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REPORT OF THE 8TH BIOPESTICIDES EXPERT GROUP SEMINAR ON NICHE USES OF HIGHLY SPECIFIC BIOCONTROL PRODUCTS

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INTER-ORGANIZATION PROGRAMME FOR THE SOUND MANAGEMENT OF CHEMICALS
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Foreword

This report summarises the discussion and outcomes of an OECD Expert Group on BioPesticide (EGBP) seminar on niche uses of highly specific biocontrol products. This one-day seminar was held on 26 June, 2017 at OECD headquarters in Paris, France, one day before the annual meeting of the EGBP, a sub-group of the OECD Working Group on Pesticides (WGP). The seminar was the eighth in a series of EGBP (formerly the BioPesticides Steering Group, BPSG) seminars that focus on bio-pesticide related issues of interest to OECD governments and other stakeholders.

The seminar was chaired by Jeroen Meeussen (European Union Minor Uses Coordination Facility), chair of the EGBP. Forty-one experts from ten OECD member countries, the European Commission, Costa Rica, the People's Republic of China, the Business and Industry Advisory Committee to the OECD (BIAC), the International Biocontrol Manufacturers Association (IBMA) and research institutes/universities participated in the Seminar. The list of participants can be found at Annex 2.

The seminar was organised to present highly specific biological solutions for crop protection and to illustrate the hurdles and issues which pesticide registrants face, as well as to work towards the delivery of workable solutions to bring highly specific biological plant protection products to farmers.

The summary of seminar participants' observations, conclusions and recommendations are included in the first part of this report. The seminar programme is presented in Annex 1. The abstracts of presentations are compiled in Annex 3, while presentations are provided in Annex 4.

This document is being published under the responsibility of the Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology, which has agreed that it be declassified and made available to the public.

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Introduction

This report presents the results and recommendations of an OECD Seminar on issues related to the usage of highly specific biocontrol products as a solution for plant protection. Its aim is to provide an overview of the issues associated with this topic from the perspective of research, industry and regulatory experts, and to provide input to the potential future development of recommendations for possible further OECD work.

The seminar focused on promoting a dialogue on "Niche Uses of Highly Specific Biocontrol Products" and initiating a process to make recommendations for improvements to the registration of highly specific biocontrol products by exchanging information on:

- organisations' and industry's experiences, challenges and problems encountered in the registration of highly specific biocontrol products; and
- regulatory approaches for the registration of highly specific biocontrol products.

Participants

People attending the OECD Seminar included:

- members of the OECD Working Group on Pesticides (WGP) and Expert Group on BioPesticides (EGBP);
- invited experts from key stakeholder groups such as the pesticide industry and manufacturers of biopesticides (BIAC and IBMA);
- invited experts from research institutes (academia), and
- regulators and evaluators from governmental or intergovernmental bodies.

Purpose and Scope of the Seminar

The main objectives of the EGBP Seminar on 'Niche Uses of Highly Specific Biocontrol Products' included:

- identify key issues and challenges in the registration of highly specific biocontrol products;
- deconstruct regulatory hurdles to facilitate adoption on a broader scale of niche market solutions;
- work towards the delivery of workable solutions to bring highly specific biological plant protection solutions to farmers;
- provide updates of national and international activities and initiatives in bringing highly specific biocontrol products to the market;
- exchange information on OECD countries' current activities in facilitating the registration of highly specific biocontrol products;

- exchange information between scientists, stakeholders and regulators on what is needed for the registration of highly specific biocontrol products;
- suggest and discuss options for further steps for OECD countries and key stakeholders in OECD and non-OECD countries to address the identified issues, and
- recommend possible further improvements to address regulatory issues and processes in the area of highly specific biocontrol products.

In particular, the following issues and statements were discussed during the Seminar:

- What are possible solutions to overcome regulatory hurdles?
- The more specific a product is the less impact it has on the environment.
- The more specific a product is the greater the expected efficacy on a target.
- The more specific a product with complex modes of action, in general the less chance of resistance development.
- The more specific a product is the smaller the size of the market.
- The more specific a product is the higher the impact from regulatory costs.
- The use of highly specific biological products is even more restrictive for speciality crops where markets are limited.
- The availability of highly specific biological products is essential for Integrated Pest Management (IPM).

With the focus on "Niche Uses of Highly Specific Biocontrol Products", the goals of this Seminar were to:

- promote a dialogue on "Niche Uses of Highly Specific Biocontrol Products"; and
- initiate a process to make recommendations for improvements to the registration of highly specific biocontrol products.

Structure of the Seminar

The Seminar programme is provided in Annex 1. Invited speakers included:

- International experts in this field;
- Government representatives; and
- Representatives from industry (IBMA) and research institutes.

Presentations were grouped under three sections covering different aspects of highly specific biocontrol products, as follows:

- Introduction
- Research Institutes' and Stakeholders' Experience and Perspectives
- Government Experience and Perspectives

There was a short discussion after each set of presentations and a more general discussion at the end of the seminar.

Summary of Presentations and Discussions

All abstracts and slides of presentations are presented in Annexes 3 and 4.

Introduction to the Seminar

The OECD and the work of OECD-EGBP and general introduction to the seminar on 'Niche Uses of Highly Specific Biocontrol Products'

by the EGBP and Seminar Chair, Jeroen Meeussen, European Union Minor Uses Coordination Facility [PPT 1]

At the beginning of the seminar, the Chair invited a tour de table for the participants of the seminar to introduce themselves. The Chair continued by giving a presentation on the history of OECD and the work of the OECD Expert Group on BioPesticide (EGBP), as well as a general introduction to the seminar. He explained that the topic 'Niche Uses of Highly Specific Biocontrol Products' was selected based on discussions held in the BPSG meeting in June 2016 related to the issue of highly specific invertebrates and pheromones and their registration data requirements. He mentioned that the focus of the seminar is to present highly specific biological solutions and illustrate the challenges and issues which registrants and regulators currently face, as well as to work towards the delivery of workable solutions to bring safe highly specific biological plant protection products to the farmers. The Chair also explained that the scope of the seminar was to discuss: (1) possible solutions to overcome regulatory hurdles, (2) the relation between specificity of a product and impact on the environment, (3) the relation between specificity of a product and size of market, and the impact on regulatory costs, (4) the higher restriction of speciality crops due to the limited market, and, lastly (5) the importance of availability of highly specific biological products for IPM programmes. He pointed out that the presentations of the seminar, therefore, would focus not only on examples of highly specific biological plant protection products but also on specific government or organisation's experiences, challenges and problems encountered in the registration of these products. In this respect, possible solutions should also be highlighted. Lastly, the Chair closed his presentation by sharing the goal of the one day seminar which is to promote a dialogue among participants and to initiate a process for drawing recommendations that could facilitate the registration of highly specific biocontrol products.

Research Institutes' and Stakeholders' Experience and Perspectives

Overview of Niche Uses of Highly Specific Biocontrol Products: How to bring solutions to farmers

by David Cary (International Biocontrol Manufacturers Association) [PPT 2]

The presenter started by explaining one of the main problems faced by the current agricultural system that involves the loss of plant protection products due to multifactorial issues such as failure to accommodate new plant protection products and resistance development. The presentation aimed to summarise the difficulties encountered during the registration and use of highly specific biocontrol products. It was emphasised that the problem solving strategy should change from incident based problem solving to holistic problem solving. The presenter stated that the niche products need to be treated differently from the traditional plant protecting products. The main reason is the high cost involved for the research, development and registration of traditional plant protecting products (estimated $286 million in 2014) and the opportunities that exist for these products to be used for big crops and the time to market these traditional products was11.3 years in 2014. In contrast, the highly specific tools and tools for niche markets are often produced by small and medium enterprises. It is an innovative industry and looking for new solutions in the way they should be regulated. The presenter also indicated that all the actors, including policymakers, regulators, researchers, industry, farmers and food value chain should work together to solve the difficulties in issues related to the registration of highly specific biocontrol products. The possible solutions suggested from the presenter are: (1) global or regional positive list, (2) no renewal requirement, (3) notification procedure for active substances, (4) no requirement for product authorisations or a single regional product authorisation, (5) ability to allow a minor use on the label without needing a major use and (6) concurrent active substance approval and a regional product authorisation in a single step. Lastly, the presenter stated that there is need for a holistic approach to agriculture that prevents pest and pest disease explosion and makes use of all available tools, including highly specific biological plant protection products that could minimise any potential risk to human health and the environment. In conclusion, the speaker suggested that only through the use of true IPM, a new true green revolution can be achieved.

Niche Uses of Semiochemicals

by Vittorio Veronelli (CBC Europe, Italy) [PPT 3]

The presenter started by introducing the long history behind the discovery of semiochemicals and their use as plant protection products. The history of semiochemicals began in 1879 when insect chemical communication was first recorded, but it was only in 1978 when the first semiochemicals were registered and used in agriculture. Since then,

the global use of semiochemicals has been expanding; adoption of pheromones for pest control currently exceeds a million hectares worldwide. More than 8,000 semiochemicals (mostly straight chain lepidopteran pheromones, SCLP) have been identified and approximately 200 of them are commercialised, mostly for monitoring traps. Only 50 of them are available for mating disruption (MD) and not more than 20 are applied at a global level. Just five semiochemicals cover 80% of world uses. In addition, out of 150 SCLP formulations currently registered in the US and the EU, 40% of these are for only one pest and one crop. Before going further into the problems faced by using semiochemicals, the presenter also emphasised the characteristics and the importance of pheromones. Due to their species specificity and because they work only at the adult stage and provide 'birth control' rather than damage the pest, low amounts are used and no residues would be expected in any case of use. After that, the presenter introduced a few cases of pheromone minor uses where registration hurdles, market size and lengthy mutual recognition procedures made the registration and use of pheromones difficult. In conclusion, the presenter summarised the limitations of the current regulation for semiochemicals and suggested possible solutions. He explained that crop label extensions on products containing pheromones should be flexible and easy as pests are typically polyphagous and able to adjust to a variety of plants. Also, since a crop in a specific country is minor or very minor, an easier authorisation process and/or decreased registration fees should apply. When a product is registered and widely applied in a country, its registration should be facilitated in another country, especially if the border is practically just administrative like in the European Union. Lastly, for invasive pests moving across borders, mating disruption products already registered in one country can help prevent pest expansion faster if the regulation would support fast authorisation of these products.

Molecular factors defining specificity and host range of baculoviruses

by Johannes A. Jehle, Jörg T. Wennmann (Julius Kühn-Institute (JKI), Darmstadt, Germany) [PPT 4]

In the beginning, the presenter provided some general information on baculoviruses by describing their structure, characteristics and host range. Furthermore, he explained the biology that makes baculoviruses such a specific biocontrol agent. Baculoviruses are produced in an occlusion body, which is a protein matrix wherein active baculoviruses are embedded. The occlusion body provides the baculoviruses with protection against physical (shearing, UV, heat, pH) and chemical (detergents, enzymes) factors, ensuring their stability. The baculoviruses infect only insect larvae and not adults, with two stages of infection. In the primary infection, the baculoviruses start the infection in the midgut, which is then spread through the larvae and starts the secondary infection. In terms of a baculovirus life cycle, there are two virus phenotypes: one is the occlusion derived virus (ODV) that provides environmental persistence, infection of midgut and horizontal transmission from insect to insect, and the other is the budded virus that is for secondary infection and transmission from cell to cell. The presenter also mentioned some additional characteristics of baculoviruses, which make them different from other invertebrate pathogens as they are not toxigenic, they do not produce secondary metabolites and it is not possible for them to harm or grow on mammals. The presenter then stated the fives conditions needed for a successful infection to occur, which are: (1) pH in midgut lumen >9, (2) per os infectivity factors (PIF) proteins on ODV, (3) apoptosis inhibition, (4) viral

transcription and (5) DNA replication. After the detailed explanation of each of these processes, the presenter explained that baculoviruses host specificity is unique and there are no related viruses outside arthropods. Since host specificity and host range depend on successful virus-host interaction during replication which relies on many factors, one factor missing would result in blocking of the replication. Lastly, he concluded that there is a discrepancy between ecological benefits based on high specificity and very narrow host range and commercial value as well as discrepancy between registration expenses and market value. Therefore, further facilitation of registrations for small markets will be needed for the use of baculoviruses in the future.

Niche Uses of Baculoviruses

by Philip Kessler (Andermatt Biocontrol, Grossdietwil, Switzerland) [PPT 5]

First, the presenter explained the basis and biology of baculoviruses in terms of their mode of action- how they cause infection primarily to the host and secondarily from one cell to another within the host. Then, he mentioned that because baculoviruses are only found in insects and have a narrow host range, they are safe for both users and consumers, they do not affect plants, mammals or aquatic organisms, they do not have adverse effects on beneficial insects and do not produce metabolites or toxins. On the other hand, he talked about the challenges of using baculoviruses in terms of virus biology, production (*in vivo*), distributor and end user. Overall, the challenges would be that baculoviruses are labour intensive, time intensive, and difficult to store. After that, the presenter also stated the past and current uses of baculoviruses. The first use of baculoviruses was recorded in 1970s and today, there are more than 50 baculoviruses products with more than 180 registrations worldwide in about 30 countries. There are only 9 main producers of baculovirus products today, and when comparing to other pesticides products, the market is still very small. The presenter also gave 3 examples of challenges of baculovirus products in niche market, which include *Adoxophyes orana* granulovirus (AoGV), *Spodoptera exigua* MNPV and *Phtorimaea operculella* GV. In these examples, the main challenges of baculoviruses products were that the market is too small to be cost effective and that the regulatory hurdle for market entry is too high. In addition, the presenter introduced the Consensus Document on information used in the assessment of environmental applications involving baculoviruses, which is an OECD publication (Series on Harmonization of Regulatory Oversight in Biotechnology, No.20), where it was stated that baculoviruses are safe and do not cause harm to human health and the environment. This document is mainly accepted by the EU and Canada and partly accepted by the US and Australia. In conclusion, the presenter suggested ways to improve the challenges of using baculoviruses products: (1) harmonise dossier formats, (2) harmonise and adjust data requirements, (3) accept available guidance, (4) accept scientific rationales, (5) adjust fees for niche market products, (6) prioritise assessment of low risk products and (7) no re-registration procedures for low-risk products.

Niche Uses of Bacteriophages

by Roma L. Gwynn (Rationale, United Kingdom) [PPT 6]

First, the presenter talked shortly about the bacterial phytopathogens and the economic importance of them as they cause significant damage to large number of crops during cultivation and storage and that they can be difficult to control. Despite the importance of bacterial phytopathogens, there are not that many biocontrol products on the market, whereas there are numerous for fungal diseases. After that, the presenter provided general information on bacteriophages, starting from their biology. Bacteriophages are the most abundant organisms in the world found in a wide range of substrates such as soil, water, plants, and animals. They act as antibacterial agents, with different bacteriophages being specific to different hosts. For almost every bacterial species, at least one bacteriophage exists that can specifically infect that particular bacterial group. In terms of structure, bacteriophages consist of 3 parts: capsid (head), collar and phage tail. Regarding their life cycle, bacteriophages first attach to the cell surface of bacteria, then release DNA into the cell, proliferate into numeral numbers, and hence lead bacteria to burst and die (lytic pathway). There is also the lysogenic pathway but for plant protection the lytic pathway is used. The presenter also mentioned that current taxonomic status for bacteriophages is not clear because it is complex and continually evolving, and thus an alternative classification could be based on morphotype, host genus and pathogenicity. The key aspects for using bacteriophages as a biocontrol product are: (1) high virulence, (2) high specificity to host, (3) rapid mode of action, and (4) short persistence without host. Bacteriophages are mainly used in food of animal origin against human pathogens, whereas their use as plant protection products is currently very limited. In addition, the presenter explained that bacteriophages are considered niche products due to their high specificity, their complex large-scale production and their difficulty to be delivered to target on plants. Lastly, the presenter explained the regulatory aspects related to the biology and ecology, commercialisation and regulatory procedures of bacteriophages that should be taken into consideration. Hence, it was suggested that when a new regulatory framework is developed to address specific issues like in the case of bacteriophages, all the above mentioned aspects should be taken into account.

Two examples of fungal biopesticides that disappeared from the EU market

by Willem Ravensberg (Koppert Biological Systems, Berkel en Rodenrijs, The Netherlands) [PPT 7]

In this presentation, the speaker provided two examples of biopesticides that disappeared from the EU market, he explained the reasons why they disappeared, and gave possible solutions to bring them back to the market again. First, the presenter talked about two bio-insecticides products, which are both based on the entomopathogenic fungus *Verticillium lecanii*. These products were both developed in the 1970's in the UK, the first product targeted whitefly and thrips species, while the second product targeted aphid species. These products were registered for vegetables and ornamentals protection, using one dossier based on the species *Verticillium lecanii* with two different strains. However, during the re-registration process the Board for the Authorisation of Plant Protection Products and Biocides in the Netherlands (Ctgb) refused the joint application and asked for two new dossiers. The problem was that some studies were based on one product, some were based on the other product, and some were based on both species, whereas efficacy was generated per product. Eventually, one of the two applications was withdrawn due to the extra burden in terms of money and time and only one application for one product went through. While the loss of the product in the EU caused serial

reduction of market size in other countries, the need was still there, and the growers are still asking for the second product as it was/is considered the only effective entomopathogen against aphids in many minor (protected) crops. The second example is a fungus, which is used to control American black cherry tree *Prunus serotina*, an invasive weed in Dutch forests. It also had potential for control of other deciduous trees to prevent stump re-sprouting. The product was proved to be very effective as 90% of treated trees die in two-three years. However, since the product has only one target, the market for the product was very small. The product was placed on market as wood rot promotor because its registration as herbicide was considered too expensive. Furthermore, the cost-benefit and Return of Investment (ROI) turned negative, and hence the product was eventually withdrawn from the market too. The solutions suggested so the products can get back to the EU market were: for one of the products containing the fungus *Verticillium lecanii*, to accept the assessment of closely related and similar entomopathogenic strains through read-across, and for the sprouting inhibitor, to accept the product approval from the US and Canada through mutual recognition of data.

Niche Uses of Fungi

by Christina Donat (Bio-Ferm GmbH, Tulln, Austria) [PPT 8]

In this presentation, the speaker explained the niche uses of fungi by giving examples of *Aureobasidium pullulans* strains specifically used against fire blight in pome fruits. First, the presenter introduced the biology of the fungus *Aureobasidium pullulans* and the history of its use as a biocontrol product. In terms of biology, the fungus is an ascomycete with asexual, yeast-like reproducing cells that can be found naturally in different substrates such as soil and plant surfaces. It is also a well adapting organism, being resistant to drought and UV radiation. The two strains of the fungus were first isolated by University of Konstanz in Germany. However, the strains were stored frozen after the end of a governmental funded project. In 1998, the strains were reactivated and a product against fire blight was developed. Six years later in 2004, a company was founded to work on the international product registration and marketing of *A. pullulans* products. Since the company was founded, it has developed and submitted the dossier for product authorisations, registered them and expand their market to more countries. Studies carried out on two products showed that the products are effective and better than chemicals. Nevertheless, the presenter stressed out that the commercialisation of the products is being difficult due to the high cost of development of products and the time frame for product development and registration. Hence, for the products to be commercialised any further, important governmental/industrial support would be needed.

Niche Uses of Invertebrate Biocontrol Agents

by Lieselot van der Veken (Biobest, Westerlo, Belgium) [PPT 9]

In this presentation, the speaker introduced the Invertebrate Biological Control Agents (IBCAs) as plant protection products and explained the niche market of them. IBCAs include beneficial insects, entomopathogenic nematodes and predatory mites. In most cases, IBCAs are highly specific biocontrol products and often restricted to niche uses and currently there is an imbalance between the high registration costs and the market

potential of these products. The need for regulation of IBCAs has been recognised a long time ago in the International Convention of Biodiversity in 1992, where topics on conservation of biological diversity, sustainable use of biological components and access and benefit sharing were discussed. The IBCAs' regulation history goes back to 1996, when FAO published the International Standards for Phytosanitary Measures (revised in 2005), then the European and Mediterranean Plant Protection Organisation (EPPO) published a number of Guidelines and a positive list with IBCAs widely used in the EPPO region. After that, the OECD published Guidance for information requirements for IBCAs and REBECA, an EU Policy Support Action, took place and facilitated the regulation of IBCAs in many countries. The presenter introduced the stepwise Environmental Risk Assessment for IBCAs developed by IBMA, which is useful for a quick scan or comprehensive evaluation. In this assessment, clearly good/bad species are discovered early in the evaluation and thus saving resources and only doubtful species go through evaluation. The status of national regulation in several OECD member countries was also discussed in the presentation. Overall, the bottlenecks in the process of regulating IBCAs are: (1) lack of taxonomic reports, (2) variability in experience with authorities, (3) lack of transparent procedures, (4) lack of a standard application form (single format), and (5) unclearness on host range testing protocols. The presenter emphasised the importance of an interpretation of national biodiversity and the need for an agreement on the positive list, as species do not stop at country borders and hence the term 'national species' is difficult to be defined for IBCAs. Hence, when regulating IBCAs, three things need to be considered: (1) the added value for environmental safety, (2) how to define 'national' species, and (3) the use of cut off criteria to distinguish based on molecular data. Lastly, it was recommended to implement harmonised IBCAs' regulation within an ecological zone context (relevant a/biotic parameters limiting species distribution), use EPPO list as a positive list with safe IBCAs and establish risk categories to be used for the assessment (the safer the category, the lesser assessment required).

Government Experience and Perspectives

The U.S. Approach to the Registration of Highly Specific Biocontrol Products

by Shannon Borges (Environmental Protection Agency, Washington DC, United States) [PPT 10]

In this presentation, the speaker shared the experiences and perspectives of the US Environmental Protection Agency (US EPA) on the registration of highly specific biocontrol products. In the US, pesticides which are classified as biopesticides include both microbials and biochemicals. Some of these biopesticides can be highly specific and, in general, the more targeted the biopesticide for the intended pest, the more targeted the data requirements are. However, the specificity of biopesticides needs to be supported by scientific data. According to the US EPA, the benefits of biopesticides include: (1) fewer risks compared to other types of pesticides, (2) low environmental persistence leading to reduced potential for exposure, (3) decreased use of conventional pesticides, (4) reduced incidence of resistance development, (5) greater flexibility for growers and (6) the ability to address minor crop or certain pest control needs that may not be addressed by conventional pesticides. For these reasons, the Biopesticides and Pollution Prevention Division was created to facilitate the registration of biopesticides and help bring them to the market. The US EPA encourages development and use of low risk biological pesticides as alternatives to conventional pesticides by requiring lower registration fees, delivering shorter registration timelines and setting targeted data requirements. Compared to other pesticide data requirements, the biopesticides have specific tiered data requirement tables, which are different for microbials and biochemicals. To satisfy the data requirements, companies can conduct studies according to the US EPA test guidelines, cite a study from the literature, cite existing data from similar active ingredients/products (with justification and permission where needed) and/or provide a scientific rationale to address the requirement, meaning that many data requirements can often be addressed by means other than conducting a test guideline study. In conclusion, the presenter reemphasised that the US EPA recognises the benefits of biopesticides, including that they generally have a low risk profile and that USA EPA's approach to their regulation aims at facilitating and streamlining their registration by lowering registration fees, shortening time frames, reducing and asking for targeted data requirements, and, lastly, providing pre-registration consultations to focus data needs.

The Ctgb approach to the registration of highly specific biocontrol products

by Jacobijn van Etten (Board for the Authorisation of Plant Protection products and Biocides (Ctgb), Ede, The Netherlands) [PPT 11]

In the beginning, the presenter briefly went through the benefits of biocontrol products, which are: (1) lower toxicity and risk profiles for humans and the environment, (2) fit for

IPM, and (3) contribute to diversity of modes of action. Then, the challenges for placing these products on the market were acknowledged, as biocontrol products target small markets and their development and regulatory costs are relative high. However, since the biocontrol products are highly desirable and they are in line with EU and national policies, consumer wishes and grower needs, the Board for the Authorisation of Plant Protection Products and Biocides (Ctgb) has been working to increase the availability of these products. Three examples of Ctgb experience in niche products were given, including a protective agent based on *Verticillium albo-atrum* to prevent the Dutch elm disease, Mild Pepino Mosaik virus VC1 and VX1, and semiochemicals. During the assessment of these highly specific biocontrol products, the Ctgb learnt to use scientific information related to their mode of action (e.g., some plant viruses have no effect to mammals) and exposure data (e.g., some pheromones that remain behind the background values even after application) and be pragmatic and not ask for unnecessary testing. In addition, the presenter shared the experience from a Dutch project called Green Deal, which was recently finalised. The aim of the project was to stimulate sustainable growth by promoting the collaboration between all stakeholders, to resolve obstacles in the authorisation process and to have more "green" products available for Dutch growers. Some useful results from the various activities in Green Deal were as follow: (1) decision taken on 6 product dossiers and important steps are completed for 2 active substance dossiers, (2) a successful workshop on human toxicology of microorganisms used in plant protecting products was held, (3) a harmonising workshop on efficacy for biopesticides co-organised with EPPO that led to new EPPO Guidance (expected to be published in September 2017) took place and lastly (4) an evaluation manual for biopesticides is ready for publication. From this project, the lessons learnt can be summarised as follows: a pre submission meeting is important to clarify possibilities and difficulties in the registration process; high quality dossiers can support speedy assessment; a specialised "greenTEAM" as assessors can facilitate intake and assessment of the dossier; efficacy assessment should be in line with the nature of the products; and tailor made solutions for dossiers are possible. On the other hand, concerns on EU Regulation (EC) No 1107/2009 regarding placing plant protection products on the market was raised in a sense that the regulation should enable green innovation and that there are large differences in regulatory requirements of biostimulants and low risk products. Finally, as solutions it was suggested to apply 120 days for the evaluation of zonal low risk product dossiers, use different requirements for highly specific biopesticides with low risk profile and enforce non-authorised products.

Summary of Discussions, Ideas and Recommendations for Possible Future Work

Summary

The topic "Niche Uses of Highly Specific Biocontrol Products" was selected based on discussions held in the BPSG that noted that the usage of some biopesticides (e.g., invertebrates, pheromones etc.) can be highly specific to the target and that there would be benefits to clarifying what the requirements should be for their registration. These biocontrol products can be very specific due to their biology and their mode of action. Compared to conventional products their biology can make these biocontrol products very specific. The use of biocontrol products offers many advantages, for example, no or limited impact on beneficial fauna, the environment and/or on human health for operators and consumers. For that reason, biocontrol products can help national and international programmes (e.g., FAO, OECD) support sustainable agriculture. From the presentations and discussions during the seminar, participants clearly noted that: the more specific a product is the less impact it has on the environment; the more specific a product is the greater the expected efficacy on a target; and the more specific a product with complex modes of action, the less chance of resistance development. On the other hand, the more specific a product is the smaller the size of the market, and the more specific a product is the higher the impact of regulatory costs.

Different highly specific biological solutions were presented and the hurdles and issues which must currently be faced were illustrated. Throughout the seminar, the aim was to work towards the delivery of workable solutions to bring highly specific biological plant protection solutions to farmers. However, it is important to recognize that in order to bring such products to the farmer and make agriculture more sustainable, the current regulatory system and how it is applied would need to change.

The following types of biocontrol products were discussed throughout the seminar:

- Semiochemicals: Sex pheromones produced by insects which are almost unique for each species. Their function is to locate a partner for mating. These communication tools have a non-killing mode of action. They are highly volatile and work at very low levels to guide a male to a female.

- Baculoviruses: Highly specific to the insect orders Lepidoptera, Hymenoptera and Diptera; they infect the larval stages of their insect hosts. Most baculoviruses are highly selective for a single or a few closely related insect species. Host specificity and host range are the consequence of a concerted interaction of virus

and host factors which may result in successful virus replication. If this interaction is interrupted, the infection cycle is stopped. Baculoviruses have no potential to be harmful for mammals, including humans.

- Bacteriophage: A virus that infects and replicates within a bacterium. They are highly specific. Lytic phages disrupt the bacterial metabolism and cause the bacterium to lyse. In combination with the use of a cocktail of unrelated phages this form of plant protection is called bacteriophage therapy. Bacteriophage therapy may be a potential solution for antibiotic resistance.

- Fungal biopesticides: Two examples of fungal biopesticides that disappeared from the EU market were presented. For an entomopathogenic fungus, a change in the taxonomy led to a different classification of the strains, and hence an additional regulatory burden which lead to the product being withdrawn from the market. For a product to treat freshly cut stumps the market size was too small to apply for an approval. For another microorganism, all efforts have been made to register the microorganism as an active substance and sell the microbial plant protection products worldwide. However, the balance between the commercial value and regulatory costs is still in question and the company is in a fragile financial situation.

- Invertebrate BioControl Agents (IBCAs): IBCAs are beneficial insects, predatory mites and entomopathogenic nematodes that usually have high host specificity. To evaluate the environmental risk of IBCAs, a 'stepwise risk assessment scheme' has been developed by IBMA:
  - Clearly good or bad species are discovered early in evaluation (saves money and time)
  - Only doubtful species go through the whole evaluation
  - The scheme can be used for a quick scan or comprehensive evaluation

By using this scheme the likelihood and magnitude of each of the risks can be determined.

A harmonised IBCA regulation within an ecological zone context (relevant (a)biotic parameters limiting species distribution) would be welcomed. It is recommended to use the European and Mediterranean Plant Protection Organisation (EPPO) list as a positive list with safe IBCAs.

Regulatory authorities do recognise the benefits of biocontrol products which include, in general, lower toxicity and risk profiles for humans and the environment, lower environmental persistence, greater grower flexibility due to shortened re-entry and pre-harvest intervals, reduced reliance on conventional pesticides, and optional treatments that may reduce resistance development. Because of these benefits, regulatory authorities aim to facilitate the registration of biocontrol products.

Conclusions / Recommendations

A general observation made during the seminar is that in the majority of OECD member countries the procedures for the registration of a biopesticide are mostly the same as for a chemical plant protection product, even if the characteristics of the active substance and the exigencies for the risk assessment differ in many aspects. It was however noted that some of the regulatory authorities already implement measures specific to biocontrol products to facilitate their registration and this should be encouraged.

It was also highlighted that the benefits of biopesticides (i.e., low impact and low risk pest control) could be realised if authorisation processes are simplified. Data requirements can be addressed and justified with sound science and/or long-term experience of safe use. Highly specific biocontrol products can play an important role in IPM strategies and fit within a more holistic approach to agriculture. This is in line with the *OECD Vision on pesticides and sustainable pest management*.

Participants developed a number of recommendations to improve the registration of highly specific biocontrol products which need to be further considered:

- Lower registration fees, shorten registration time frames and prioritise applications for highly specific biocontrol products.
- Organise a pre-registration consultation to get specific advice on data requirements.
- Apply reduced, more targeted data requirements for certain groups of biocontrol products, e.g. Straight Chain Lepidopteran Pheromones (SCLPs) and baculoviruses.
- Consider a notification procedure for these specific groups instead of an approval process for every new SCLP, strain and/or isolate.
- Crop label extensions should be flexible and easier, to adjust to the fast changes of pest presence.
- Micro-organisms are approved at strain level, however, accept read-across for closely related and similar (entomopathogenic) strains.
- Allow a minor use without needing a major use already on the label.
- Instructions for use of these highly specific biocontrol products can be very targeted and detailed as most farmers nowadays can download these instructions on their smartphone.
- Prepare overview documents for certain groups of biopesticides (e.g., baculoviruses, bacteriophages) that are known to have specific properties. For example, baculoviruses are not known to be harmful for humans and due to their specificity have no impact on non-target organisms. Bacteriophages have characteristics quite different from other microorganism based products. Taking into account the safety and benefits of bacteriophages, there is a need to develop relevant, pragmatic and proportional mechanisms for the regulation of bacteriophage as plant protection products.
- Envisage reduced requirements for these highly specific biocontrol products for renewal. For example, is it considered useful to do a scientific peer-reviewed open literature search on the active substance dealing with side-effects on health, the environment and non-target species for an already approved baculovirus?

- Accept for some very specific biocontrol products approval from other countries through mutual recognition (when the product has been authorised under similar agricultural, climatic and environmental conditions).
- Use the European and Mediterranean Plant Protection Organisation (EPPO) list as a positive list with safe Invertebrate BioControl Agents (IBCAs).

Annex 1 – Seminar Programme

The 8th BioPesticides Steering Group

Seminar on "Niche Uses of Highly Specific Biocontrol Products"

Monday 26 June 2017

OECD, Paris, France

2 rue André Pascal, 75016 Paris

Conference Centre

Final Programme

Chair: Jeroen Meeussen, EU Minor Uses Coordination Facility

9.30 – 10.00	**Introduction** • Purpose and structure of the seminar • Tour de table to introduce participants • Presentation on the OECD and the work of OECD-EGBP and general introduction to the seminar on 'Niche Uses of Highly Specific Biocontrol Products' *by Jeroen Meeussen* (EU Minor Uses Coordination Facility)
	Research Institutes' and Stakeholders' Experience and Perspectives
10.00 – 10.25	- Overview of Niche Uses of Highly Specific Biocontrol Products: How to bring solutions to farmers *David Cary* (International Biocontrol Manufacturers Association)
10.25 – 10.50	- Niche Uses of Semiochemicals *Vittorio Veronelli* (CBC Europe, Italy)
10.50 – 11.20	**Coffee break**
11.20 – 11.45	- Molecular factors defining specificity and host range of baculoviruses *Johannes A. Jehle, Jörg T. Wennmann* (Julius Kühn-Institute (JKI), Darmstadt, Germany)
11.45 – 12.10	- Niche Uses of Baculoviruses *Philip Kessler* (Andermatt Biocontrol, Grossdietwil, Switzerland)

12.10 – 12.35	- Niche Uses of Bacteriophages *Roma Gwynn* (Rationale, United Kingdom)
12.35 – 14.00	**Lunch break**
14.00 – 14.25	- Two examples of fungal biopesticides that disappeared from the EU market *Willem Ravensberg* (Koppert Biological Systems, Berkel en Rodenrijs, The Netherlands)
14.25 – 14.50	- Niche Uses of fungi *Christina Donat* (Bio-Ferm GmbH, Tulln, Austria)
14.50 – 15.15	- Niche Uses of Invertebrate biocontrol agents *Lieselot van der Veken* (Biobest, Westerlo, Belgium)
15.15 – 15.45	**Coffee break**
15.45 – 16.10	**Government Experience and Perspectives** - The US approach to the registration of highly specific biocontrol products *Shannon Borges* (Environmental Protection Agency, Washington DC, United States)
16.10 – 16.35	- The Ctgb approach to the registration of highly specific biocontrol products *Jacobijn van Etten* (Board for the Authorisation of Plant Protection products and Biocides (Ctgb), Ede, The Netherlands)
16.35 – 17.00	**Summary of the Discussion, Ideas for Follow-up, Recommendations for possible further OECD work (with reference to the seminar outline)**
17.00	End of the seminar

Annex 2 – List of Participants

Allemagne/Germany	Mr. Herbert KOEPP Department 2: Plant Protection Products Federal Office of Consumer Protection and Food Safety (BVL)
	Dr. Ann-Kristin DIEDERICH Federal Office of Consumer Protection and Food Safety (BVL)
	Dr. Johannes JEHLE Institute for Biological Control Julius Kühn-Institute (JKI)
	Mr. Bilgin KARAOGLAN Section IV 1.3 - Plant Protection Products German Federal Environment Agency (UBA) Ecotoxicology / Environmental Risk Assessment
	Ms. Anne SCHAEFER Federal Institute for Risk Assessment (BfR)
Australie/Australia	Mr. Alan NORDEN Registration Management and Evaluation Australian Pesticides and Veterinary Medicines Authority (APVMA)
Corée/Korea	Dr. Are Sun YOU Rural Development Administration
États-Unis/United States	Ms. Shannon BORGES Biopesticides and Pollution Prevention Division U.S. Environmental Protection Agency
France	Dr. Chantal ARAR ANSES, DEPR
Japon/Japan	Dr. Hidetaka KOBAYASHI Plant Products Safety Division, Food Safety and Consumer Affairs Bureau Ministry of Agriculture, Forestry and Fisheries
	Mr. Tatsuya FUJII

	Plant Protection Division, Food Safety and Consumer Affairs Bureau Ministry of Agriculture Forestry and Fisheries
Pays-Bas/Netherlands	Ms. Marloes BUSSCHERS Board for Authorisation of Plant Protection Products and Biocides (Ctbg)
	Ms. Jacobijn VAN ETTEN Board for the Authorisation of Plant Protection Products and Biocides (Ctgb)
Royaume-Uni/United Kingdom	Mr. John DALE Chemicals Regulation Directorate Health and Safety Executive
Suède/Sweden	Ms. Camilla WANG Swedish Chemicals Agency (KEMI)
Suisse/Switzerland	Mr. Min HAHN Biotechnology Section Federal Office for the Environment FOEN
	Dr. Chantal PLANCHAMP Office fédéral de l'environnement (OFEV)
UE/EU	Ms. Flora LIMACHE DG ENV European Commission
	Mr. Jeroen MEEUSSEN European Union Minor Uses Coordination Facility
	Mr. Jérémy PINTE Directorate-General for Health and Food Safety European Commission
Costa Rica	Mr. Roger RUIZ ZAPATA State Phytosanitary Service Ministry of Agriculture and Livestock
République populaire de Chine/People's Republic of China	Ms. Mengmeng QU International Cooperation Division Institute for the Control of Agrochemicals, Ministry of Agriculture (ICAMA)
Comité consultatif économique et industriel (BIAC)/Business and Industry Advisory Committee (BIAC)	Ms. Robyn KNEEN Regulatory Affairs Biologics Bayer US LLC

	Ms. Denise MUNDAY EMEA SCAE - Valent BioSciences
International Biocontrol Manufacturers Association	Mr. David CARY International Biocontrol Manufacturers' Association
	Ms. Adi CORNELESE GAB Consulting GmbH
	Ms. Rosa CRIOLLO Regulatory Affairs Biocontrol Knoell Consult GmbH
	Dr. Christina DONAT International Biocontrol Manufacturers Association
	Dr. Roma GWYNN Rationale Biopesticide Consultants
	Mr. Evert HAMBLOK Koppert Biological Systems
	Mr. Ulf HEILIG International Biocontrol Manufacturers Association (IBMA)
	Dr. Philip KESSLER Andermatt Biocontrol AG
	Ms. Alessandra MOCCIA Suterra Europe Biocontrol S.L.
	Dr. Willem RAVENSBERG International Biocontrol Manufacturers Association
	Dr. Lieselot VAN DER VEKEN Biobest NV
	Mr. Vittorio VERONELLI CBC (Europe) Srl
IDRG	Dr. Imme GERKE IDRG
OCDE/OECD	Ms. Ye Lin JUN
	Ms. Christiana OLADINI-JAMES
	Ms. Magdalini SACHANA

Mr. Richard SIGMAN

Annex 3 – Abstracts for Presentations

The OECD and the work of OECD-EGBP and general introduction to the seminar on 'Niche Uses of Highly Specific Biocontrol Products'

by the EGBP Seminar Chair, Jeroen Meeussen, European Union Minor Uses Coordination Facility [PPT 1]

In 1961, the Organisation for Economic Co-operation and Development (OECD) was established with a trans-Atlantic and then global reach. Today the OECD has 35 member countries. More than 70 developing and transition economies are engaged in working relationships with the OECD.

OECD is a forum in which governments work together to address the economic, social and environmental challenges of interdependence and globalisation. OECD is also a provider of comparative data, analysis and forecasts to underpin multilateral co-operation.

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.

The Expert Group on BioPesticides (EGBP), previously called 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 first tasks of the EGBP consisted of:

(i) reviewing regulatory data requirements for three categories of biopesticides (microbials, pheromones and invertebrates); and

(ii) developing formats for dossiers and monographs for microbials, and pheromones and other semio-chemicals.

This was achieved in 2004 and resulted in several OECD-publications in the Series of Pesticides (No. 12, 2001; No. 18, 2003 and No. 21, 2004).

The EGBP then decided to concentrate its efforts on science issues that remain as barriers to harmonisation and work-sharing. 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 has been published in OECD Series on Pesticides No. 43, 2008.

The report of the Workshop on the Regulation of Biopesticides: Registration and Communication issues, 15 – 17 April 2008, EPA, Arlington, USA, is another publication in the OECD Series on Pesticides (No. 44, 2009). This was followed by publications of an "Issue Paper on Microbial Contaminant Limits for Microbial Pest Control Products" (OECD Series on Pesticides No. 65, 2011) and

a "Guidance to the Environmental Safety Evaluation of Microbial Biocontrol" (OECD Series on Pesticides No. 67, 2012).

More recently the following documents were published:

- Guidance Document: Outline on Pre-Submission Consultations For Microbial Pest Control Products (OECD Series on Pesticides No.81, 2016);
- Report of a Survey on Regulatory and Testing Issues for the Sensitisation Potential of Micro-Organisms: Survey Results (2014) (OECD Series on Pesticides No. 84, 2016);
- Guidance Document on Storage Stability of Microbial Pest Control Products (OECD Series on Pesticides No. 85, 2016);
- Report of a Survey on the Need for Further Guidance on Data Requirements and Updated Test Guidelines to Support the Assessment of Microbial Pesticides (OECD Series on Pesticides No. 87, 2017);
- Guidance Document on Botanical Active Substances Used in Plant Protection Products (OECD Series on Pesticides No. 90, 2017).
- From 2009 onwards the EGBP started to organise seminars which focus on key issues on biopesticides of interest to OECD governments. Until now the following seminars have been held:
- Seminar on Identity and Characterisation of micro-organisms, OECD Series on Pesticides No. 53, 2010;
- Seminar on The fate in the environment of microbial control agents and their effect on non-target organisms, OECD Series on Pesticides No. 64, 2011;
- Seminar on Characterisation and Analyses of Botanicals for the use in Plant protection Products, OECD Series on Pesticides No. 72, 2012;
- Seminar on: Trichoderma spp. for the use in Plant Protection Products: similarities and differences, OECD Series on Pesticides No. 74, 2013;
- Seminar on: Application Techniques for Microbial Pest Control Products and Semiochemicals: Use Scenarios and Associated Risks, OECD Series on Pesticides No. 80, 2015;
- Seminar on: Hazard and Risk Assessment of Secondary Metabolites produced by Microbial Pesticides, OECD Series on Pesticides No. 89, 2017;
- Seminar on: Sensitisation Potential of Micro-organisms, OECD Series on Pesticides No. 91, 2017.

A joint OECD/KemI/EU Workshop on “Microbial Pesticides: Assessment and Management of Risks” took place between the 17th and 19th of June 2013 in Saltsjöbaden, Sweden. The workshop aimed at addressing issues around both agricultural and non-agricultural microbial pesticides and their assessment from a scientific, technical and regulatory perspective. The report of this workshop is published in the OECD Series on Pesticides No 76, 2014.

Overview of Niche Uses of Highly Specific Biocontrol Products: How to bring solutions to farmers

by David Cary (International Biocontrol Manufacturers Association) [PPT 2]

Global legislative initiatives are increasingly directed towards encouraging, facilitating and providing the framework for a transition of practices in crop protection from chemical pesticide intensive systems to more holistic biologically based Integrated Pest Management (IPM) models. There are several drivers behind this move, including lower human health risks for operators and consumers, less environmental impact and a desirability of using sustainable systems that require small corrections as a result of an imbalance rather than using massive corrective measures likely to create a further imbalance.

In order to accomplish this task many varied solutions are needed by farmers and can be made available by the biocontrol industry. There is however a dilemma that the tools with arguably the safest risk profile for both human health and the environment may not be made available by the biocontrol industry because they are indeed too specific to justify the high costs related to their placing on the market. A means for permitting and facilitating these tools to become available must be found for the benefit of farmers and consumers alike.

What biological tools are we referring to? Examples of such tools can come from very disparate groups of biocontrol products (e.g. semiochemicals, baculoviruses, invertebrate biocontrol agents).

Often the very niche markets that would benefit see the broad spectrum older chemistry as the only available solutions because the markets have proved equally unattractive and uneconomic to the more targeted conventional chemical solutions. To encourage and facilitate the niche use of highly specific biological plant protection products there is an onus on all stakeholders, including industry, regional and national policymakers and competent authorities to discuss and arrive at workable regulatory solutions to enable the safest of tools to be used by our farmers to deliver even safer food whilst having the lowest impact on the environment and the health of farmers and consumers. The comparison can be easily drawn with human or animal surgery where we have moved where possible from invasive open surgery to keyhole operations with less impact on the patient and resulting in less hospital time, quicker recovery times and less impact on society through loss of time at work. The agricultural parallel is currently only blocked by our inability to devise regulatory systems to facilitate adoption on a broader scale of niche market solutions

Niche Uses of Semiochemicals

by Vittorio Veronelli (CBC Europe, Italy) [PPT 3]

Semiochemicals sex pheromones produced by insects are almost unique for each species and function to locate a partner for mating. These communication tools have non-killing mode of action between adult individuals of insect species and no relation with crops, as pests have typically several host plants, but few or some of them are agriculture crops. They are highly volatile and work at very low amounts to accomplish the function of guiding the male to a female.

More than 8.000 semiochemicals are currently identified, the large majority are straight chain lepidopteran pheromones (SCLP). Roughly 200 are produced either in large or very small scale, mostly for monitoring traps and about 50 of them are available at Kg level for mating disruption use. However, not more than 20 are applied worldwide and just 5 covers 80% of world uses in fruits, vines and forestry. About 150 SCLP formulations are currently registered between US and EU, but 40% of these are just for one pest and one crop (Codling moth in pome fruits).

The adoption of pheromones for pest control is currently exceeding a million of hectares worldwide, which is the evidence of the consistent performances of this tool. More contribution to low impact and low risk pest control could be available if authorisation process is simplified.

In pheromones crop relevance is little, as mode of action is interference to adult mating, but pest are typically polyphagous and can adjust to a variety of plants. No phytotox (for passive dispensers) and no residues in any case are expected. Crop label extensions should be flexible and easier, to adjust to the fast changes of pest presence. Each crop status is different country by country and some of them can be minor or very minor. Authorisation process and fees do not take this factor into account. When a product is registered and widely applied in a Country it should be facilitated in another especially if the border is practically just administrative like in Europe. Pests are moving fast and across borders, mating disruptors already registered in other Countries in the world can help preventing the pest expansion quickly if Regulation would support fast adoption.

Molecular factors defining specificity and host range of baculoviruses

by Johannes A. Jehle, Jörg T. Wennmann (Julius Kühn-Institute (JKI), Darmstadt, Germany) [PPT 4]

Baculoviruses are dsDNA viruses, which are highly specific to the insect orders Lepidoptera, Hymenoptera and Diptera; they infect the larval stages of their insect hosts. So far, more than 700 different baculoviruses have been isolated from different insect species, many of them are highly selective for single or few, closely related insect species. Host specificity and host range are the consequence of a concerted interaction of virus and host factors which may result in successful virus replication. If this interaction is interrupted, the infection cycle is stopped. Abortion of virus infection can occur during release of infective virions from viral occlusion body, virion entry into the midgut, transcription and DNA replication, virus replication and spread of infection. The infection process of baculoviruses is very well studied. Several viral genetic factors, such as peroral infection factors, inhibitors of apoptosis, RNA and DNA polymerase functions and others are crucial for a successful infection process. The presentation will provide an overview on the current knowledge of the infection process and viral factors defining the specificity and host range of baculoviruses.

Niche Uses of Baculoviruses

by Philip Kessler (Andermatt Biocontrol, Grossdietwil, Switzerland) [PPT 5]

One characteristic of many biopesticides is their narrow host range. Particularly baculoviruses are characterised by a narrow host range, including only one single or few closely related insect species. This represents a lot of advantages, e.g., protecting the beneficial fauna, or harmlessness towards human health, but it significantly reduces the potential market size for such products. The procedures for the registration of a biopesticide are mostly the same as for a chemical plant protection product, even if the characteristics of the active substance and the exigencies for the risk assessment differ in many aspects. Despite of available guidance from OECD and well documented safe use of baculoviruses for insect pest control since more than 40 years, the costs to fulfil existing requirements for registration dossiers as well as the cost for fees and the registration timelines are out of scale. It is impossible for the industry to make the development of biopesticides for small-sized markets cost-effective. The registration of niche products based on baculoviruses in the European Union such as Adoxophyes orana granulovirus (AoGV), or Spodoptera exigua nucleopolyhedrovirus (SeMNPV) were too long and too expensive before these products became cost-effective. Consequently, very effective and economic friendly solutions might disappear again from the market due to unbearable investment in periodic re-registration processes. New baculovirus products against significant pest insect such as tomato leaf miner, cut worms, or light brown apple moth might never be developed and commercialised, due to the high

investments in niche markets. Harmonisation and adaptation of registration requirements and procedures are urgently needed. Registration fees need to adapted considering that many microbial products such as baculoviruses are niche market products.

Niche Uses of Bacteriophages

by Roma L Gwynn (Rationale, United Kingdom) [PPT 6]

Bacterial diseases cause significant economic crop losses across a wide range of crops in cultivation and in storage. 85% of plant diseases are cause by fungi and the rest are mainly bacterial phytopathogens of which there are 38 species (approximately). However, of the 455 biological control product available for plant disease control globally only 12 products claim some effectiveness against bacterial diseases and of these, most are general disease claims not specific to a bacterial species. Therefore, there is a need for more biopesticide-based plant protection products for bacterial plant diseases.

Bacteriophages are bacterial viruses which are well known and documented to be highly specific organisms that infect and kill bacteria. In nature, they are the most abundant self-replicating organisms, present in significant numbers in water sources, on food and as normal commensals of humans and animals. Humans and animals naturally ingest large numbers of bacteriophage. Bacteriophages only infect bacteria and consequently, they cannot be considered as direct pathogens for humans, animals or plants.

Bacteriophage have been developed for use in the high value food technology area where they have been granted Generally Recognised as Safe (GRAS) status in the USA and their use approved for a number of food processing and packing industries. There is currently one product developed for use in agriculture and approved in Canada and USA: Bacteriophage of Clavibacter michiganensis (subsp. michiganensis) in tomato.

Due to their host specificity bacteriophages can be considered to have a low risk profile for humans and the environment. However, this specificity to the host bacteria, even to strain level can make commercialisation difficult. Potential commercial products need to be mixtures of strains, often tailored to the bacterial plant disease by geographical area. Large-scale production requires them to be produced on the host bacterial plant pathogen which is often not amenable to consistent in vitro cultivation. After which, the host bacteria need to be removed from the active substance, usually by a costly filtration method. Therefore, while there is a high demand for bacterial plant protection products, commercialisation of bacteriophages is for niche uses, it is complex and costly.

It is anticipated that bacteriophage-based plant protection products would be considered microbial biopesticides. Bacteriophage, however, have characteristics quite different from other microorganism based products. Taking into account the safety and benefits of bacteriophage, there is a need to develop relevant, pragmatic and proportional mechanisms for the regulation of bacteriophage as plant protection products.

Two examples of fungal biopesticides that disappeared from the EU market

by Willem Ravensberg (Koppert Biological Systems, Berkel en Rodenrijs, The Netherlands) [PPT 7]

Two bio-insecticides based on the entomopathogenic fungus *Verticillium lecanii*, the strain Ve2 – can be used for control of aphids, the strain Ve6 – is for control of whitefly and thrips. Both products are

mainly for use in protected vegetables and ornamentals. They were developed in the 1970's in the UK at the Glasshouse Crops Research Institute and Tate and Lyle started to manufacture them, from 1985 on Koppert took over. The product with the Ve2 strain was registered in the UK in 1979, the product with the Ve6 strain followed in 1981, the products were registered based on one dossier of Mycotal and Vertalec, derived from the species *Verticillium lecanii* and the two strains. Some studies were based on Ve6, some on Ve2, some on both, efficacy was generated per product, and applications were made per product. The product with the Ve2 strain was approved in the UK, North Ireland, Finland, Denmark, Switzerland, Norway and Japan; the product with the Ve6 strain in the UK, North Ireland, Netherlands, Finland, Denmark, Greece, Italy, Austria, Switzerland, Turkey, Kenya, New Zealand and Japan.

Registration in the EU was then required through application for approval within EG 91/414 and List 4 procedure (Reg. 112/2002), the Netherlands was the Reference Member State (RMS), and one dossier was submitted for both strains and both products. In the meantime the taxonomy had changed and the strains were now classified as follows: the *Verticillium lecanii* Ve6 strain had become *Lecanicillium muscarium*, and the *Verticillium lecanii* Ve2 strain, *Lecanicillium longisporum*. The Ctgb refused the joint application and required two new dossiers. Koppert withdrew the application for the product with the Ve2 strain, and continued with the product with the Ve6 strain only, due to extra burden in terms of money and time.

Chondrostereum purpureum is a fungus causing wood rot through wounds in trees and shrubs: silverleaf and is considered sometimes as a disease in apple, pear. *Chondrostereum purpureum* was used to control American black cherry tree, *Prunus serotina*, an invasive weed in Dutch forests. It also had potential for control of other deciduous trees, to prevent stump re-sprouting. It was developed through over 10 years of research in Wageningen UR, the Dutch Forestry Department, and Koppert. Application was by brushing mycelial suspension on freshly cut stumps. The formulation was freshly delivered product on demand. The results were good, treated trees (90%) died in a two-three years. The market of the product containing *Chondrostereum purpureum* was very small, only uses in the Netherlands and Germany with the only target *Prunus serotine*, in nature reserves, and treatments were partly subsidised. The product was placed on market as wood rot promotor because registration as herbicide was considered too expensive. The Ctgb required an official approval and therefore the product was withdrawn.

Suggested solutions for approval of the products with the *Verticillium lecanii* Ve2 strain and *Chondrostereum purpureum* as niche products could be:

- the products with the *Verticillium lecanii* Ve2 strain: accept closely related and similar entomopathogenic strains through read-across
- Sprouting inhibitor: accept sprouting inhibitor product approval from USA and Canada through mutual recognition

Niche Uses of Fungi

by Christina Donat (Bio-Ferm GmbH, Tulln, Austria) [PPT 8]

Long time ago there were two strains of Aureobasidium pullulans. They were isolated in the orchard of a monastery by a young PhD student in a research project at the University of Konstanz in Germany (1989). After the end of the governmental funded project they were put into sleep in a - 80°C storage. In 1998, the strains were reactivated by Stefan Kunz, and a product against fire blight was developed. In 2004, a company was founded as a future investment of a larger group of enterprises. Since then all efforts were made to register the microorganism as active substances not only against fire blight and sell the microbial plant protection products worldwide. However, the commercial value is still in question.

Niche Uses of Invertebrate Biocontrol Agents

by Lieselot van der Veken (Biobest, Westerlo, Belgium) [PPT 9]

{abstract not available}

The U.S. Approach to the Registration of Highly Specific Biocontrol Products

by Shannon Borges (Environmental Protection Agency, Washington DC, United States) [PPT 10]

In the U.S., pesticides classified as biopesticides include both microbials and biochemicals. These biopesticides can have broad uses, or they may be highly specific for their target pest and more limited in their scope of use. This quality is among several benefits of biopesticides that are recognised by the U.S. EPA, which also include lower toxicity and risk profiles for humans and the environment, lower environmental persistence, greater grower flexibility due to shortened re-entry and pre-harvest intervals, reduced reliance on conventional pesticides, and optional treatments that may reduce resistance development. Because of these benefits, the U.S. EPA recognises the need for such products, and utilises an approach to regulation to facilitate their entry into the marketplace. The U.S. EPA encourages biopesticide registration by requiring lower registration fees and shorter registration time frames compared to conventional pesticides, as well as a more targeted set of data to support registration. While the U.S. EPA recognises the advantages to biopesticides, they are still subject to the same legal standards as other pesticides; low risk must be demonstrated by applicant/registrant companies. To aid in understanding the registration process and how these standards can be met, the Biopesticides and Pollution Prevention Division encourages discussions with companies prior to registration to clarify EPA's expectations regarding fees and deadlines and to ensure that data requirements best fit the needs of risk assessment. These efforts, along with the approach described above, streamline the process of registration for biopesticides.

The Ctgb approach to the registration of highly specific biocontrol products

by Jacobijn van Etten (Board for the Authorisation of Plant Protection products and Biocides (Ctgb), Ede, The Netherlands) [PPT 11]

{abstract not available}

Annex 4 – Slides of Speakers' Plenary Presentations

Please refer to the separate publication for full Annex 4

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[PPT 1] Presentation on the OECD and the work of OECD-EGBP and general introduction to the seminar on 'Niche Uses of Highly Specific Biocontrol Products'
Jeroen Meeussen (EU Minor Uses Coordination Facility)

[PPT 2] Overview of Niche Uses of Highly Specific Biocontrol Products: How to bring solutions to farmers
David Cary (International Biocontrol Manufacturers Association)

[PPT 3] Niche Uses of Semiochemicals
Vittorio Veronelli (CBC Europe, Italy)

[PPT 4] Molecular factors defining specificity and host range of baculoviruses
Johannes A. Jehle, Jörg T. Wennmann (Julius Kühn-Institute (JKI), Darmstadt, Germany)

[PPT 5] Niche Uses of Baculoviruses
Philip Kessler (Andermatt Biocontrol, Grossdietwil, Switzerland)

[PPT 6] Niche Uses of Bacteriophages
Roma Gwynn (Rationale, United Kingdom)

[PPT 7] Two examples of fungal biopesticides that disappeared from the EU market
Willem Ravensberg (Koppert Biological Systems, Berkel en Rodenrijs, The Netherlands)

[PPT 8] Niche Uses of fungi
Christina Donat (Bio-Ferm GmbH, Tulln, Austria)

[PPT 9] Niche Uses of Invertebrate biocontrol agents
Lieselot van der Veken (Biobest, Westerlo, Belgium)

[PPT 10] The US approach to the registration of highly specific biocontrol products
Shannon Borges (Environmental Protection Agency, Washington DC, United States)

[PPT 11] The Ctgb approach to the registration of highly specific biocontrol products
Jacobijn van Etten (Board for the Authorisation of Plant Protection products and Biocides (Ctgb), Ede, The Netherlands)