insects. How should regulatory managers from industries, regulators from governments, or environmental scientists deal with such risks? Scientific and technical guidance on the safety evaluation for regulatory reasons is scarce and therefore we have developed an environmental risk decision tree in cooperation with the Dutch Ministry of Environment and the National Board for the Authorisation of Plant Protection products and Biocides. This decision tree enables stakeholders to assess whether the environmental risks are acceptable, taking into account the efficacy, characterisation, identification, use pattern, emission, exposure and environmental effects of MPCPs.

Item 6-5

Microbial Review Templates

Denis Rochon and Brian Belliveau

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Health Canada's Pest Management Regulatory Agency (PMRA) began developing microbial review, or data evaluation, templates in 2001 for Canada-only registration purposes, but with a view to eventually apply them to the North American Free Trade Agreement Technical Working Group on Pesticides Joint Review (NAFTA JR) of microbial pesticides. NAFTA harmonized data evaluation templates by this time had already been developed for the human health (toxicology and exposure) and

environment (ecotoxicology and fate) review of conventional chemical pesticides. Microbial-specific templates were first modelled after the conventional chemical templates for standard toxicology and ecotoxicology/fate studies, but many modifications were required to account for study protocol differences such as the assessment of infectivity and pathogenicity end points and single dose (maximum hazard) testing of microorganisms instead of multiple dose (definitive) toxicity testing of chemical products. The PMRA also developed unique microbial review templates for assessing product characterization and analysis data as well as for core published papers, the general review of literature, and occupational/bystander exposure and dietary exposure assessments. Because so many microbial submissions/dossiers rely on waiver rationales in lieu of actual test data, the PMRA also developed waiver review templates for most study requirements.

The microbial review templates were shared with member countries of the OECD BioPesticides Steering Group in 2005 for review and comment. This project was undertaken to facilitate the future global review of microbial submissions as well as assist EU members with their 4th List programme review of microbial dossiers. Since 2005, the microbial review templates continue to undergo revisions and improvements.

Item 6-6

Review templates experiences

Annabel Waggoner, US EPA

The initial data reviews in the US are done by a contractor with close supervision by BPPD specialists. One of our projects is to develop these templates for our contractors to use to provide them with better guidance on what information we need for our final assessment and to better support classification of the submitted data into acceptable, supplementary or unacceptable categories. We have revised some of these templates to incorporate our review information and have received feedback on these from both our contractors and our BPPD reviewers. We will continue to provide this information to PMRA Canada to better harmonize our review procedures.

Item 7-1

Canadian perspective on efficacy requirements for registration of Biological Control Agents

Pierre Beauchamp, Pest Management Regulatory Agency

An overview of microbial products reviewed for registration in Canada in the last five years and of trends in Canadian registration will be discussed. A summary of the main characteristics and difficulties associated with the efficacy data reviewed up to now will be presented followed by proposed solutions to improve the quality of the efficacy data package regarding consistent description and usefulness of the mode of action of the products, the use of rationales, the level of performance justification and expectations, new types of claims.

Item 7-2

Industry perspective on efficacy requirements for registration of Biological Control Agents

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For the International Biocontrol Manufacturers Association (www.IBMA.ch)

Biological Control Agents (BCA) are used as plant protection agents in agriculture and horticulture either in conventional or organic production systems and are often important components of Integrated Pest/Crop Management (IPM/ICM). In the context of this presentation, the focus will be on products based on; micro-organisms, natural products or semiochemicals (including pheromones), collectively termed 'biopesticides'.

In EU member states, current regulations require efficacy data to be provided in support of inclusion of an active substance on Annex 1. The recent Rebeca project reports (Deliverable 24) that registration costs for Annex 1 inclusion (active ingredient listing) is €1,890,000 where efficacy represents 21% of these costs. Once Annex 1 inclusion is completed, manufacturers are required to register each product in each member state where they intend selling. This is usually with a requirement to supply efficacy data for each use (crop/pest situation). Typically, this needs to be done to GEP standards, over at least two years, with up to 10 good trials per pest/crop situation although requirements can vary depending on target organisms, efficacy obtained, and national requirements. So, for BCA manufacturer's, development of efficacy data in support of registration represents a significant cost.

Current requirements for biopesticide efficacy data are based on a system developed for chemical based plant protection products. While some EU regulatory organisations are showing flexibility to accommodate biopesticides within existing guidelines, there remain issues with a system that was developed for one type of product now being used for very different types of products. Some of the underlying principles and the related methodologies for chemical plant protection product efficacy evaluation, are not applicable to biopesticides; for example, the dose response curve for chemical products is generally linear but this is not the case for many biopesticides, and each BCA can have its own distinctive dose response curve which then requires a different method of evaluation.

Another major difference is that most biopesticides are used as population management/manipulation tools to bring pest/disease incidence below economic damage thresholds rather than for eradication. This marked difference in use means that what is considered as 'efficacy' may need reconsideration, many products with less than an 80% control may still be useful to a grower. Indeed, in an IPM system where it is important to maintain a balance, growers can actively seek products which have a small and temporal effect.

This presentation reflects the biological control manufacturer industry views on the issues surrounding the efficacy requirements for registration of biopesticides and considers whether the differences between the European and USA systems account, at least in part, for there being more BCA products available in the USA than in the European Union.

Item 7-3**Efficacy*****William Schneider***, EPA, US

The US efficacy studies are officially entitled “Product Performance” studies. These Product Performance regulations are published in part 158.640 of section 40 of our Code of Federal Regulations (40CFR). This part of our data requirement regulations was not updated when we published the newly revised data requirement regulations for conventional and biopesticides. Our product performance data requirement and guidelines workgroup has been meeting regularly on this project. The US currently requires each registrant to ensure through testing that his products are efficacious when used in accordance with label directions and commonly accepted pest control practices. However, the product performance regulation requires applicants to submit the efficacy data only for products that bear a claim to control pest microorganisms that pose a threat to human health and their vectors. The current rule notes, however, that we can ask for submission of efficacy data on a case-by-case basis. In actual practice we have been asking for efficacy data for pesticides that control public health pests, i.e. mosquito control pesticides and rodenticides, for those pesticides that control pests whose control cannot be readily observed by the user, e.g. termites, and for pesticides that directly control human pathogens, i.e. antimicrobial pesticides. The latter category includes pesticides that control organisms producing mycotoxins and we have reviewed efficacy data for two microbial pesticides that control aflatoxin-producing *Aspergillus flavus* species. Most of the efficacy studies we review are for products that would fall into the EU biocide category. However, we have some of the same regulatory issues that might be encountered for other agricultural biopesticide efficacy studies, particularly in selecting appropriate label language for describing the level of control for that product without necessarily implying that the product is not useful.

Item 9-1**Evaluation of Straight-Chained Lepidopteran Pheromones (SCLPs): Lessons learned based on the experience with the 4th list of the 91/414 EU review program*****Wolfgang Bergermayer*** and ***Alexandra Fischer***

Austrian Agency for Health and Food Safety (AGES), Institute for Plant Protection Products Evaluation & Authorisation, Vienna, Austria

Introduction

A total of 11 companies formed a task force and submitted one single dossier for 32 active ingredients, all members of the Straight-Chained Lepidopteran Pheromones (SCLPs), including the substance classes of acetates, aldehydes and alcohols as well as different blend mixtures. Austria as Rapporteur Member State (RMS) prepared the Draft Assessment Report (DAR) for the EU review program in accordance with the Commission Directive 91/414/EEC. As guidance for writing the DAR we used primarily the “*OECD SERIES ON PESTICIDES Number 12, Guidance for Registration Requirements for Pheromones and Other Semiochemicals Used for Arthropod Pest Control*” ENV/JM/MONO(2001)12 (in this abstract referred to as OECD No. 12), as recommended in the “*Guidance document on the preparation of dossiers and draft assessment reports for substances covered in the fourth stage of the review programme referred to in Article 8(2) of Council Directive 91/414/EEC (Sanco/10393/2004 –*

rev.4)”. In the **OECD No. 12**, the data and studies required for evaluation and risk assessment are defined and a number of waiving arguments is provided.

Here, we will present our experiences with the evaluation of SCLPs and our opinion on the usefulness of the **OECD No. 12**.

Results

First of all, we would like to discuss the definition of SCLPs given in **OECD No. 12**, as the current definition does not cover all of the 32 active ingredients (a.i.) notified in the course of the EU program. In our opinion, the definition of SCLPs needs to be revised or adapted in order to cover them all.

For each submission of a dossier the notifiers should be obliged to submit all relevant available studies or information. It should not happen that data available to notifiers are not submitted, just because in accordance with **OECD No. 12** these data could potentially be waived. This should also apply to existing studies or information, which are not required in Appendix 1 to **OECD No. 12**. We would like to stress that the misinterpretation of waiving arguments (such as “data may be waived for TGAI, if the substance is a member of a well characterized group e.g. SCLPs”) as justification for non-submission of existing and available data has to be avoided. This should be clearly stated in **OECD No. 12**.

A further problem we were confronted with was that in the SCLP dossier a number of values for physical-chemical parameters were given without any reference. In all cases references are required and must be accessible for the evaluators.

In Appendix 1 to the **OECD No. 12** a list of requirements for data or information is given and each requirement has been assigned a status of “R” (required) or “CR” (conditionally required). In principle this list is very useful, however, we suggest (1) a stricter definition of “R” and “CR” and (2) certain waiving arguments should be defined more clearly.

Additionally, information concerning important issues, e.g. vapour releasing rate/effectiveness and analytical methods for monitoring, should be required. Therefore, the **OECD No. 12** has to be revised.

In the **OECD No. 12** it is stated that “application rates of up to 375 g SCLP/ha/year are generally understood to result in exposure levels which are comparable to natural emissions”. However, the rationale for this assumption/value is based on an unpublished letter (Maloney, R.; 1999). This letter should be made accessible for all users of the **OECD No. 12**. Independently, in our opinion the maximum application rate (comparable to natural emissions) should be recalculated on the base of current research results on pheromone release rates.

Furthermore, in our opinion more guidance is required for formulations other than solid matrix dispensers, because additional problems or requirements could arise from e.g. sprayable microcapsule suspensions (such as technical application, risk of inhalation by operator, ingestion by birds and mammals).

Conclusion

Although the **OECD No. 12** is basically useful for SCLPs formulated in solid matrix dispensers with an application rate of less than 375 g a.i./ha/year, it should be clearly stated which requirements are absolutely necessary and cannot be waived (e.g. concerning identity and physical-chemical parameters; refer to definition of “R”). For other cases (i.e. semiochemicals other than SCLPs, formulations other than solid matrix dispensers and application rates of more than 375 g a.i./ha/year) more detailed guidance is necessary.

Item 9-2**Pheromones*****William Schneider, US EPA***

The US regulates pheromones/semiochemicals as part of their biochemical class of pesticides. The biochemical pesticide definition and the biochemical pesticide data requirements were just updated to better fit with our experiences since the regulation for these was last published in 1984. The regulation of biochemical pesticides are also affected by some of our regulations in section 40 of our Code of Federal Regulations (40CFR) that exempt some substances from regulation as pesticides. The pheromones are particularly affected by 40CFR152.25(b), which exempts pheromones and substantially similar substances when used in pheromone traps. We've also exempted all substances when used to attract pests for survey or detection purposes (40CFR152.10(b)). Pheromones are also allowed to be used on up to 250 acres of land for experimental purposes without requiring an Experimental Use Permit as compared to all other pesticides which can only be tested on up to 10 acres. Our Biochemical Pesticide Data Requirements are organized much like our Microbial Pesticide data requirements to describe what studies are actually required. The Human Health and the Nontarget Organism / Environmental Fate table are organized into three Tiers and have many specific footnotes that give further information on when we might actually need that particular study. Before revising our data requirements, we did a survey of what data was actually required for Biochemical Pesticides registered between 1995 and 2003. This analysis included 6 pheromones and the new requirements reflect our past practices. The main changes to the new data requirements is that all arthropod pheromones are exempted from Nontarget and Environment Fate data requirements, and all straight chain lepidopteran pheromones are exempted from human health data requirements. The residue data would still not be required because it is only required if Tier II or Tier III toxicity data is required. Of course we still evaluate each new submission on a case-by-case basis considering the use patterns, the inert substances in the product, and the information verifying that it is actually a pheromone/semiochemical. Canada (PMRA) has published a proposal to establish a class of biopesticides like our biochemical pesticides with similar data requirements (PRO2007-02). They are currently using a harmonized pilot program and are evaluating public comments on their proposal.

Item 10-1**Communications*****Mike Mendelsohn, US EPA***

We post helpful information and guidance on our website for our registrants. We generally recommend that registrants that are new to the regulatory process hire a consultant. We post a list on our website. If a company is based outside the US they must have a US representative for their product. We engage in direct communications to help an applicant early in the process. We have a Biopesticide Classification Committee that will give an official decision on whether any given product qualifies to be a Biopesticide or would have to be instead submitted to the Registration Division for conventional chemical pesticides or to the Antimicrobial Division. All pre-registration communications are considered to be confidential until an application is officially submitted. We have pre-registration meetings with potential

applicants at which we can discuss what data would actually be needed for the submission and they can summarize our agreements on this for our signoff. Once an application is submitted, it is announced in the Federal Register and is put in a docket for the public to view on the internet. We solicit public comments on these submissions. Some of the data is protected by our laws regarding involving Confidential Business Information. We stay in close contact with the applicant during the review process and ask for clarification and/or additional information as needed. We also publish announcements of our assessments for any registration or permit approvals and add that to the public docket. Some of the US states also require regulation of pesticides and usually use our assessments and/or data to expedite their process. We often engage in direct communication with those states to assist them and we have standing committee meetings to resolve any general or policy issues.

Item 10-2

Communication and Registration

Bernard J. Blum, head International Affairs – IBMA

The registration of pesticides as well as Biopesticides is a process which is designed in order to ensure that quality products are brought to the market. Authorities are designated in each country as well in the EU in order to assess the fitness of candidate products and ensure that they will not endanger the environment not the public health. Additionally to the manufacturers and the regulatory authorities, several other stakeholders are due to be involved in one way or the other in the process. The paper describes the reasons for such a dialogue which has to take place at all the stages of the regulatory process and its implementation. The presentation covers more in details the necessary both-ways communication which should be established between the evaluation body and the industrial applicant and mention some important issues which remain to be solved.

Item 10-3

Communication: How to initiate a dialogue between all stakeholders on the regulation of Biological Control Agents (BCAs) – The UK Biopesticide Scheme

John Dale, PSD, York, United Kingdom

Traditionally in the UK there have never been a large number of approved biopesticide-type products available in market place; pre-2003 there were only four actives. Therefore, following discussions with growers, manufacturers and policy makers PSD launched a Biopesticides Pilot Project in June 2003. This was seen as a way of learning more about this sector, encouraging potential applicants to open dialogues with PSD and also offer reduced fees; often quoted as the main obstacle to product availability.

The pilot led to further discussions with IBMA-UK, R&D bodies, academia and a large number of pre-submission meetings with potential applicants. It also resulted in three new products being successfully approved containing pheromone, viral and fungal active substances.

Building on the success of the Biopesticides Pilot Project; 2006 saw PSD launch a full-scale Biopesticides Scheme. The aim of the scheme is to increase the number of products entering the market that are alternatives to conventional pesticides. The scheme covers a range of biopesticides including products containing micro-organisms, pheromones, semiochemicals and plant extracts. There is also scope to consider other novel alternatives which do not easily sit within a specific category and as such the data requirements are assessed on a case by case basis.

The key elements of the scheme itself are:

- The appointment of a 'Biopesticide Champion', who provides an initial contact for product innovators/manufacturers, and steers them through the approval process.
- Appointment of 'Biocontacts' in each of the specialist areas of risk assessment to provide guidance on specific scientific and regulatory issues.
- Encouraging potential applicants to meet with PSD at the earliest possible stages of product development.
- Providing specific guidance to applicants (via pre-submission meetings), flagging up possible hurdles to address and identifying the best way forward for their product.
- A fee for evaluation that is approximately a quarter of the cost of a conventional pesticide.
- A new dedicated Biopesticide area on the PSD website to support those making applications. The information in this area will continue to grow with further information and guidance on the regulatory and scientific aspects of the process.

Our 'Biocontacts' actively seek opportunities to engage with potential applicants and have attended a number of biopesticide related seminars and conferences. In March 2007, PSD also organised a one day seminar for all stakeholders to provide an overview of the Biopesticide Regulatory Process' and was attended by over 60 participants.

Since the introduction of the scheme six biopesticide products have now successfully been guided through the system and are approved for use in the UK. A further three other products are currently under evaluation. A number of other companies are discussing possible applications with PSD or have submitted draft dossiers as part of the pre-submission process. We also hold a regular dialogue with IBMA-UK. These developments have been welcomed and highly praised by industry both on a national and international level.

In summary, the keys to the scheme's success have been; an opening of communication to dispel myths about the regulatory process, a commitment from PSD to listen more closely to these often inexperienced applicants' special concerns. It allows us to dedicate time in explaining the system and its requirements to them before the raising of a fee. We found that by starting this communication at the earliest opportunity, applicants have targeted their resources more efficiently often resulting in more reliance on information already in the public domain rather than the generation of new data. As regulators we continually aim to provide as much flexibility as possible and look at providing regulation at an appropriate level. Working with the IBMA-UK, has helped deliver a consistent message on these issues to a wide selection of our stakeholders.

ANNEX 3

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