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

**Annex to the Report of the 8th Biopesticides Steering Group Seminar on Niche Uses
of Highly Specific Biocontrol Products**

**Series on Pesticides
No. 95**

Dr. Magdalini SACHANA
Tel: +33 (0) 1 85 55 64 23; Email: magdalini.sachana@oecd.org

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Annex 4 – Slides of Speakers' Plenary Presentations

[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'

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[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

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[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)

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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)

Presentation 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)



**SEMINAR ON “NICHE USES OF
HIGHLY SPECIFIC BIOCONTROL
PRODUCTS”**

26 June 2017, OECD, Paris
OECD Expert Group on BioPesticides

Jeroen Meeussen
 Chair of the OECD Expert Group on Biopesticides




My Background



- ▶ Untill October 2010: Ctgb
- ▶ October 2010 – July 2015: DG Sante
- ▶ Since September 2015: EUMUCF
- ▶ Since 2005: Chair of the EGBP

ctgb





- **A few words about OECD**
- OECD Work on (Bio)Pesticides
- Today's seminar: purpose, scope and structure



**OECD: The Organisation for Economic
Co-operation and Development**



OECD

- Started after **World War II**
- Transformed in **1961** into the Organization for Economic Co-operation and Development with 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 (Brazil, Russia, India, China and South Africa)

OECD – What is OECD?

A forum in which governments work together to:

- Co-ordinate and harmonise **policies**;
- Discuss issues of **mutual concern**;
- Work together to respond to **international problems**.

A provider of **comparative statistics** and **economic and social data** with more than 250 publications per year.



OECD – How do pesticides fit in all this?

One of the fields in which OECD is actively involved is the **sustainability of agriculture**.



OECD-WGP (Working Group on Pesticides)

The OECD work on **agricultural 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**;
- **reduce risks** to human health and the environment.





- A few words about OECD
- **OECD Work on (Bio)Pesticides**
- Today's seminar: purpose, scope and structure



- The **BioPesticides Steering Group** (BPSG) was established by the WGP in 1999 to help member countries to **harmonise** the methods and approaches used to **assess biological pesticides**.
- New name: **Expert Group on BioPesticides (EGBP)**.





Biological Pesticides:

- Macro-organisms
- Microbial pesticides
- Semiochemicals
- Plant extracts/Botanicals




The first tasks of the BPSG consisted of:

- reviewing regulatory **data requirements** for three categories of biopesticides;
- developing **formats for dossiers and monographs** for microbials, and pheromones and other semio-chemicals.



OECD-Publications (I)

Registration requirements:

- for **pheromones** (Series on Pesticides, No. 12, 2001)  **under revision**
- for **microbial pesticides** (Series on Pesticides, No. 18, 2003)
- for **invertebrate biocontrol agents/IBCA**s (Series on Pesticides, No. 21, 2004)

OECD-EGBP

The EGBP then decided to concentrate its efforts on **science issues** that remain as barriers to harmonisation and work-sharing.



OECD-Publications (II)


- Working Document on the **Evaluation of Microbials** for Pest Control (Series on Pesticides No. 43, 2008)

This document is essentially a set of examples/case studies aimed at helping the regulatory authorities to deal with these issues in the safety assessment of microbial pesticides.




OECD-Publications (III)

- Issue Paper on **Microbial Contaminant Limits** for Microbial Pest Control Products (Series on Pesticides No. 65, 2011)
- Guidance to the **Environmental Safety Evaluation** of Microbial Biocontrol Agents (Series on Pesticides No. 67, 2012)
- Guidance Document: Outline on **Pre-Submission Consultations** for Microbial Pest Control Products




OECD-Publications (IV)

- 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)
- 



OECD-Publications (V)

- Guidance Document on **Botanical Active Substances** Used in Plant Protection Products (OECD Series on Pesticides No. 90, 2017)
 - Guidance Document on **Semiochemical Active Substances and Plant Protection Products** (DRAFT)
 - Guidance document for the assessment of the **equivalence of technical grade active ingredients** for identical microbial strains and isolates (DRAFT)
- 

Workplan 2013-2016 and 2017-2020

- Promote **communication** and **exchange of information** among regulatory authorities of participating countries
- Organise **seminars** and **workshops** on topics of common interest



OECD-Seminars (I)

1. Report of Seminar on "**Identity and Characterisation of micro-organisms**", OECD Series on Pesticides No. 53, 2010)
2. Report of 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)
3. Report of Seminar on "**Characterisation and Analyses of Botanicals for the use in Plant protection Products**", OECD Series on Pesticides No. 72, 2012)

OECD-Seminars (II)

4. Report on Seminar on “*Trichoderma* spp. for the use in Plant Protection Products: similarities and differences” (OECD Series on Pesticides No. 74, 2013)
5. Report of Seminar on “Application Techniques for Microbial Pest Control Products and Semiochemicals: Use Scenarios and Associated Risks”, (OECD Series on Pesticides No. 80, 2015)
6. Report of Seminar on “Hazard and Risk Assessment of Secondary Metabolites produced by Microbial Pesticides”, (OECD Series on Pesticides No. 89, 2017)
7. Report of Seminar on: “Sensitisation Potential of Micro-organisms”, (OECD Series on Pesticides No. 91, 2017)

OECD-BPSG workshops

- Workshop on the Regulation of Biopesticides: **Registration and Communication Issues**; 15-17 April 2008, EPA, Arlington, USA
- Workshop on Microbial Pesticides: **Risk Assessment and Risk Management**; 17-19 June 2013, Saltsjöbaden, Sweden






- A few words about OECD
- OECD Work on (Bio)Pesticides
- **Today's seminar: purpose, scope and structure**



Seminar on Niche Uses of Highly Specific Biocontrol Products

The topic "Niche Uses of Highly Specific Biocontrol Products" was selected based on the discussions that the usage of some invertebrates and pheromones can be **highly specific** and that it should be clarified what the **requirements should be for their registration**.

Focus of the seminar is to **present highly specific biological solutions** and to **illustrate the hurdles** and issues which must currently be faced, as well as to work towards the delivery of **workable solutions** to bring highly specific biological plant protection **solutions to farmers**.



Seminar - Scope

Discussion on:

- 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 **smaller the size of the market**, but the **higher the impact of 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 IPM programmes**.

Seminar - Structure

Presentations focussed on:

- **government, research and stakeholder** experience and perspectives,
- followed by **discussion** after each set of presentations.



Seminar - Results

With the focus on “niche uses of highly specific biocontrol products”, the goals of this seminar are

1. for participants to **promote a dialogue**, and
2. to initiate a process to make **recommendations** for improvements to the **registration of highly specific biocontrol products**.



Seminar on Niche Uses of Highly Specific Biocontrol Products



**I wish you an interesting and
useful seminar!**

Presentation 2

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

David Cary (International Biocontrol Manufacturers Association)



**An overview of
Niche Uses of
Highly Specific
Biocontrol
Products: How to
bring solutions to
farmers**

David Cary Executive Director IBMA



Greening policies

- FAO
 - Sustainable Development Goals
 - 5 Principles of Sustainable Food and Agriculture
- OECD
 - Green Growth and Sustainable Development
 - Sustainable Agriculture
- China
 - China's No.1 Central Document
- USA
 - Green Chemistry Awards
 - Better for the Environment
- EU
 - Sustainable Uses Directive
 - EU Sustainable Agriculture Group 40 point implementation plan



What is wrong with the current agricultural system?

Surface look

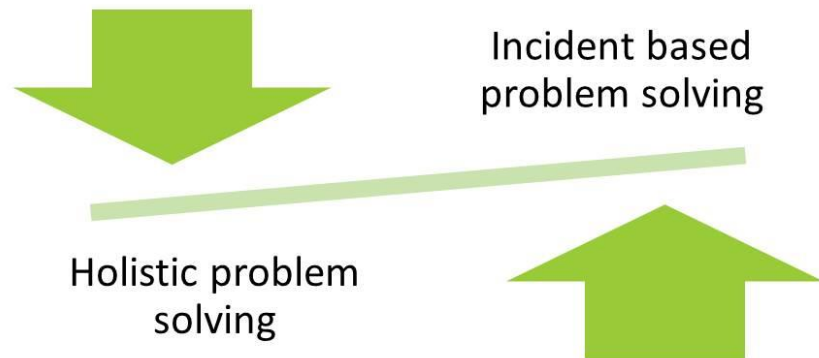
- Plentiful food since 1st green revolution
- Good quality food
- More reliability of production
- Cheap food
- Plentiful choice of food

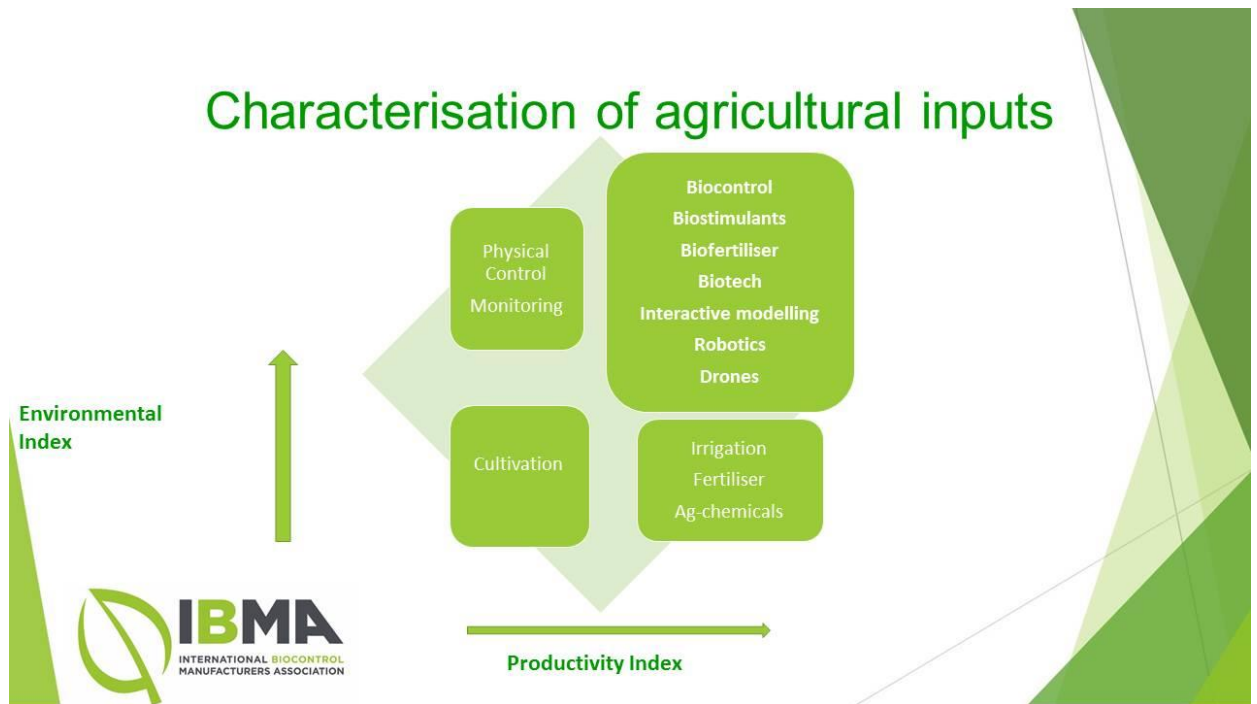
In depth look

- Resistance development
- Increase of invasive pests and diseases
- Pendulum of pest and disease occurrence
- Imposed produce quality standards
- Direct costs only accounted for
- Loss of PPPs due to multifactorial issues
- Failure to accommodate new PPP solutions



Problem solving needs to change





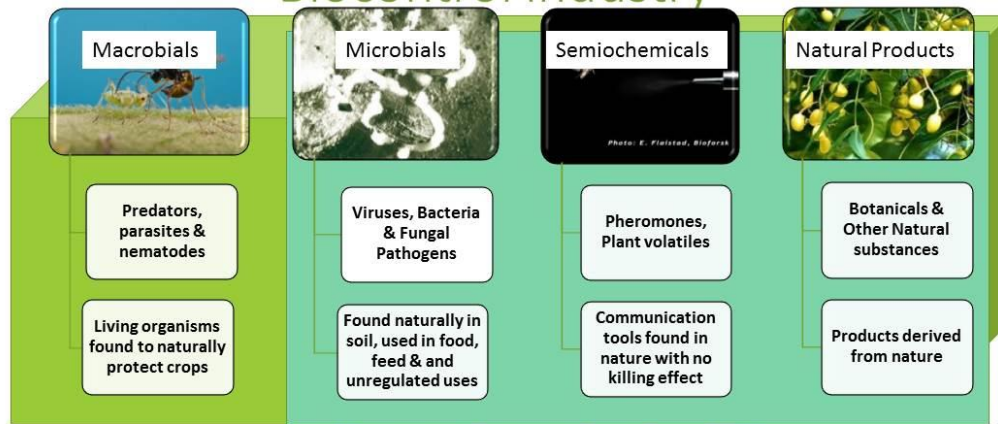
Why do niche products need to be treated differently?

- Cost of developing and registering traditional PPPs was estimated at \$286M* in 2014
- Time to market for traditional PPPs in 2014 was 11.3 years*
- It is no wonder the number of R&D companies producing PPPs is now reduced from 15 pre 2000 to the top 6 companies having >75% market share in 2005 and by end of 2017 2 of those will have merged leaving 4
- PPPs have had to be blockbusters or silver bullets for economic prudence as they are only viable on the big crops in the big markets
- Highly specific tools and tools for niche markets often produced by SMEs cannot come to the market using this model forced on us by regulation and the resultant structure of the Agchem market



* Phillips McDougall Agri Futura Magazine April 2016 No. 198

The products: “innovative green tools” of the Biocontrol industry



Not usually regulated as PPPs

Regulated as PPPs

All groups can have niche solutions

Specificity

- What do we mean by specificity
 - Species specific products
 - Pheromones
 - Baculoviruses
 - Weak strains of host specific viruses
 - Invertebrate Biocontrols, Specific uses, Bacteriophages, etc..



Unique attributes

- Activity on non-target species
- Corrective technologies without impacting other control mechanisms
- A part of agroecology
- Often without major uses



Who can/need to help with the issue

- Policymakers
- Regulators
- Researchers
- Industry
- Farmers
- Food value chain



What are possible solutions

- Global or regional positive list
 - EPPO list for IBCAs
 - FAO list of MBCAs
 - EU 2003/2003 proposed list of microbial biostimulants
- No renewal requirement
- Notification only procedure for a.s. ie EU and SCLPs
- No requirement for product authorisations or a single regional product authorisation
- Ability to allow a minor use without needing a major use
- Concurrent a.s approval and a regional product authorisation in a single step
- Think outside the box!!!



Engagement during the seminar

- Understand the type of products that have already been lost
- Understand what solutions are available
- Understand the specificity / niche markets
- Understand that if we are to bring such products to the farmer and make agriculture more sustainable - the system and how we apply it has to change
- Understand if we don't apply a system designed for these specific solutions that in the main they will not be available and they are arguably because of the specificity the most sustainable tools we could use
- Think of ways we can work together to solve this common issue



Holistic Agriculture



- Prevention of pest & disease explosion
- Use of all available tools
- Minimise risk to human health and the environment

Only through use of true IPM

A new true green revolution




***Thank you for attending now
is time for us all to actively
participate in this seminar
and only then can we solve
our dilemma together***



Presentation 3

Niche Uses of Semiochemicals

Vittorio Veronelli (CBC Europe, Italy)





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Niche uses of semiochemicals

OECD - 8th BioPesticidesExpert Group


Vittorio Veronelli - Paris 26th March 2017

Semiochemicals... a long work

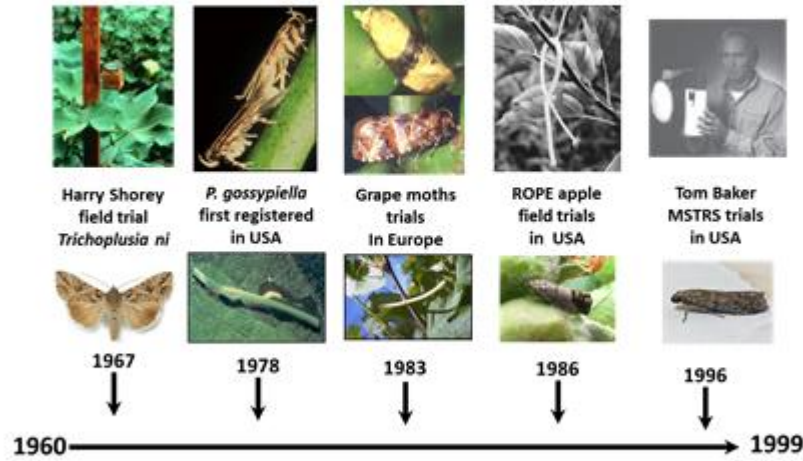
Year	Scientist(s)	Key Contribution
1879	Jean-Henry Fabre	first records insect chemical communication
1940	Bruno Götz	hypothesis on Mating Disruption of Grape moths
1959	Adolf Butenandt	identifies Bombykol From <i>B. mori</i>
1959	P. Karlson & M. Luscher	Suggested Pheromone
1960	Morton Beroza	Suggested Mating Disruption
1967	Harry Shorey	conducts first MD field trial (<i>T. ni</i>)

1870s — 1930 ————— 1990





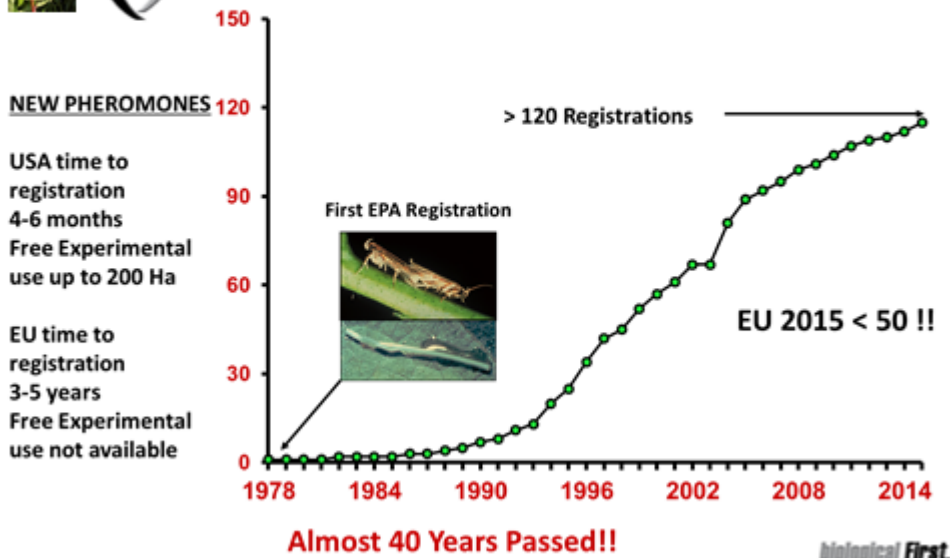
Semiochemicals an established technology



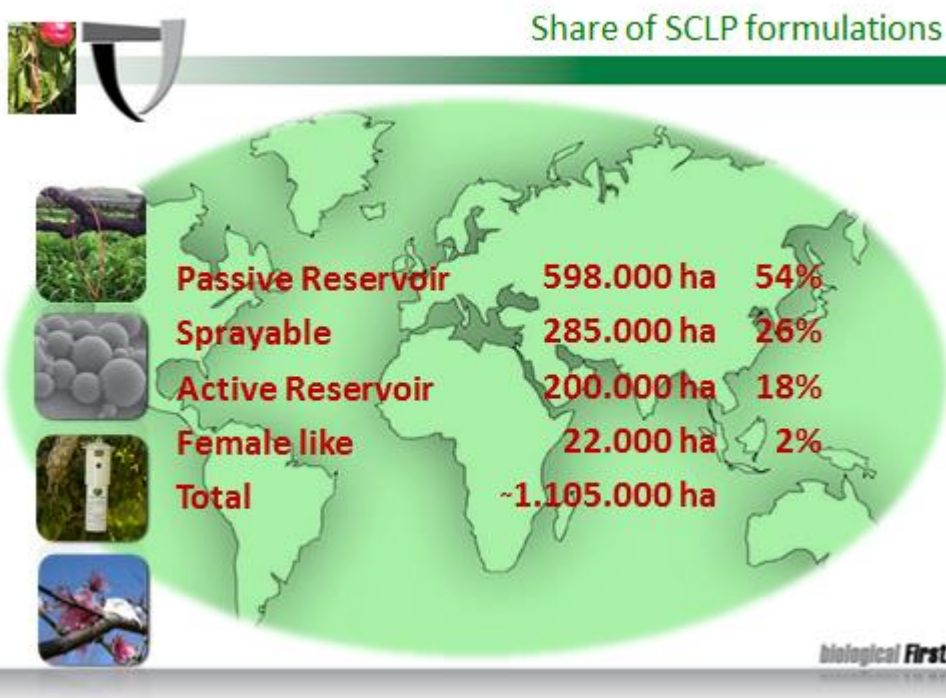
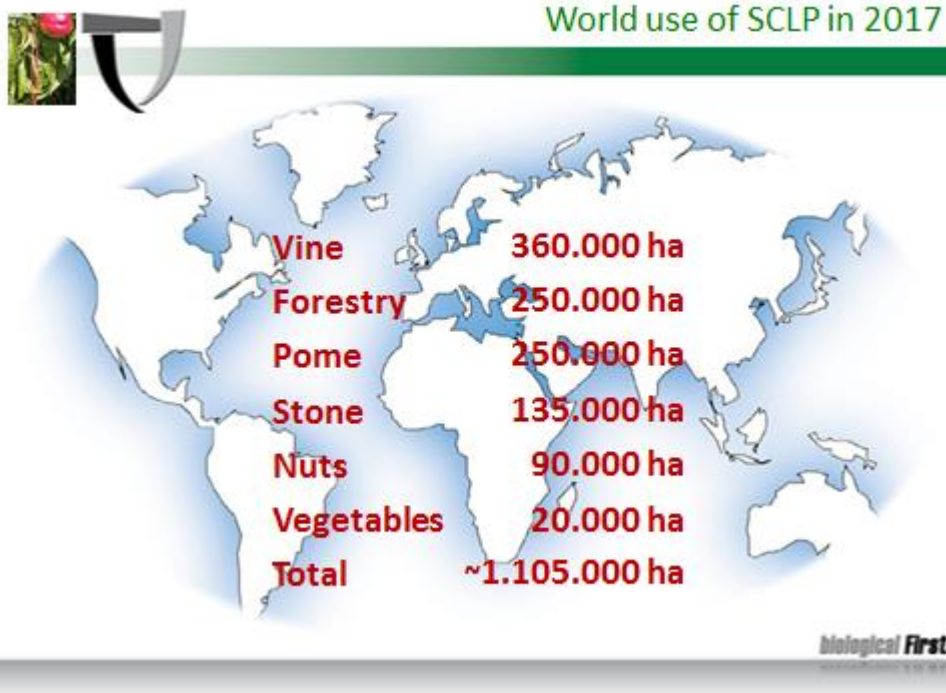
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USA vs EU available formulations

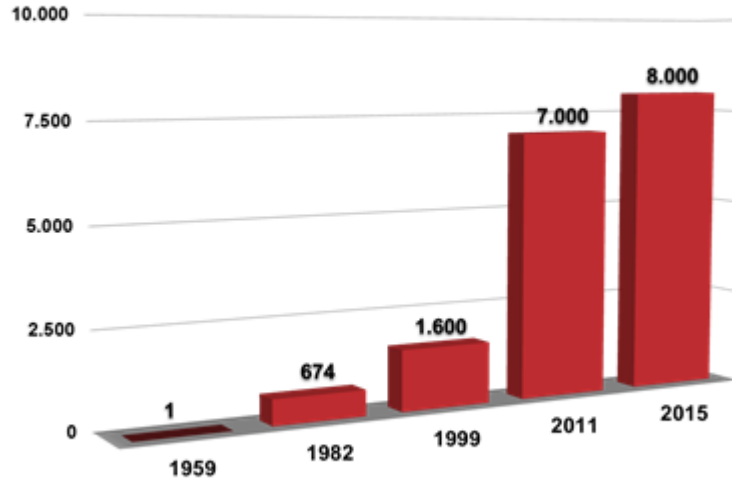


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Identification of Semiochemicals



Pherobase > 8,000 Pheromones & Semiochemicals

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Market available Semiochemicals

Species	Common name	Pheromone components
<i>Adoxophyes orana</i>	Summerfruit tortic	Z9-14:Ac (80), Z11-16:Ac (10)
<i>Adoxophyes homana</i>	Smaller leaf tortic	Z9-14:Ac (80), Z11-16:Ac (20), Z11-16:Ac (4), (10M)-16:Ac (2)
<i>Agarita thapsalis</i>	Small leaf tortic	Z9-10:Ac (10), Z11-16:Ac (90)
<i>Agropyrenia valisaria</i>	Roadside leafhopper	Z11-16:Ac (80), Z11-16:Ac (20)
<i>Carpocapsa pomonella</i>	Peach fruit moth	Z13-20-10:OT (80), Z13-19:Ac (20)
<i>Orbia suppuratrix</i>	Rice stem borer	Z11-16:Ac (80), Z13-19:Ac (10), Z9-16:Ac (10)
<i>Choristoneura dimorpha</i>	Western grape budworm	Z11-16:Ac (80), Z11-16:Ac (10)
<i>Quila pomonella</i>	Codling moth	ZZ9-10:Ac
<i>Cryoblabes gnathalis</i>	Honeydew moth	Z11-16:Ac (20), Z13-19:Ac (80)
<i>Phlogothra vitana</i>	Grape berry moth	Z9-12:Ac
<i>Ephyra pomonella</i>	Light brown apple moth	Z11-16:Ac (80), ZZ9-11:Ac (20)
<i>Scotinotia scotinaria</i>	Western pine shoot borer	Z9-12:Ac (87), Z9-12:Ac (13)
<i>Spodoptera ambigua</i>	European grape berry moth	Z9-12:Ac
<i>Grapholita dimorpha</i>	Plum fruit moth	Z9-12:Ac
<i>Grapholita molesta</i>	Oriental fruit moth	Z9-12:Ac (80), Z9-12:Ac (20)
<i>Heliothis virescens</i>	Indian meal moth	Z11-16:Ac (87), Z9-16:Ac (13)
<i>Heliothis virescens</i>	Tobacco budworm	Z11-16:Ac (84.8), Z9-14:Ac (15.2), Z11-16:Ac (0.12), Z11-16:Ac (0.12)
<i>Heliothis zea</i>	Corn earworm	Z11-16:Ac (80), Z9-16:Ac (20)
<i>Hormia nigropuncta</i>	Tea tortic	Z9-12:Ac (80), Z11-16:Ac (20)
<i>Hormia confinis</i>	Tea tortic	ZZ9-12:Ac (20), ZZ9-12:Ac (80), Z9-12:Ac (20)
<i>Heliothis virescens</i>	Tomato pinworm	Z9-12:Ac (94), Z9-12:Ac (6)
<i>Loxia obsoleta</i>	European grape leaf moth	ZZ9-12:Ac
<i>Osma riciniella</i>	Colombian bark moth	Z11-16:Ac, Z11-16:Ac
<i>Rhyacionia caryocarpae</i>	Bluegrass leafworm	Z11-16:Ac (80), Z9-16:Ac (20)
<i>Rhyacionia caryocarpae</i>	Rhik bollworm	Z11-16:Ac (20), Z11-16:Ac (80)
<i>Rhyacionia caryocarpae</i>	Apple leafminer	Z10-14:Ac (81), ZZ9-12:Ac (19)
<i>Rhyacionia caryocarpae</i>	Omnivorous leafminer	Z11-16:Ac (10), Z11-16:Ac (90)
<i>Ruella ypsilon</i>	Diamondback moth	Z11-16:Ac (80.2), Z11-16:Ac (19.8), Z11-16:Ac (1)
<i>Plutella maculipennis</i>	Archievala plum moth	Z11-16:Ac
<i>Spodoptera exigua</i>	African army worm	Z9-14:Ac (80), ZZ9-12:Ac (20)
<i>Spodoptera frugiperda</i>	Fall armyworm	Z9-14:Ac (81.9), Z11-16:Ac (17.7), Z9-12:Ac (0.22), Z11-16:Ac (0.4)
<i>Spodoptera litura</i>	Saturniid worm	ZZ9-12:Ac (10), Z9-16:Ac (90)
<i>Spodoptera litura</i>	Egyptian cotton leafworm	ZZ9-12:Ac (80), ZZ9-12:Ac (20)
<i>Spodoptera litura</i>	Common cutworm	ZZ9-12:Ac (80), ZZ9-12:Ac (20)
<i>Synanthedon acris</i>	Peachtree borer	ZZ9-12:Ac
<i>Synanthedon acris</i>	Cherry tree borer	ZZ9-12:Ac (20), ZZ9-12:Ac (80)
<i>Synanthedon</i>	Apple cleaning moth	ZZ9-12:Ac
<i>Synanthedon</i>	Lesser peachtree borer	ZZ9-12:Ac
<i>Synanthedon</i>	Currant cleaning moth	ZZ9-12:Ac
<i>Trichoplusia ni</i>	Cabbage looper	Z11-16:Ac (80.9), Z11-16:Ac (19.1)
<i>Trichoplusia ni</i>	Tomato leafminer	ZZ9-12:Ac (80), ZZ9-12:Ac (20)
<i>Trichoplusia ni</i>	Crape root borer	ZZ9-12:Ac (80), ZZ9-12:Ac (20)
<i>Trichoplusia ni</i>	Leaf-miner	ZZ9-12:Ac (80), ZZ9-12:Ac (20)

- >8,000 semiochemicals identified
large majority are SCLP
- Roughly 200 produced (g/kg scale)
mostly for monitoring traps
- About 50 available at Kg level
all SCLP for Mating Disruption
- ONLY 20 widely applied
on world basis
- JUST 5 covers 80% of world uses
only fruit and forest
- 150 SCLP formulations registered
40% are just for one pest & one crop

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Sex Pheromones specificity

- **Species specific**
sex pheromones semiochemical produced by insect are almost unique for each species and function to locate partner for mating
- **Non killing mode**
just a way of identify species and individuals
- **Only for adult stage**
it's a birth control, not damage control, it has no relation with crop
- **Not crop specific**
insect pest have typically several host plants, few or some of them are agriculture crops
- **Volatile and Low amounts**
very low persistence and very low amounts to accomplish the function of guiding the male to female
- **Consider the pest size**
insect world is different, amount is different
- **Preventive approach**
prevents damages caused by offspring, up to pest eradication in some conditions



Photo: E. Floistad, Bioforsk

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Sex Pheromones characteristics

Straight Chained Lepidopteran Pheromones

<i>Synanthedon tipuliformis</i> Currant moth E2,Z13-octadecadienyl acetate	$\text{CH}_2(\text{CH}_2)_2\text{CH}=\text{CH}(\text{CH}_2)_6\text{CH}=\text{CH}(\text{CH}_2)_2\text{OCOCH}_3$
<i>Lobesia botrana</i> Grapevine moth E7,Z9-dodecadienyl acetate	$\text{CH}_2\text{CH}_2\text{CH}=\text{CHCH}=\text{CH}(\text{CH}_2)_6\text{OCOCH}_3$
<i>Grapholita molesta</i> Oriental fruit moth Z-8-dodecenyl acetate	$\text{CH}_2(\text{CH}_2)_2\text{CH}=\text{CH}(\text{CH}_2)_7\text{OCOCH}_3$
<i>Cydia pomonella</i> Codling moth E8,E10-dodecadienol	$\text{CH}_2\text{CH}=\text{CHCH}=\text{CH}(\text{CH}_2)_7\text{OH}$

Fatty Acids

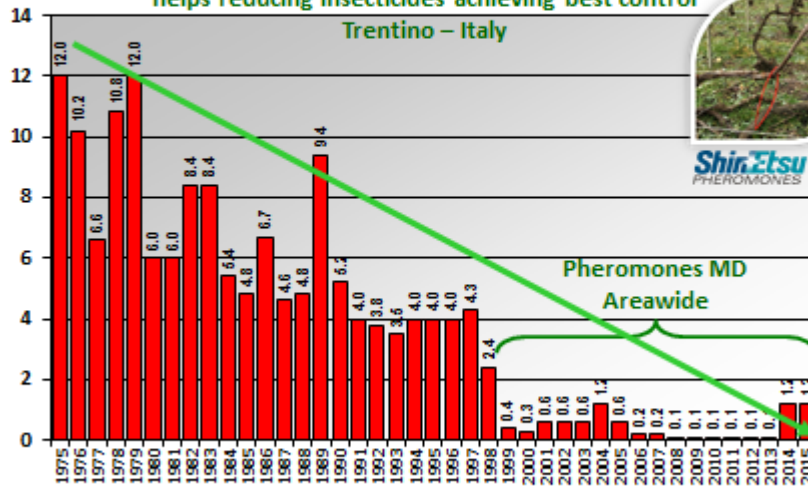
Oleyl alcohol Z9-octadecenol	$\text{CH}_2(\text{CH}_2)_2\text{CH}=\text{CH}(\text{CH}_2)_7\text{OH}$
Linoleic acid Z,Z-9,12-octadecadienoic acid	$\text{CH}_2(\text{CH}_2)_2\text{CH}=\text{CH}(\text{CH}_2)_4\text{COOH}$
Oleic acid Z9-octadecenoic acid	$\text{CH}_2(\text{CH}_2)_2\text{CH}=\text{CH}(\text{CH}_2)_7\text{COOH}$

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Pheromones facts

grape moths areawide pheromone Mating Disruption helps reducing insecticides achieving best control

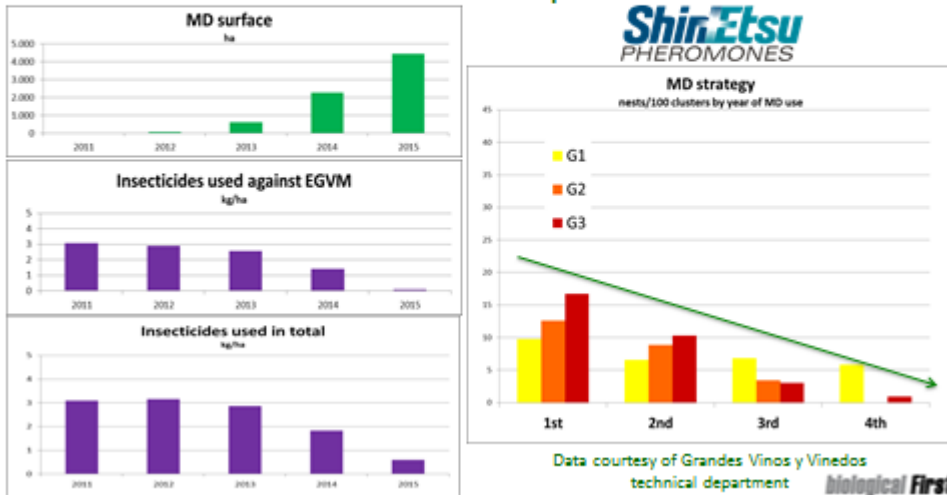


Data courtesy of Mezzacorona Winery

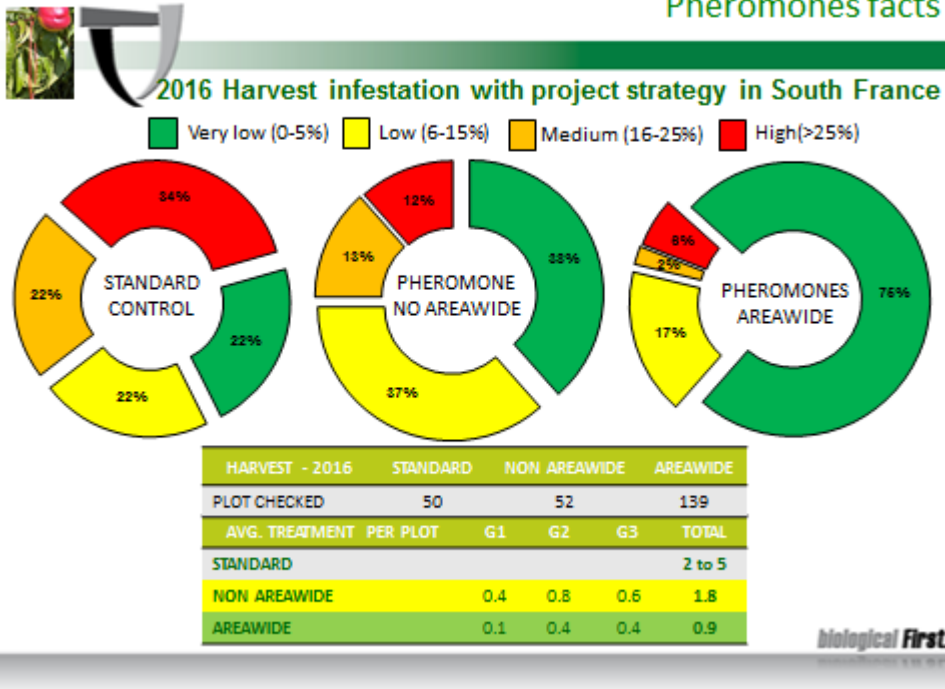


Pheromones facts

grape moths areawide pheromone Mating Disruption helps reducing insecticides achieving best control
Carinena - Spain



Pheromones facts



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Pheromone facts



EUROPEAN GRAPEVINE MOTH ERADICATED FROM CALIFORNIA

Release #16-030 Sacramento August 16, 2016

Agricultural officials confirm eradication of grape pest, lift quarantine restrictions

"Eradicating EGVM has been a top priority for USDA-APHIS, and together with industry, state and local officials, growers, university scientists and extension services, we were able to successfully invest in and implement the right tools to safeguard California grapes. The collaborative strategies used by the EGVM eradication project will be a model for addressing future pest incursions."

(Among other measures up to 9,000 Ha of vineyards applied pheromones during the program from 2011 to 2016)



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Pheromone minor uses (1)

- ***G. funebrana* in plums - Holland**

Plums are grown on about 20 hectares in Holland. *G. funebrana* is a key pest, as in most of plums orchards in Europe. A well known moth for which pheromone MD is applied in many European countries since a decade on several thousand hectares. The growers cost for the product is about 160 Euro/ha/season.

A total market of 3.000 Euro a year!

Producers association (NFO) wanted to get the product authorized, but the MR process from Germany (same Zone) cost 12.000 Euro which would take decade to be recovered. It was supported by growers but yet an annual tax of 1.300 Euro has to be paid to Dutch authorities.

- **Leafrollers in Cherry – Denmark**

Leafrollers is a generic name given to a large number of moths due to their behavior. Very often they share a number of common components in their pheromone blends though in different proportions, but can be disrupted by using mixed blends of mimics. Typical species are *A. orana*, *P. heparana*, *A. podana*, *A. ljugiana* etc. Danish growers had problems in 2016 on Cherries and advisors requested a label extension of another product authorized on Apples and Pears for Leafroller. It was granted this year with fees 1.500 Euro ? Market ?

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Pheromone minor uses (2)

- ***Cossus cossus* (European Goat Borer)**

a secondary pest wood borer attacking several trees including Cherry, Pear and Apple. It is occasional, but difficult to control because larvae are in the wood. Pheromone is known and available, MD can be a good option...but registration ?

- ***S. vespiiformis* - stone fruit; *S. myopaeformis* - apple; *S. tipuliformis* - persimmon** three woodborers that can cause high damages to orchards trees. The occurrence is occasional and limited. MD is good solution as for most borers moth, but....



- ***Zeuzera pyrina* – (Leopard moth)**

a big moth woodborer, originally affecting pear trees, but recently found on olive carob, hazelnut, pomegranate, mainly favored by irrigation. MD was registered on pear and olive, it works very well, but how to predict where the pest will move next ?...Label extension..?

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Pheromone minor uses (3)

- ***Cacoecimorpha pronubana* (Carnation tortrix)**
a pest originally of flowers, but recently found on soft fruits (blackberry), again MD works well and is ready available because in Japan another species, pest in tea orchards, has same pheromone blend. But market is too small for the registration hurdles...
- ***Pandemis heparana, Adoxophyes orana* (Leafrollers)**
typically secondary pest in apples, but in southern areas found in peaches and plums. In apple orchards they are associated with *Cydia pomonella* (Codling moth) and MD dispensers have been developed combined for all pests, but in peach and plums there is no Codling moth. Separate dispensers are required, but...another registration...
- ***Epiphyas postvittana* (Light Brown Apple moth)**
a moth originally of Australia and New Zealand, spread to California and lately UK. Damaging grapes and berries. MD was developed in Australia and successfully applied. Would be ready for Europe except for the Regulation hurdle...

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Pheromones and invasive pests

- **The *Tuta absoluta* (SA Tomato moth) case**
landed in Europe (Spain) in 2006, pheromone first identified in 1996, mimic pheromone and MD dispenser completed development in 2009, dossier application in 2010, FIRSEU REGISTRATION (Protected Crops) granted January 2016 in Italy.
Not yet available in all EU Member states due to lengthily MR procedures.
MD Efficacy very high, reduction of standard insecticides very high. Tomato in greenhouse is minor crop in all EU.
- **The *Tecia solanivora* (Potato tuber moth) case**
first detected in Europe (Spain, Galicia) in September 2015. Field and storage pest exclusively of potato. Sex pheromone first identified in 1995. Dispenser formulation ready developed and tested in Colombia in 2004. Can prevent spreading of pest, but inclusion and full registration will take 5-6 years...could be too late to control. Meanwhile only conventional insecticides are applied...



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Pheromone present and future contribution

in IPM

- **Apple, Pear**

25 years of use on *C. pomonella* and leafrollers in all countries of EU have reduced the insecticides use. In northern areas some species of leafrollers are different and rotating seasonally. Technically is easy to include their pheromones in the dispensers, but not easy for Regulation...

- **Grape**

25 years of use in EU on *L. botrana*, *E. ambiguella* and *A. lujungiana* brought to more than 250.000 ha of grape with virtually no chemical spray. Other secondary pest appear and need to be controlled in same way to keep the insecticides at lowest level, again the Regulation will slow the solution.

- **Bell peppers**

O. nubilalis (European Corn borer) was originally developed for corn but found use in bell peppers greenhouses production to support IPM with beneficial insects for a zero residue production. Use could be extended to other crops...

- **Rice**

C. suppressalis in Spanish rice fields is controlled without insecticides...

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Limits of current Regulation

- **Target pest can affect different crop**

in pheromones crop relevance is little, as mode of action is interference to adult mating. However pest are typically polyphagous and can adjust to a variety of plants. No phytotox (for passive dispensers) and no residues is expected. Crop label extensions should be flexible and easier.

- **A crop in specific Country is minor or very minor**

MR or Authorization process and fees do not take this into account. When a product is registered and widely applied in a State should be facilitated in another especially if the border is practically just administrative like in EU.

- **Invasive species affecting crops**

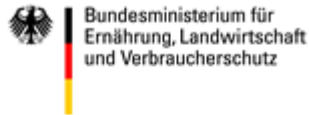
pests are moving across borders, MD already registered in other Countries in the world can help preventing the pest expansion in fast way if Regulation would support fast adoption.

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Presentation 4

Molecular factors defining specificity and host range of baculoviruses

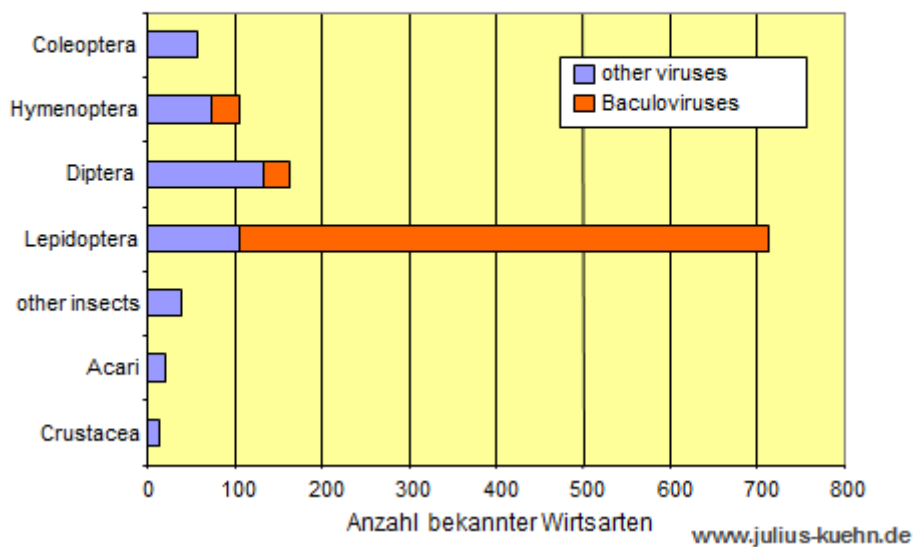
Johannes A. Jehle, Jörg T. Wennmann (Julius Kühn-Institute (JKI), Darmstadt, Germany)



Molecular factors defining specificity and host range of baculoviruses

Johannes A. Jehle & Jörg T. Wennmann
Julius Kühn-Institut, Darmstadt, Germany

Virus Frequencies in Arthropods



Characteristics of Baculoviruses



- rod shaped virions embedded in an occlusion body
- > 120 Baculovirus genomes fully sequenced
- dsDNA genome, 80 - 180 kb, 100 - 150 genes
- from more than **700** insect species isolated
- huge undiscovered diversity expected
- specific for Lepidoptera, Diptera, Hymenoptera
- Specific for single species

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Host Range of some Baculoviruses



Virus	Insect species	Insect families
<i>Autographa californica</i> MNPV (alfalfa looper)	73	13
<i>Mamestra brassicae</i> MNPV (cabbage moth)	36	4
<i>Helicoverpa zea</i> SNPV (corn earworm)	7	1
<i>Cydia pomonella</i> GV (codling moth)	4	1
<i>Cryptophlebia leucotreta</i> GV (false codling moth)	1	1
<i>Spodoptera exigua</i> MNPV (beet army worm)	1	1

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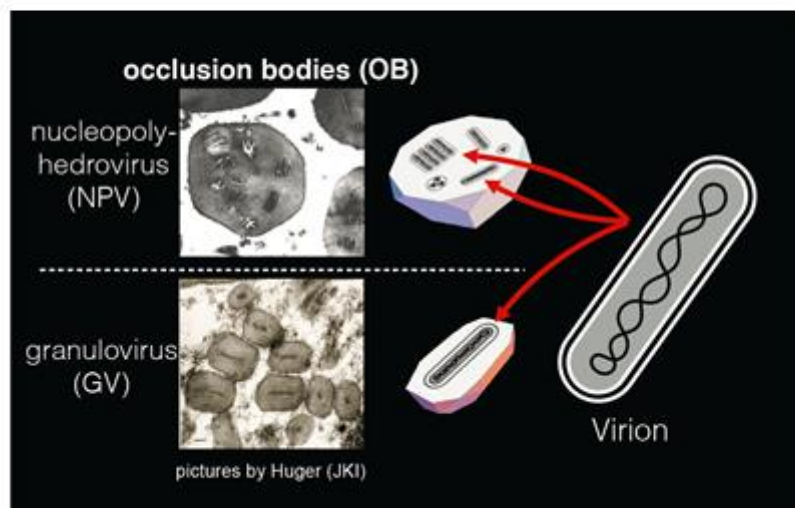


Why are they so specific?

Its their biology!

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The Occlusion Body (OB)

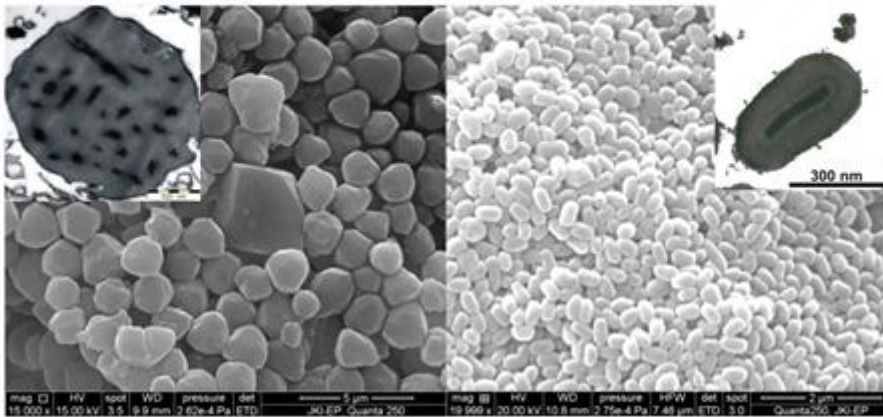


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The OB – a natural Formulation



Provides protection against physical (shearing, UV, heat, pH) and chemical (detergents, enzymes) factors

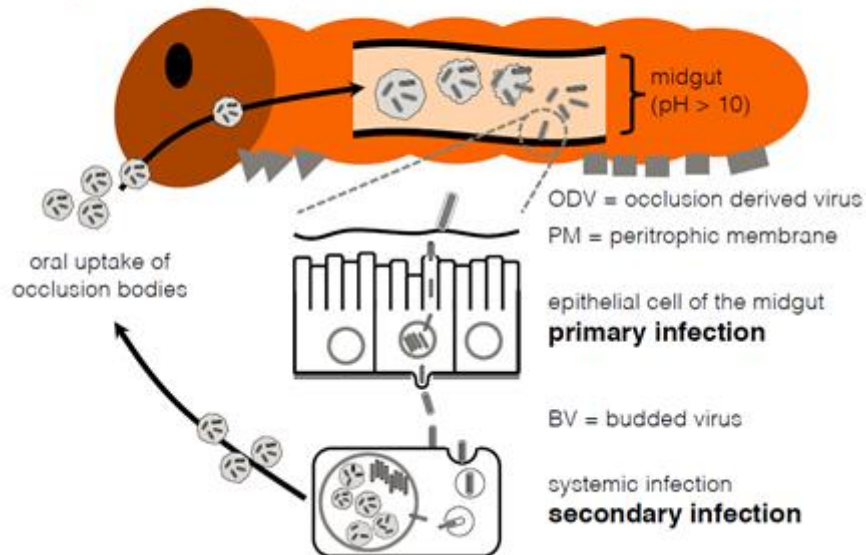


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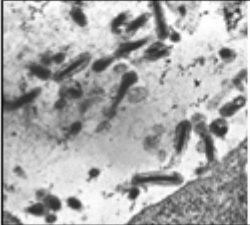

Baculovirus Infection of Insect Larvae



example: nucleopolyhedrovirus




One Life Cycle – Two Virus Phenotypes


EM	Phenotype	Biological function
	 Occlusion Derived Virus (ODV)	<ul style="list-style-type: none"> • environmental persistence • peroral (= primary) infection of midgut • horizontal transmission from insect to insect
	 Budded Virus (BV)	<ul style="list-style-type: none"> • secondary infection • transmission from cell to cell


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Baculovirus-infected Codling Moth Larvae




healthy





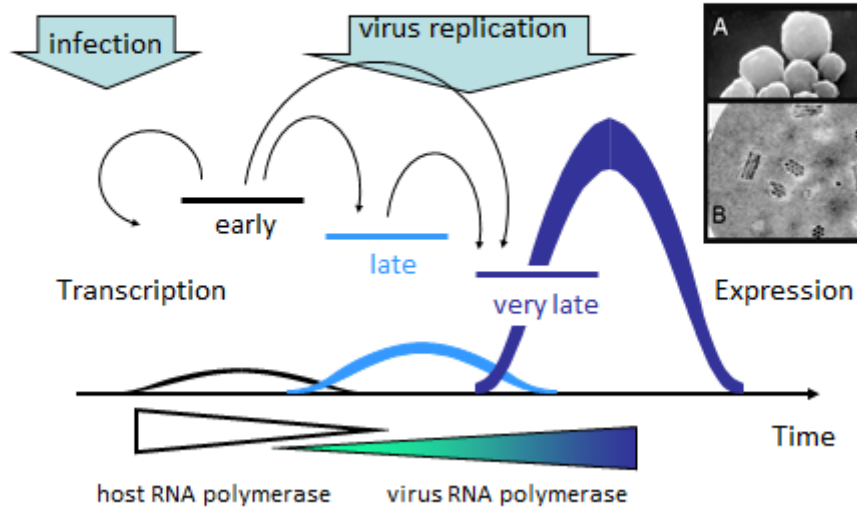
Infected L1 larvae



Infected L4 larvae

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Baculovirus Gene Regulation



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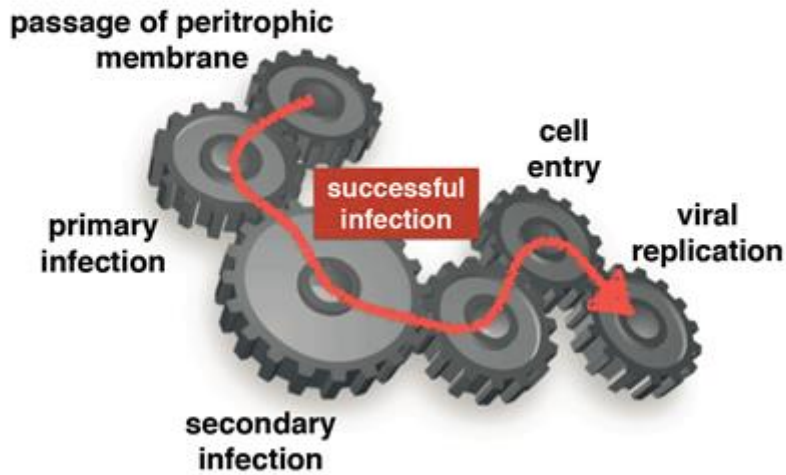
What makes Baculoviruses different from other Invertebrate Pathogens?



- Not toxigenic
- No secondary metabolites
- Highly conserved infection process adapted to different host species
- Small genomes, strains well described
- Strain variability considerably low
- No potential to harm or grow on mammals
- QPS (Qualified Presumption of Safety) Status by EFSA
- EU: Registration on species level not on strain level
- EU: Potential of being considered as low-risk product

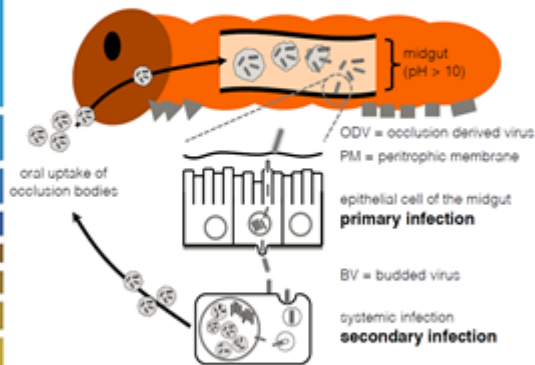
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What is needed to make a successful Infection?



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Factors defining Host Specificity



1. pH in Midgut lumen >9
2. PIF Proteins on ODV
3. Apoptosis
4. Viral Transcription
5. DNA Replication
6. ...

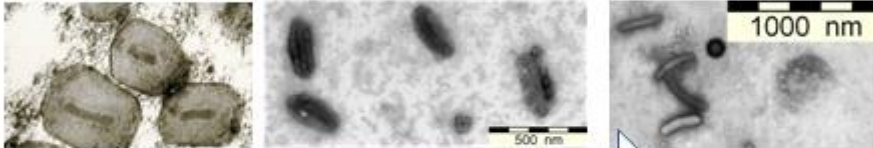
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Peritrophic Matrix and Midgut Milieu

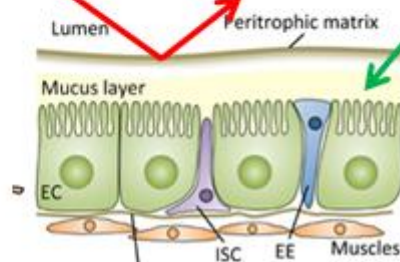


GV: 300 x 500 nm
NPV: 1-5 μm

30–60 nm x
250–300 nm



Increasing time of incubation at pH 9



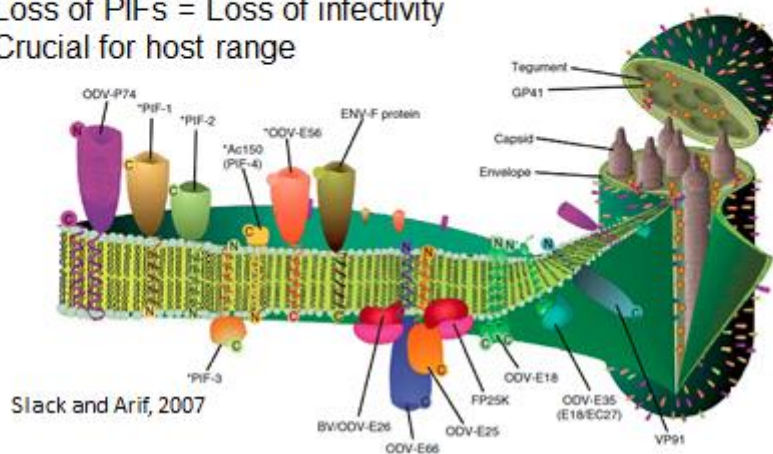
PM:
Chitin microfibrils
and proteins,
Sieve <100 nm

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Per os infectivity Factors (PIFs)

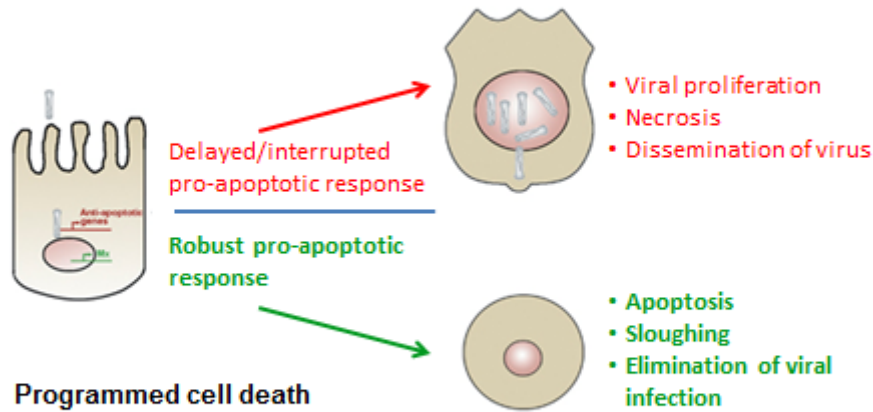


- Localized in membrane of ODFs
- Binding and Fusion Proteins
- Interact with cellular receptor in midgut
- Loss of PIFs = Loss of infectivity
- Crucial for host range



Slack and Arif, 2007

Baculovirus Inhibition of Apoptosis

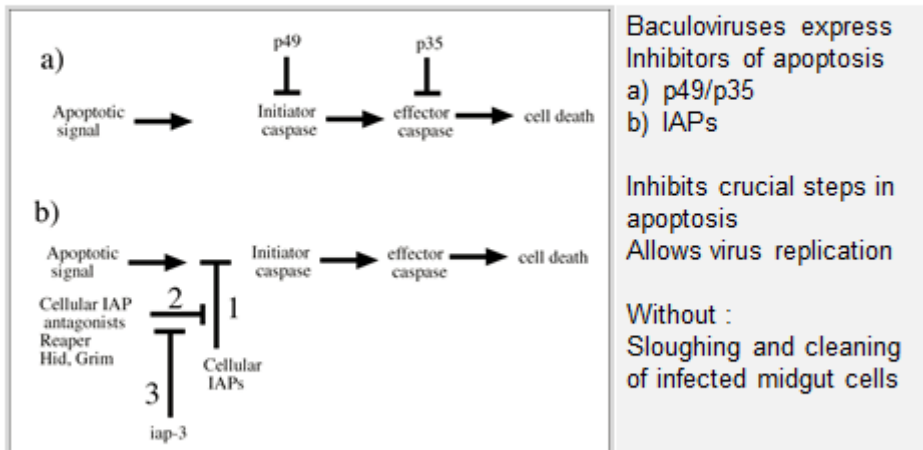


Programmed cell death

- Development (metamorphosis)
- Malfunction of cell cycle (DNA damage, unscheduled DNA replication and RNA synthesis)
- Anti-viral mechanism

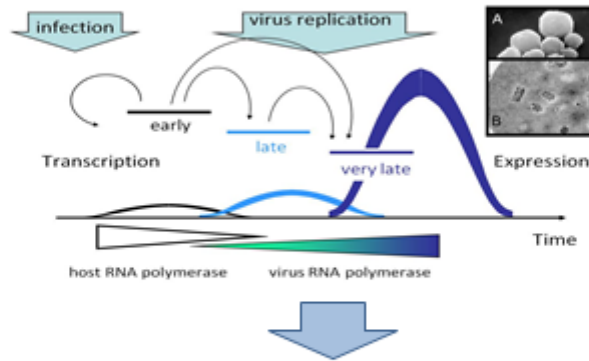
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Baculovirus Inhibition of Apoptosis



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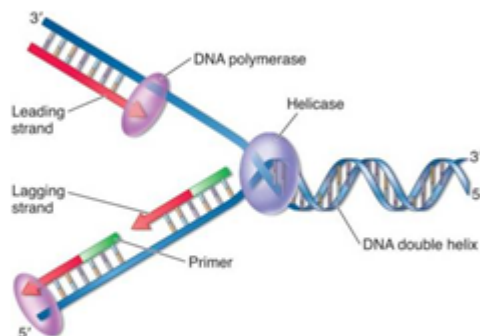
Baculoviral RNA Polymerase



Viral RNA Polymerase
 Consists of several subunits (p74, lef-4, lef-8, lef-9)
 Recognizes specific baculoviral promoters
 Transcription of late and very late proteins

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Change of virulence by Change of Helicase



	Sf9	BmN
AcMNPV	+	-
BmNPV	-	+
AcMNPV + signatures of BmNPV helicase	+	+

- AcMNPV and BmNPV 93% identical genome sequence
- Val556Leu, Ser564Asn, Phe577Leu in Helicase extends host range to BmN cells
- AcMNPV helicase toxic to BmN cells?

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Summary and Conclusion (I)



- Baculovirus host specificity is unique
- Host specificity is the consequence of 140 Million years of coevolution with insect hosts
- No related viruses outside arthropods
- Host specificity and host range depend on successful virus-host interaction during replication
 1. pH in Midgut lumen >9
 2. PIF Proteins on ODV
 3. Apoptosis
 4. Viral Transcription
 5. DNA Replication



Many factors needed for a successful infection
One factor missing results in block of replication

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Summary and Conclusion (II)



- The narrower host range the smaller the market
- Most baculoviruses are single pest applications
- Discrepancy between ecological benefits and commercial value
- Absolutely safe to humans and mammals
- Repetitions of Ecotox and human Tox studies still necessary?
- Several pre-Directive 91/414 products are still missing
- Harmonization impeded local solutions
- Discrepancy between registration expenses and market value
- Further facilitation of registrations for small markets needed



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Presentation 5

Niche Uses of Baculoviruses

Philip Kessler (Andermatt Biocontrol, Grossdietwil, Switzerland)



**where Nature
leads Innovation**

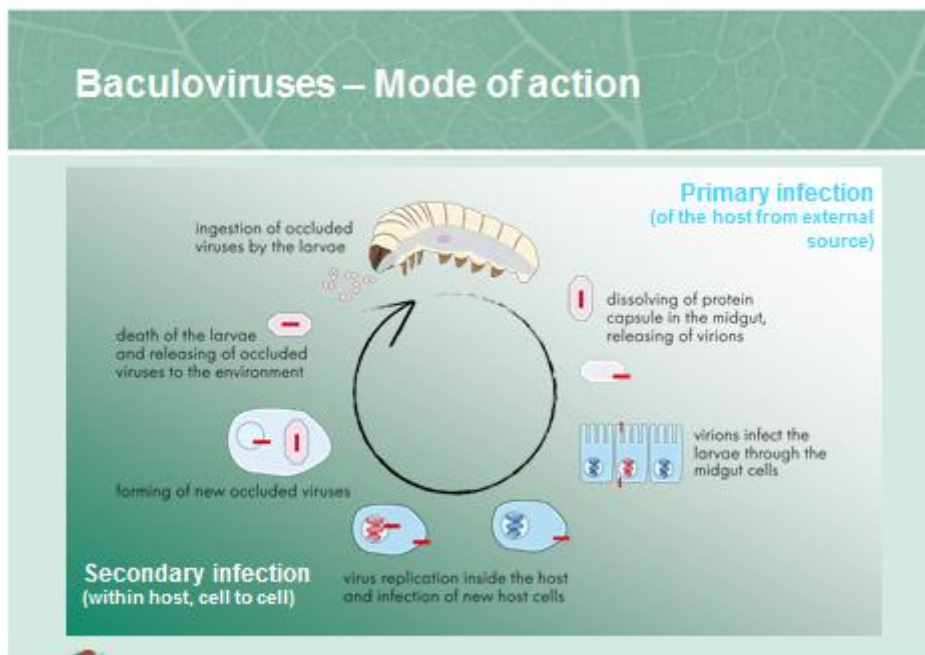


12.09.2018



Niche Uses of Baculoviruses
Philip Kessler,
Director International Market Development, Andermatt Biocontrol AG
OECD 8th BPSG
Seminar on "Niche Uses of highly Specific Biocontrol Products"
Paris 26. June 2017





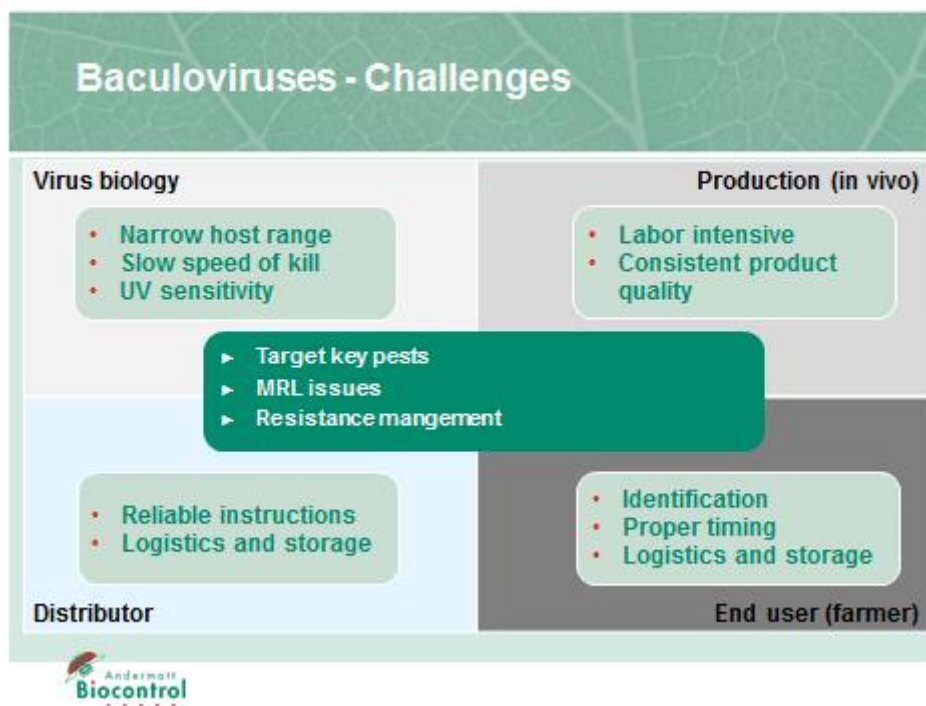
Toxicology and Ecotoxicology

Only found in insects (mainly lepidopteran species)

OECD Consensus Document No 20

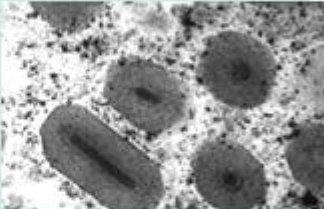

- Safe for user and consumer
- No effects to plants, mammals or aquatic organisms
- Narrow host range, no adverse effects on beneficial insects
- No production of metabolites or toxins





Uses of baculoviruses

- 1970s first use of NPV
- 1987 first registration of GV
- Today
 - More than 50 baculovirus products, of which ca. 24 HaNPV and 16 CpGV products
 - >180 registrations worldwide
 - > 30 countries
- **Main producer:**
 - AgBitech (AU), Andermatt Biocontrol (CH), Arysta (FR), Biotepp (CA), Certis (USA), Henan Jiyuan Baiyun Industry (CN), Kenya Biologics (KE), River Bioscience (ZA), Serbios (IT), further Indian and Chinese producers

Adoxophyes orana granulovirus (AoGV)

Adoxophyes orana GV: Timelines

- Dossier submitted to RMS in 2004
- Conclusion for "Annex-1 inclusion" by EU COM in 2012
- **Eight years** after application for Annex-1 inclusion, application for mutual recognition in MS can be submitted



Adoxophyes orana GV: Costs

- Registration costs up to 1 Mio € (fees, consultants, studies and field trials)
- Fluctuating market for CAPEX
- Estimated annual turnover of 50'000 to 200'000 €



Return of investment, when CAPEX (AoGV) already needs to be re-registered. Why to register CAPEX in the EU?



Spodoptera exigua MNPV: used in IPM in protected pepper production in Spain

SeMNPV used in IPM to control *Spodoptera exigua* in protected pepper production in Almeria, Spain

- 2007: SeMNPV F1 - first inclusion in Annex-1
- 2010: 2 new isolates of SeMNPV on Annex-1
- Since 2009: applications of three SeMNPV products submitted to Spain (Spod-X[®], Spexit[®], Virex[®])
- Since 2009: Emergency authorisations issued yearly limited to the Province of Andalucía
 - Too late in the season
 - No marketing strategies possible
 - Remains a spot business
- **2015** **Renotification for SeMNPV necessary:** SeMNPV not notified by Andermatt for Annex1 renewal of SeMNPV in 2017
- **2016** National approval for Spexit in Spain



Phtorimaea operculella GV

- **BIOCOMES**
- EU funded project 2012-2017
- Development of new biocontrol tools
- PhopGV against Tomato leaf miner (*Tuta absoluta*)
- TLM x Tomato -> Niche market
- Regulatory hurdle for market entry



 **BIOCOMES**
New biological control products
for sustainable farming and forestry



OECD Environment, Health and Safety Publications Harmonization of Regulatory Oversight in Biotechnology No.20

Consensus Document on Information used in the Assessment of Environmental Applications involving Baculovirus

Baculoviruses are safe and do not cause hazards to human health and to the environment

- **EU : mainly accepted**
- **USA: partly accepted**
 - Cell-culture studies
 - Non-target studies
- **Canada: mainly accepted**
- **Australia: partly accepted**
 - non-target studies on indigenous leps
 - caddies flies
- **Japan, South Korea: no experience**
- **Brazil (non-OECD): not yet accepted**
 - new specific studies



To take the hurdles

Leaders

- CpGV, HaNPV, CrleGV

Struggling or failed ...

- AoGV, SeMNPV, SpliNPV, SINPV, MbNPV, AgipNPV, AcMNPV

On the start

- PxGV, SfNPV, EppoNPV, PhopGV, LdMNPV, more?



How we can improve

- Harmonize dossier formats (e.g. accept OECD data format)
- Harmonize and adjust data requirements (e.g. for microbial a.i.)
- Accept available guidance (e.g. from OECD)
- Accept scientific rationales
- Adjust fees for niche market products
- Prioritise assessment of low risk products
- No re-registration procedures of low-risk products



Global organisation such as OECD, FAO, etc. can give valuable guidance



Presentation 6

Niche Uses of Bacteriophages

Roma Gwynn (*Rationale, United Kingdom*)



Bacterial phytopathogens – economically important

- 85% plant diseases cause by fungi – rest bacteria, viruses
- Bacterial phytopathogens = 38 species (approximately)
- Bacterial diseases cause economic losses in cultivation and storage

Israel, soft rots in potato: yield reduction 20–25%



Soft rots in carrot



70-80 % crop loss in Tomato



Xanthomonas sp. in brassicas



Bacterial phytopathogens – seed borne

Crop	Disease
Wheat	<i>Pseudomonas syringae</i> pv. <i>syringae</i> , <i>Xanthomonas campestris</i> pv. <i>translucens</i>
Maize	<i>Pantoea stewartii</i> subsp. <i>stewartii</i> , <i>Clavibacter michiganensis</i> subsp. <i>Nebraskensis</i>
Rice	<i>X. oryzae</i> pv. <i>oryzae</i> , <i>X. oryzae</i> pv. <i>oryzicola</i> , <i>Acidovorax oryzae</i>
Bean	<i>P. syringae</i> pv. <i>phaseolicola</i> , <i>Curtobacterium flaccumfaciens</i> pv. <i>flaccumfaciens</i> , <i>Xanthomonas campestris</i> pv. <i>phaseoli</i> and <i>X. fuscans</i> var. <i>fuscans</i>
Soybean	<i>P. syringae</i> pv. <i>glycinea</i>
Chickpea	<i>Rhodococcus fascians</i>
Cereals, grasses	<i>Rathayibacter</i> sp.
Alfalfa	<i>C. michiganensis</i> subsp. <i>insidiosus</i>
Tomato, pepper	<i>Pseudomonas syringae</i> pv. <i>tomato</i> (tomato), <i>P. syringae</i> pv. <i>syringae</i> , <i>Xanthomonas</i> spp., <i>Clavibacter michiganensis</i> subsp. <i>Michiganensis</i>
Carrot	<i>Xanthomonas campestris</i> pv. <i>carotae</i>
Onion	<i>Pantoea ananatis</i> , <i>Burkholderia cepacia</i>
Crucifers	<i>Xanthomonas campestris</i> pv. <i>campestris</i> , <i>P. syringae</i> pv. <i>alisalensis</i> (broccoli), <i>Pseudomonas</i> spp. (crucifers)
Cucurbits	<i>P. syringae</i> pv. <i>lachrymans</i> , <i>Acidovorax citrulli</i>
Lettuce	<i>Xanthomonas campestris</i> pv. <i>vitians</i>



Bacterial phytopathogens – vegetative transfer

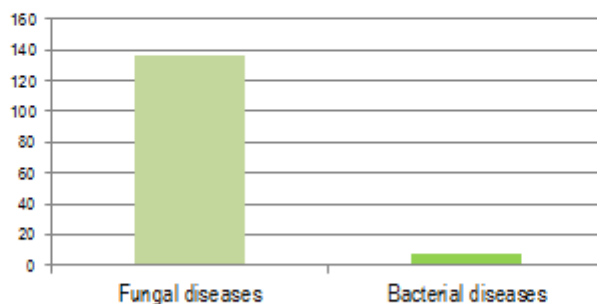
Crop	Disease
Potato	<i>Clavibacter michiganensis</i> subsp. <i>sepedonicus</i> , <i>Ralstonia solanacearum</i> , <i>Streptomyces scabies</i> , <i>Candidatus Liberibacter</i> sp., <i>Pectobacterium/Dickeya</i> spp.
Citrus	<i>Candidatus Liberibacter asiaticus</i> , <i>Xylella fastidiosa</i> subsp. <i>pauca</i> , <i>Xanthomonas citri</i>
Strawberry	<i>X. fragariae</i>
Grape, almond	<i>Xylella fastidiosa</i> subsp. <i>fastidiosa</i> ,
Pear, apple, quince	<i>Pectobacterium amylovora</i>
Sugarcane	<i>Leifsonia xyli</i> subsp. <i>xyli</i> , <i>Xanthomonas albilineans</i>
Cassava	<i>Xanthomonas campestris</i> pv. <i>cassavae</i>
Banana	<i>X. campestris</i> pv. <i>musacearum</i>
Roses, ornamentals	<i>Agrobacterium tumefaciens</i>

- Propagation production systems offer ideal conditions for bacterial reproduction and spread



Bacterial phytopathogens - products

Number of diseases for which there are biocontrol products

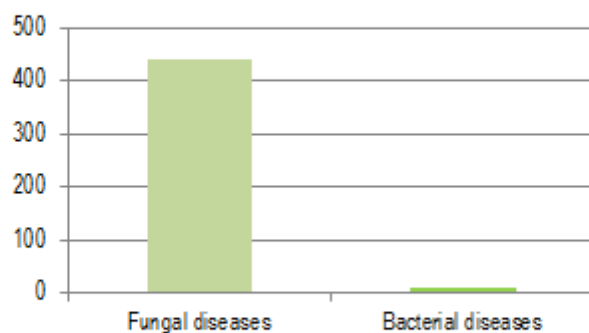


From BCPC Manual of biocontrol agents



Bacterial phytopathogens - biocontrol products

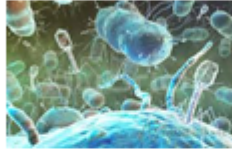
Number of Biocontrol Products



From BCPC Manual of biocontrol agents



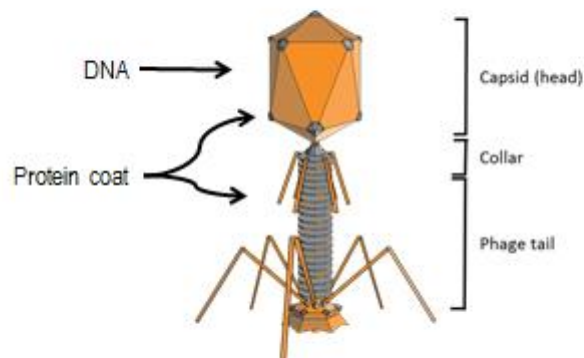
Bacteriophage – biology



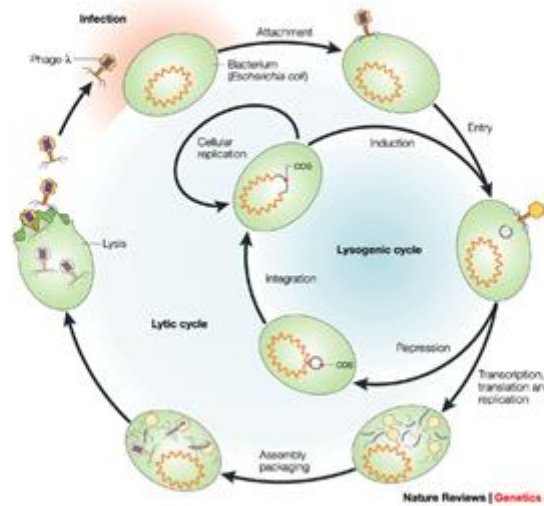
- The most abundant organisms in the world (10^{31} on Earth)
- Abundant in wide range of ecological niches such as soil, water, plants and animals
- Act as antibacterial agents, with different bacteriophage being specific to different hosts
- For almost every bacterial species - at least one bacteriophage that can specifically infect that particular bacterial group



Bacteriophage – bacterial viruses



Bacteriophage – Life cycle

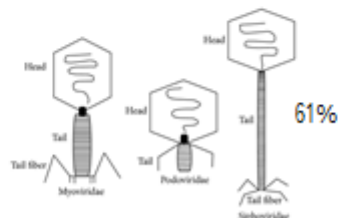


Bacteriophage – current taxonomic situation

Bacteriophage taxonomy is complex & continually evolving:

- ICTV (International Committee of Taxonomy of Viruses): use virion properties & nucleic acid (not fully agreed approach)
- Alternative: classification according to morphotype, host genus & pathogenicity (approach accepted by PMRA, Canada)

>96% bacteriophage 'tailed' with double-stranded DNA (order Caudovirales)



Bacteriophage – key aspects for products



- High virulence
- High specificity to host
- Rapid mode of action
- Short persistence without host



Bacteriophage - commercialisation

Mainly applications to food of animal origin against human pathogens (e.g. *Listeria*, *Salmonella* spp.)

- Listex P100 (Microcos, The Netherlands): approvals in the US, Canada, NZ, Zealand, Australia & The Netherlands for use on meat, fish, vegetables and cheese
- ListShield, SalmoFresh & EcoShield (Intralytics, USA)

One bacteriophage plant protection product approved in Canada (PMRA) and USA (IR4 supported):

- AgriPhage-CMM (Omnilytics): Bacteriophage of *Clavibacter michiganensis* (subsp. *michiganensis*) in tomato



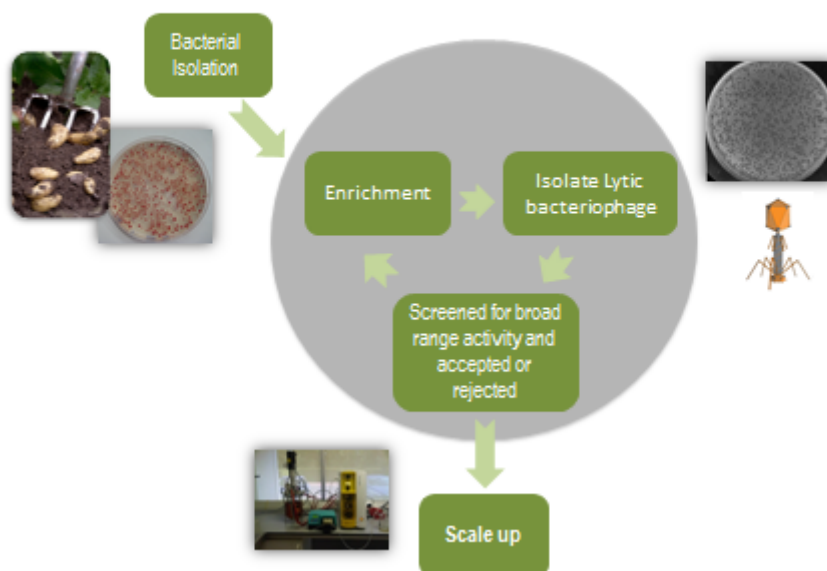
Bacteriophage – commercialisation - regulation

Conclusion of PMRA review of bacteriophage of *Clavibacter michiganensis* (subsp. *michiganensis*)

- By nature, bacteriophage are viruses that are **only capable of infecting bacteria**.
- Bacteriophage are not capable of infecting animals, plants, or fungi and are not capable of producing any toxins outside their hosts because they are not metabolically active. Bacteriophage rely on the bacterial host's metabolism for reproduction and survival. Bacteriophage themselves are **not considered to be toxic**.
- Also, since the host bacterium, *C. michiganensis* subsp. *michiganensis*, does not produce toxins nor is it otherwise considered to be harmful to humans, the infection of these bacteria by bacteriophage of *Clavibacter michiganensis* (subsp. *michiganensis*) will not alter the bacterial population in a way that could be harmful to humans.
- Although the relative exposure of people to bacteriophage of *Clavibacter michiganensis* (subsp. *michiganensis*) may increase from the use of AgriPhage-CMM, there have been no reports of adverse effects or incidents resulting from the direct exposure to naturally occurring bacteriophage.



Bacteriophage – common approach to production



Bacteriophage – why are they niche products?

Specificity of bacteriophage to disease

- Market potential limited as product highly specific
- Specific to disease strains – need mixture of phage genotypes
- Disease strains vary geographically – may need to tailor phage strain mixture to geography



Bacteriophage – why are they niche products?

Large-scale production

- Production only on host bacteria – host may not be amenable to *in vitro* cultures
- Bacterial hosts often disease complexes – need to produce several host bacteria
- Production only on host bacteria – double cultivation in production
- Must clean-up plant pathogen from active substance – ultra filtration needed



Bacteriophage – why are they niche products?

Delivery to target on plants

- Delivery of product to plants – need **host** disease – may limit bacteriophage persistence
- Bacteriophage susceptible to environmental conditions - on-plant persistence can be short
- Diseases often within plants – specific **inoculation** to get phage to disease sites?
- Bacterial soft rots – in root zone – difficult delivery



Bacteriophage – regulatory aspects

Aspects of biology and ecology

- Specificity of relationship between bacterial host strain and bacteriophage genotype
- Specificity of disease complex to crop(s)
- Need mixtures of multiple bacteriophage which may need to be altered regionally
- Bacteriophage specificity and mode of action = good safety profile for humans and environment
- Need bacteriophage with lytic life cycle for PPP
- Lysogenic cycle: confirm absence of potential virulence factors and/or antimicrobial resistance genes in both host bacteria and bacteriophage



Bacteriophage – regulatory aspects

Aspect of commercialisation

- *In vitro* production
- Need to produce mixed strain/genotype cultures
- Cultured on host diseases – must remove for market acceptability
- Downstream processing removes host bacteria and all other microorganisms - active substance is only bacteriophage culture – no contaminants
- Usually formulated in buffer solution – simple formulation
- Long-term storage – low temperature, distribution – room temperature
- Need balance between market size and regulatory costs



Bacteriophage – regulatory aspects

Aspect of regulatory procedures

- Virus of microorganisms – new PPP technology
- Bacteriophage are not specifically referred to in any PPP regulations
- Use of bacteriophage as PPP for agriculture and horticulture is a relatively new technology - no guidance documents to allow interpretation of the data requirements
- Closest parallel in biopesticide regulation – baculoviruses ?



Presentation 7

Two examples of fungal biopesticides that disappeared from the EU market

Willem Ravensberg (Koppert Biological Systems, Berkel en Rodenrijs, The Netherlands)



Two examples of fungal biopesticides that disappeared from the EU market

Willem Ravensberg, PhD
Koppert Biological Systems
The Netherlands
OECD EGBP, 26 June 2017, Paris
Seminar on "Niche Uses of Highly Specific Biocontrol Products"



Mycotal and Vertalec

- Mycotal and Vertalec are bio-insecticides based on the entomopathogenic fungus *Verticillium lecanii*
- Vertalec: strain Ve2 - for control of aphids
- Mycotal: strain Ve6 - for control of whitefly and thrips

Vertalec



- Developed in the 1970's in the UK at the Glasshouse Crops Research Institute (GCRI) and Tate and Lyle as manufacturer, from 1985 on Koppert
- Targeted at aphid species in cucumber, tomato, peppers, chrysanthemum
- *Myzus persicae*, *Aphis gossypii*, *Macrosiphoniella sanborni*, *Macrosiphum euphorbiae*
- First bio-insecticide registered in the UK in 1979



Mycotal



- Developed in the 1970's in the UK at the Glasshouse Crops research Institute (GCRI) and Tate and Lyle as manufacturer, from 1985 on Koppert
- Targeted at whitefly and thrips species in cucumber, tomato, peppers, etc.
- *Trialeurodes vaporariorum*, *Thrips tabaci*, *Frankliniella occidentalis* a.o.
- Second bio-insecticide registered in the UK in 1981

Registration



- One dossier of Mycotal and Vertalec based on the species *Verticillium lecanii* and the two strains
- Some studies based on Ve6, some on Ve2, some on both
- Efficacy generated per product
- Applications per product
- Approvals per product
- Vertalec: registered in UK, North Ireland, Finland, Denmark, Switzerland, Norway and Japan
- Mycotal registered in UK, North Ireland, Netherlands, Finland, Denmark, Greece, Italy, Austria, Switzerland, Turkey, Kenya, New Zealand and Japan

Re-registration



- Application for approval within EG 91/414 and List 4 procedure (Reg. **112/2002**)
- RMS- Netherlands
- One dossier submitted for both strains
- Taxonomy changed: 2 new species
 - Mycotal strain *Verticillium lecanii* Ve6 → *Lecanicillium muscarium*
 - Vertalec strain *Verticillium lecanii* Ve2 → *Lecanicillium longisporum*

Re-registration



- One dossier submitted for both strains
- Ctgb refused the joint application and required two new dossiers
- Not acceptable for Koppert due to registration history, and other comparable submission: *Trichoderma harzianum* Task Force dossier with 4 strains that also ended up in a new taxonomic classification as 3 species.

Re-registration



- Koppert withdrew Vertalec application
- And continued with Mycotal only
- Main reason: extra burden in terms of money and time to large for Vertalec
- Vertalec annual turnover € 50,000 due to niche market
- Versus total costs € 2-300,000 to register

Vertalec



- Due to loss of product in EU, remaining market even smaller, ultimately we stopped production and withdrew from Japan, Switzerland, etc.
- Request from PMRA and growers to register in Canada, several times, but could not honoured
- Small market also due to high RH requirement of Vertalec
- Still growers ask for Vertalec, it was/is the only effective entomopathogen against aphids in many minor (protected) crops

Biochon



- Biochon is a fungus causing wood rot through wounds in trees and shrubs: silverleaf
- Ubiquitous fungus *Chondrostereum purpureum*
- Considered sometimes as a disease in apple, pear
- Used to control American black cherry tree *Prunus serotina*, an invasive weed in Dutch forests
- Also potential for control of other deciduous trees
- To prevent regrowth after cutting, stump re-sprouting

Biochon



- Over 10 years of research in Wageningen UR and Dutch Forestry Department, and Koppert
- Application method: brushing mycelial suspension on freshly cut stump
- Product development: Koppert
- Formulation: freshly delivered product on demand
- Results: very effective
- Tree (90%) dies in a two-three years

Biochon



- Biochon market very small, NI and Germany
- Only target: *Prunus serotina*
- Nature reserves, etc.; treatment partly subsidized
- Placed on market as wood rot promotor
- Registration as a herbicide too costly
- Also request from water authorities: willows, alder, poplars

Biochon



- Market less than € 30,000 per annum
- Used during 1997-2001
- Ctgb required registration as herbicide
- Costs-benefit and ROI negative
- Withdrawal from the market



Similar products

- Mycotech Paste- from Myco-Forestis Corporation Canada
 - Registered in Canada in 2002 - 2008
 - Registered in USA in 2005 (?)
- Chontrol Paste – from MycoLogic inc.
 - Registered in USA in 2004
 - Registered in Canada in 2007



Solution for EU market

- Vertalec: accept closely related and similar entomopathogenic strains through read-across
- Sprouting inhibitor: accept sprouting inhibitor product approval from USA and Canada through mutual recognition

Presentation 8

Niche Uses of fungi

Christina Donat (Bio-Ferm GmbH, Tulln, Austria)

BIOTECHNOLOGICAL PLANT PROTECTION



Niche Uses of fungi in biocontrol

Example:

Aureobasidium pullulans strains DSM14940 and DSM14941
against fire blight in pome fruits

Christina Donat

20.06.2017

www.bio-ferm.com

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BIOTECHNOLOGICAL PLANT PROTECTION



The main players are...

***Aureobasidium pullulans*, DSM 14940 and DSM 14941**



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Aureobasidium pullulans

- Ascomycete with asexual, yeast-like reproducing cells (blastospores)
- Natural occurrence in the environment (soil, plant surface)
- Well adapted, resistant to drought and UV radiation



Aureobasidium pullulans
under the microscope, on an agar plate and dried to granules

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History:

1989 University Konstanz, Chair of Phytopathologie:

about 500 microbial isolates: Schiewe und Mendgen 1992; Falconi 1993; Schiewe 1993; Falconi und Mendgen 1994, ...

1996: End of the research projects at Uni-Konstanz; strains were stored frozen

1998- 2001: Research project fire blight (BBA Darmstadt, governmental research institute, BMBF Bundesministerium für Bildung und Forschung) – among others also *A. pullulans* tested

2001: Bio-Protect GmbH founded, Konstanz, further development of *Aureobasidium pullulans* strains
Further 5 years research founded by Baden Württemberg till 2005

- Blossom Protect™

BÖLW fire blight project University of Konstanz: 2004-2011 field trials

- 6 pack Tox, field trials Germany, first emergency use registrations,

2004: bio-ferm GmbH, founded by the Erber Group in Tulln, Austria:
production, registration and marketing of *A. pullulans* products



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Global Presence

~1400 employees in more than 120 countries. Own Business Units in 37 countries

ERBER Group



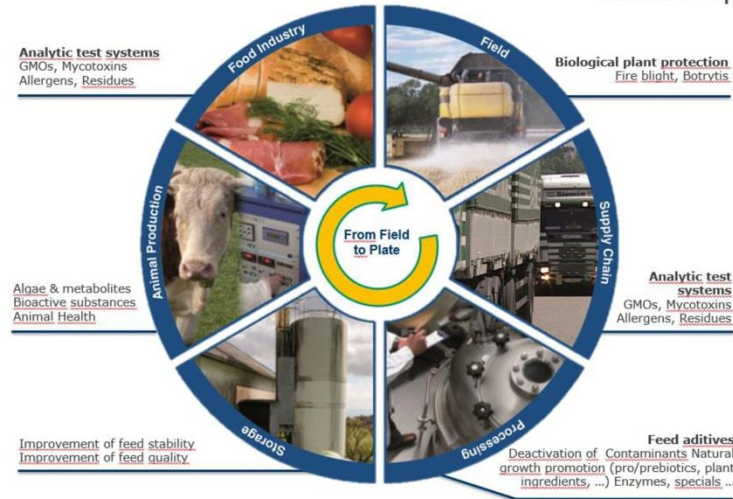
BIOMIN • ROMER LABS • SANPHAR • BIO-FERM • EFB Pioneers • Partners • Performers

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ERBER Group

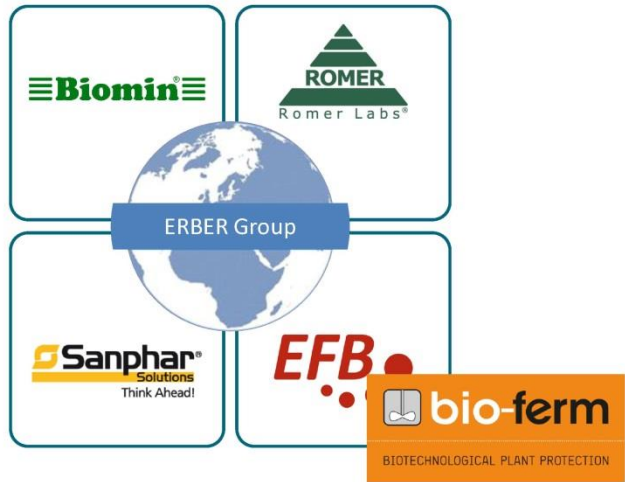


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ERBER Group is a group of healthy and profitable businesses which are aligned for organic growth on a global scale and show a strong ability to innovate



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Science cluster Tulln:



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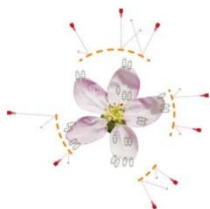
- 2005: Start with the dossier for Annex I inclusion – 1.5 employees
Emergency use permits in several EU countries
Tox, Ecotox, Fate, Field trials
- 2007: submission of the dossier Blossom Protect™, start development Botector®
- 2009: Provisional registration of Blossom Protect™ and Botector® in Austria
- 2012: Registration and entry into the U.S. market
- 2014: USA: Blossom Protect™ on 6.000 ha in use
- 2014: Cooperation with Nufarm in Australia, France, Portugal, Canada
- 2017: 8 employees (+ Erber group in the back)

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Blossom Protect™



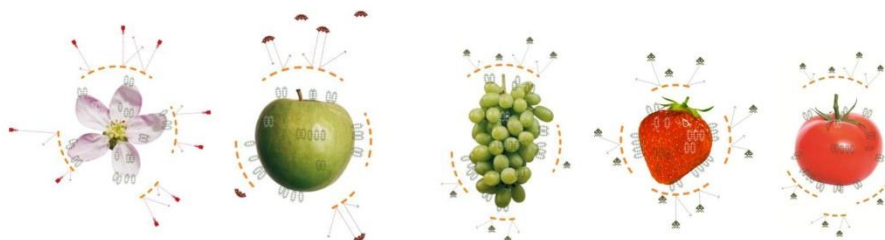
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Blossom Protect™™

Botector®®

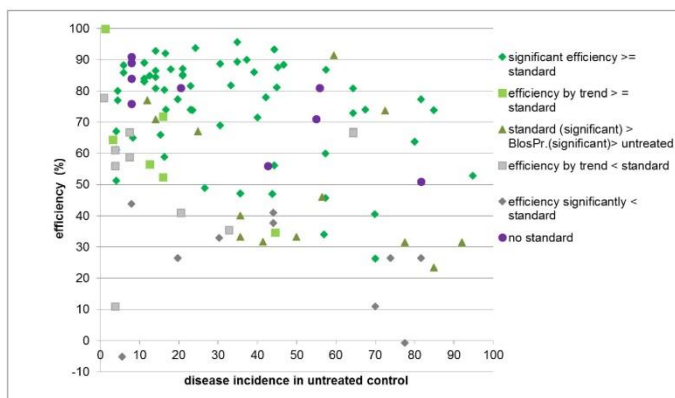


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Blossom Protect™ against fire blight:
110 trials 2003-2016



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Scale up the production:



Marketing:



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Europe



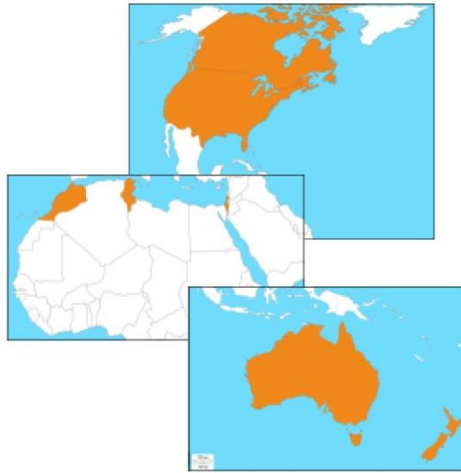
- < 2014 **Provisional Registrations**
(Art. 8(1) | Dir. 91/414) and
Emergency Use Permits
(Art. 53 | Reg. 1107/2009)
Final registrations (not EU)
- 2014-01 **EU Approval of *A. pullulans***
- 2014-07 **Final Registrations**
(zonal procedure, pending in
C-EU and S-EU)

Transition period:
Provisional Registrations
remain valid until final registration
(e.g. Austria, Belgium, Netherlands,
Poland, Portugal...)
Emergency Use Permits

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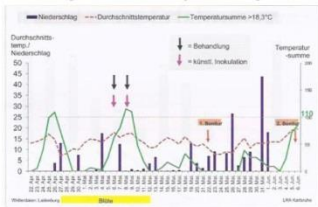
- Canada**
 - ✓ Blossom Protect™ since 2012
 - ✓ Botector® since 2014
- United States**
 - ✓ Blossom Protect™ since 2012
 - ✓ Botector® since 2012
- Morocco**
 - ✓ Botector® since 2009
- Tunisia**
 - ✓ Blossom Protect™ since 2016
 - Botector® *pending* since 2016
- Israel**
 - ✓ Blossom Protect™ Research Permit
- Australia**
 - Botector® *pending* since 2016
- New Zealand**
 - Blossom Protect™ *pending* since 2014

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Conclusion:
Fire blight is a tricky pathogen:



Relevant fire blight infections in Europe: 2007, 2012.

Aureobasidium pullulans DSM 140941 and 14940 no youngsters anymore:
 (1989) - 2005 - 2017: 28 years
 some million € governmental foundation, some million € industry investment



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Presentation 9

Niche Uses of Invertebrate biocontrol agents *Lieselot van der Veken (Biobest, Westerlo, Belgium)*



Niche Uses of Invertebrate biocontrol agents and regulation of exotic IBCA's; status, hurdles and prospects

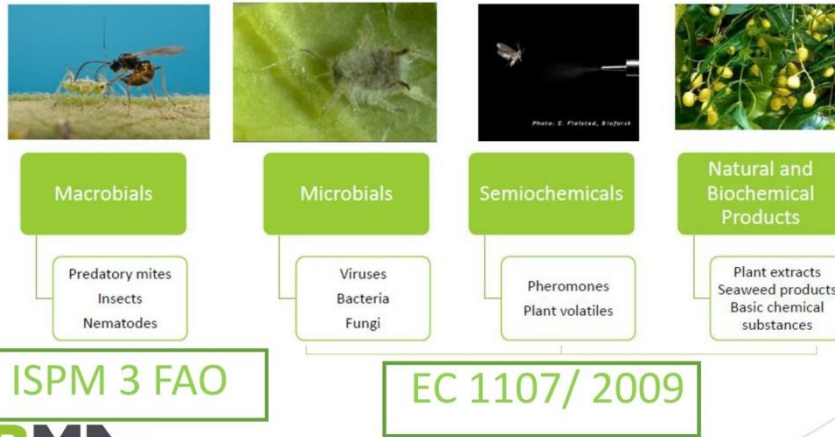
Dr. Lieselot Van der Veken (Biobest NV)
Chairwoman Invertebrates Biocontrol Agents professional group IBMA
OECD EGBP Seminar June 26th 2017



Biocontrol's (BC) offer:

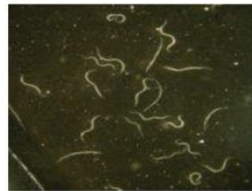


IBMA: 4 professional groups according to product categories



IBCA's

- Invertebrate Biological Control Agents include insects, entomopathogenic nematodes and predatory mites



The cradle of commercial biocontrol

KOPPERT
BIOLOGICAL SYSTEMS

1967

- Jan Koppert- cucumber grower
- Chemical PPPs gave health and resistance problems
- Looking for alternatives
- *Phytoseiulus persimilis* against spidermite (CH)
- *Encarsia formosa* against whitefly
- Positive results and effects



Why BC solutions are highly specific and often restricted to niche use

- High costs compared to market potential
- Economic potential of single products often does not exceed € 0,2 mio
- 1107/2009 EC regulated products often do not make the cut when registration costs come in the picture
- Imidacloprid turnover 2003: 590 mio € (Agrow 2004) commensurates with estimated registration cost of chemical PPPs (€ 200 mio),

• **Is this the case for any BCA?**



Ehlers, 2011

Why IBCAs are highly specific and often restricted to niche use

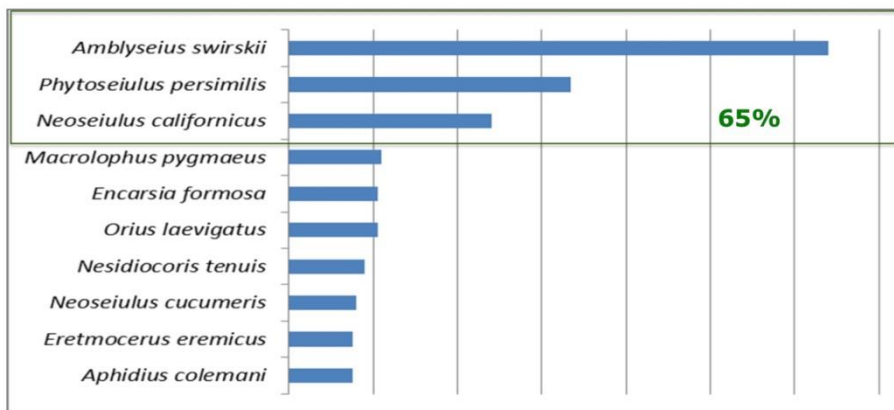


- 2000: BC market share were 55% IBCAs and 26% Microbials
- Economic potential of single products often limited
- Host specificity of IBCAs (eg. *Phytoseiulus persimilis* vs. *Tetranychidae*, parasitoids)
- Successful introduction is highly depended on technical support
- Limited shelf life requires high demanding distribution logistics
- Regulatory hurdles: Convention of BioDiversity CBD



Ehlers, 2011

Predatory mites most important IBCA's



Top-10 of biocontrol agents used in greenhouses (turnover)

J Klapwijk

Phytoseiulus persimilis against spidermite in tomato and strawberry



Source: Biobest



Highly specific uses of IBCAs in niche markets



Source: Entocare

Regulation of IBCAs



Convention on Biological Diversity

International Convention of Biodiversity (CBD 1992)

Ratifications: (# 194) Almost all EU countries, S-AM, ~~(USA)~~

1 Conservation of Biological diversity

"prevent the introduction of all alien species and, when prevention fails, to control as far as possible species that threaten indigenous ecosystems, habitats or species"

2 Sustainable use of biological components

3 ABS (Access and Benefit Sharing)



SUD EC 128/2008

- Art. 14 '*Member States shall take all necessary measures to promote low pesticide-input pest management, **giving wherever possible priority to non-chemical methods** so that professional users of pesticides switch to practices and products with **the lowest risk to human health and the environment** among those available for the same pest problem*'



IBCA Regulation history:

- **1996** FAO ISPM 3 (IPPC)
- **1997** EPPO / CABI on Safety and Efficacy of Biological Control in EU: endorsement ISPM 3
- **1999** EPPO Guidelines for the first import of exotic BCAs for research under contained conditions
- **2000** EPPO Guidelines for import and release of exotic BCAs
- **2002** EPPO positive list with IBCAs widely used in the EPPO region
- **1998-2002** ERBIC; detailed criteria for RA and IBCA ranking (safety)
- **2003** OECD Guidance for information requirements for IBCAs
- **2003** IOBC/WPRS Commission for the Harmonisation of Regulation of IBCA's
- **2005** FAO: revised version of ISPM 3
- **2006** Bigler *et al.* 2006: book as framework for ERA of IBCAs
- **2006-2008**: REBECA (EU Policy Support Action)



(Ehlers, 2011)

How to perform ERA for IBCAs?

Identify risks of introducing exotic natural enemy

- **Establishment** and/or **dispersal** in non-target habitat
- Non-target **host range**
- (In) direct effects on **non-target organisms**

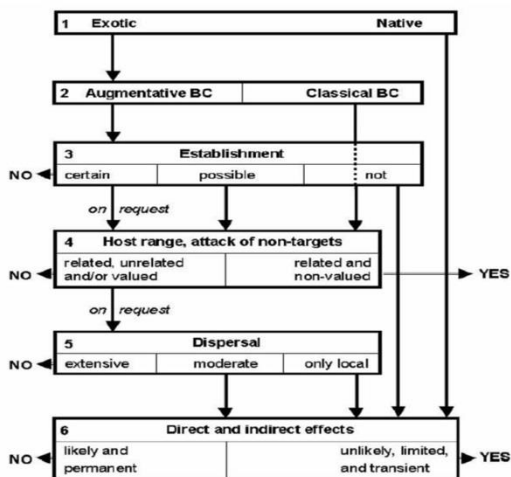
Determine likelihood and magnitude of each of the risks

Quantify risk and apply cost-benefit analysis (**also for other control methods!!!**)

(Van Lenteren, 2006)



Stepwise risk assessment : from 5 to 1 scheme



- Clearly good or bad species are discovered early in evaluation (saves resources)
- Only doubtful species go through whole evaluation
- Useful for quick scan or comprehensive evaluation

Van Lenteren, 2006



Literature

<http://archives.eppo.org/EPPOStandards/biocontrol.htm>

European and Mediterranean Plant Protection Organization
Organisation Européenne et Méditerranéenne pour la Protection des Plantes

Safe use of biological control
Sécurité de la lutte biologique

Import and release of non-indigenous biological control agents

Specific Scope

This standard gives guidelines for the import, release and regional application procedures for non-indigenous biological control agents (BCAs).

Specific approval and amendment

Revisions approved in 2010-09.

Introduction

Non-indigenous organisms, including biological control agents, may pose risks to agricultural and natural ecosystems if they establish in the environment. Their introduction into countries should be done with great care after assessment of the risks. The release ('historical liberation into the environment', IBC, 1995) of a non-indigenous biological control agent often follows a period in which relevant research has been carried out. The first import, for research, should have been carried out following the notification procedure of EPPO Standard PM 6/1 *First import of exotic biological control agents for research under controlled conditions*, and the research will have provided information in support of the safety and efficacy of the organism when it is in due course released. This guideline is mainly concerned, therefore, with the release of biological control agents after a period of research, either in the importing country, or in another country, notified to the EPPO member state, or in another country, notified to the EPPO member state, or in another country, notified to the EPPO member state.

The requirements for release of a biological control agent are more severe than for first import for research purposes. If the organism is to be released for classical biological control, it is intended that it should establish itself and control one or more pests, possibly permanently. If it is intended to be used for immediate release or for seasonal establishment, it will be released on an experimental scale first, then separately at full scale¹ and the risks arising from this release should be estimated according to this Standard. The relevant precautions apply whatever the scale of the first release, as undesirable consequences may be irreversible.

ISPM No. 3 (*Guidelines for the export, shipment, import and release of biological control agents and other beneficial organisms*) provides that Governments should designate a National Authority responsible for implementation. For the purpose of import and release of non-indigenous biological control agents, this National Authority should function as appropriate official receiver. Each country should decide what type of submission



PM 6/2 (2)

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ASSESSING RISKS OF RELEASING EXOTIC BIOLOGICAL CONTROL AGENTS OF ARTHROPOD PESTS

J.C. van Lenteren,¹ J. Bale,² F. Bigler,³ H.M.T. Hokkanen,⁴ and A.J.M. Loomans⁵

¹Laboratory of Entomology, Wageningen University, 6700 EH, Wageningen, The Netherlands; email: j.c.vanlenteren@wur.nl

²School of Biosciences, University of Birmingham, Birmingham B15 2TT, United Kingdom; email: j.j.bale@bham.ac.uk

³Swiss Federal Research Station for Agroecology and Agriculture, Zürich CH 8046, Switzerland; email: franc.bigler@fhnw.ch

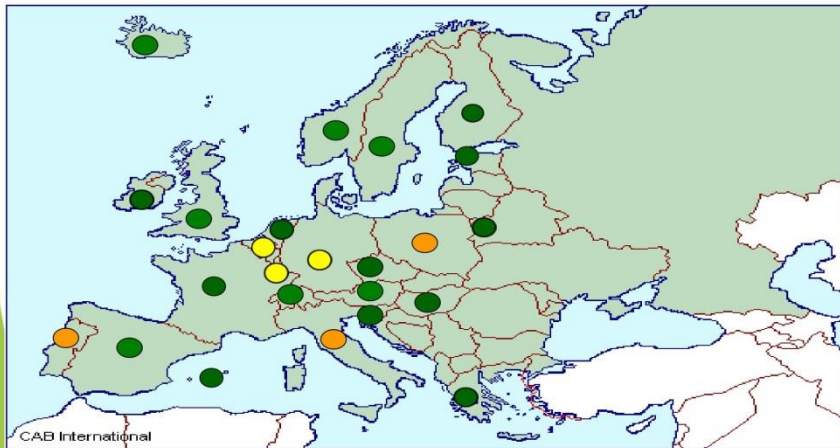
⁴Department of Applied Biology, University of Helsinki, FIN-00014, Finland; email: hehokkan@mappi.helsinki.fi

⁵Section Entomology, Plant Protection Service, 6700 HC Wageningen, The Netherlands; email: a.j.m.loomans@minisc.nl

Key Words: environmental risk assessment, host range, establishment, dispersal, nontarget effects

Abstract: More than 5000 introductions of about 2000 species of exotic arthropod agents for control of arthropod pests in 196 countries or islands during the past 120 years rarely have resulted in negative environmental effects. Yet, risks of environmental effects caused by releases of exotics are of growing concern. Twenty countries have implemented regulations for release of biological control agents. Soon, the International Standard for Phytosanitary Measures (ISPM3) will become the standard for all biological control introductions worldwide, but this standard does not provide methods by which to assess environmental risks. This review summarizes documented nontarget effects and discusses the development and application of comprehensive and quick-scan environmental risk assessment methods.

Status of national regulation in European countries:



- Implemented (16)
- In preparation (2)
- No regulation



International Regulation



- NAPPO region: NAPPO application: US, CAN and MEX
- Rest of the world : country specific (often PRAs) **ISPM 3**



Bottlenecks

- Lack of taxonomic reports
- All IBCA's are seen as potential IAS
- Variability in experience with authorities
- Procedure not transparent
- Responsibilities of dossier evaluation unclear
- Product specific regulation with biopesticide- like procedures
- Subspecies interpretation of native
- Lack of full implementation of EPPO guidelines
- Different formats of (EPPO) application form
- Lack of clarity about host range testing protocols



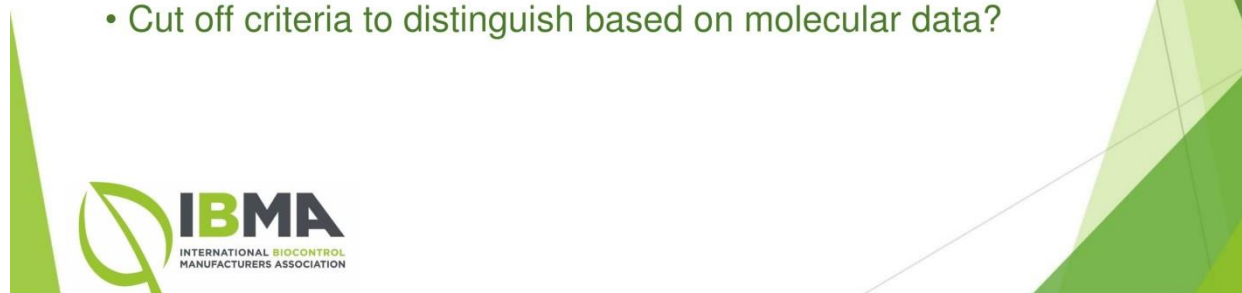
1 Interpretation of native below species level

'National biodiversity'



Considerations

- Added value for environmental safety?
- How to define 'national' species?
- Cut off criteria to distinguish based on molecular data?



IBMA position paper on the interpretation of 'native' is available



Position paper on the interpretation of 'native' in invertebrate biocontrol agent regulations

IBMA member companies produce a broad range of solutions for the biological control of pests and diseases. These products provide economically competitive alternatives to the use of Plant Protection Products, and as such generate considerable ecological benefits. As an ecologically responsible industry it is obviously vital to us that our products have low environmental impact. For this reason, IBMA has engaged early-on with academic experts in the field of biocontrol to pro-actively develop stringent guidelines for ecological impact assessment of non-native species. These guidelines were published as EPPO standards PM 6/1(1) First import of exotic biological control agents for research under contained conditions and PM 6/2(2) Import and release of non-indigenous biological control agents. Our industry has complied with these standards to warrant the ecological safety of our natural pest control solutions. We only produce and market natural species, using material for our rearing as it has been collected from nature. Our industry has an excellent record in providing environmentally benign and acceptable solutions for crop protection. By providing alternatives for registered plant protection products, important ecological benefits have been realized.

In various European countries we work together with the authorities to develop appropriate and workable regulations that allow for a sound environmental impact assessment, without generating unnecessary hurdles to making our ecological solutions available to farmers. As such we offer to work with national authorities in order to avoid the potential risks associated with the use of non-native species.



2 Studies on request for non-native species

- Efficacy data for new applications: TBD
- No adoption of the EPPO positive list as such



3 Procedural hurdles

- Efficacy data per crop
- Invertebrate registration falls under national plant protection law and is treated in a biopesticide-like manner
- Procedures overshadow the fairly feasible content of a dossier



4 Good practice

- Balanced registration application; based on EPPO list (PM 6/3)
- Clear procedures
- Open Communication with evaluators
- Application dealt with in timely matter



Prospectives

- Harmonized IBCA regulation within an ecological zone context (relevant a/biotic parameters limiting species distribution)



Species distribution or environmental niche = abstract multidimensional space, in which a set of biotic and abiotic conditions allow a species to maintain a viable population (Hutchinson, 1957; Schnitzler *et al.*, 2012).



EPPO standard PM 6/3: 'Positive list'

List of biological control agents widely used in EPPO region, created in 2001

- Facilitates decisions on import/ release of BC agents within EPPO
- First listings based on expert judgement: Quick scans
- Joint EPPO-IOBC panel: updating of list
- Criteria:
 - Native in large part of EPPO region or
 - used in 5 EPPO countries for at least 5 years with
 - no reported negative environmental effects or significant non-target effect
- Removal of species when it does no longer meet criteria (Appendix 3, documented!)



- Use EPPO list as a positive list with safe IBCA's
- Risk categories: ranking according to risk:
 - *Develop tools based on these categories: the safer the category, the lesser assessment required*
 - *For specialist parasitoids less data required as for generalist predators*



- Expected vs perceived risk



Positive list and harmonized application format in agro-ecological zone context with relevant (a)biotic parameters limiting natural species distribution

according to regional IPPC offices:

- NAPPO
- OIRSA, CA, COSAVE,
- EPPO
- NEPP0, IAPSC
- PPPO, IAPSC, APPPC



Species distribution or environmental niche = abstract multidimensional space, in which a set of biotic and abiotic conditions allow a species to maintain a viable population (Hutchinson, 1957; Schnitzler *et al.*, 2012).

Position paper: Why 'national species' do not make sense in case of IBCA's

- 1. Widespread genetic exchange (highly mobile insects)
- 2. No added protection to the national flora and fauna
- 3. Seriously hamper the development of clean and safe alternatives for crop protection
- 4. Unfeasible to have production plant in each country
- 5. Unconstitutional in terms of European laws on free trade to favor national producers over other EU producers.



Presentation 10

The US approach to the registration of highly specific biocontrol products

Shannon Borges (Environmental Protection Agency, Washington DC, United States)

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

June 26, 2017

The 8th Expert Group on BioPesticides Seminar
Paris, France

Shannon Borges
Senior Scientist
Biopesticides and Pollution Prevention Division
Office of Pesticide Programs
U.S. Environmental Protection Agency



Biopesticides in the U.S.

- Biopesticides are derived from natural materials
- In the U.S., biopesticides fall into three main categories
 - Microbial Pesticides
 - Biochemical Pesticides
 - Plant Incorporated Protectants (PIPs)



Microbial Pesticides

- Microorganisms with pesticidal effect
- Consist of:
 - Eukaryotic microorganisms (e.g., protozoa, algae, fungi)
 - Prokaryotic microorganisms (e.g., bacteria)
 - Autonomous replicating microscopic elements (e.g., viruses)
- Target various pests
 - Insects
 - Bacterial and fungal plant diseases
 - Plants
 - Nematodes



Microbial Pesticides

Examples of Microbial Pesticides:

Bacteria

- *Bacillus thuringiensis* subspecies
- Other *Bacillus* species
- *Pseudomonas* species
- *Streptomyces* species
- *Agrobacterium* isolates

Fungi

- *Beauveria bassiana*
- *Trichoderma* species
- *Clonostachys rosea*

Baculoviruses

- *Helicoverpa zea* NPV
- *Cydia pomonella* GV

Plant viruses

- Tobacco mild green mosaic tobamovirus (TMGMV)

Yeast

Protozoa

GE microbes

Products of microbes



Biochemical Pesticides

- Naturally occurring substance or synthetically derived equivalent
- History of human exposure with minimal toxicity
- Non-toxic mode of action to target pest(s)
 - Desiccant
 - Suffocating agent (e.g., soybean oil)
 - Abrasive agent (e.g., diatomaceous earth)
- Determined by Biochemical Classification Committee



Biochemical Pesticides

Examples of Biochemical Pesticides:

Semiochemicals (Pheromones)

- n-Tetradecyl acetate – a mating disruptor for codling moth

Insect growth regulators

- Azadirachtin

Herbicides

- Vinegar (acetic acid)

Repellents

- Coyote and fox urine - repel deer and other animals
- Capsaicin – repel birds, mammals

Floral attractants and Plant Volatiles

- 1-Octen-3-ol attractant in electric bug traps

Insect & Nematode Control

- Soybean oil

Plant pathogen & Microbial Control

- Potassium silicate (induces Systemic Acquired Resistance)
- Laminarin (induces Systemic Acquired Resistance)



Highly Specific Biopesticides

- Biopesticides can be highly specific
 - Pheromones
 - Certain baculoviruses
- Others are more “broad spectrum”
 - Fungal entomopathogens
 - Biochemical insecticides (e.g., neem oil, diatomaceous earth)
- Others can be somewhere in the middle
 - *Bacillus thuringiensis* – subspecies can target specific insect orders, but within those orders there are nontargets of concern
- In general, the more targeted the biopesticide for the intended pest, the more targeted the data requirements
 - Must be supported



How EPA Views Benefits of Biopesticides

- Generally pose fewer risks compared to other types of pesticides
- Low environmental persistence leading to reduced potential for exposure
- Can be target specific
- When used as part of IPM program, can decrease use of conventional pesticides
- When used in rotation with conventional pesticides, can reduce incidence of resistance development
- Often require reduced restricted entry interval and have no pre-harvest interval – greater flexibility for growers
- May address minor crop or obscure pest control needs that are not addressed by conventional pesticides



BPPD's Role Within OPP

- Biopesticides and Pollution Prevention Division - created to facilitate registration of biopesticides to help bring them to the market
 - Microbial Pesticides Branch
 - Biochemical Pesticides Branch
 - Environmental Stewardship Branch
- Committed to encouraging development and use of low risk biological pesticides as alternatives to conventional pesticides
- Employs multiple measures to facilitate application process
 - All science and registration activities are performed within BPPD
 - Shorter registration timelines
 - Targeted data requirements
- Promotes IPM initiatives and coordinates Pesticide Environmental Stewardship Program



Pesticide Registration – Primary Statutes

- Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA)
 - Legal standard: No unreasonable adverse effects to man or the environment
 - Considers both risks and benefits
 - Lower toxicity, targeted efficacy = reduced risks, increased benefits
- Federal Food, Drug, and Cosmetic Act (FFDCA)
 - Legal standard: Reasonable certainty of no harm
 - Establishes tolerances (maximum residue level) in or on food or animal feed
 - Most biopesticides are granted tolerance exemptions
- Pesticide Registration Improvement Act (PRIA) and extensions
 - Establishes deadlines for registration
 - Requires fees for registration activities
 - Biopesticides – fees are reduced, timelines shorter
 - Small business fee waivers allowed



Pesticide Data Requirements

- **Product Characterization**
 - Identity of the active ingredient (a.i.), product formulation, discussion of formation of impurities, manufacturing process, analysis of samples, physical and chemical characteristics
- **Human Health**
 - Acute and subchronic toxicity, pathogenicity (microbial pesticides), developmental toxicity, mutagenicity
 - Food safety assessment (residue data or tolerance exemption)
- **Environmental**
 - Nontarget organism toxicity, pathogenicity (microbial pesticides)
 - Environmental fate
 - Endangered species

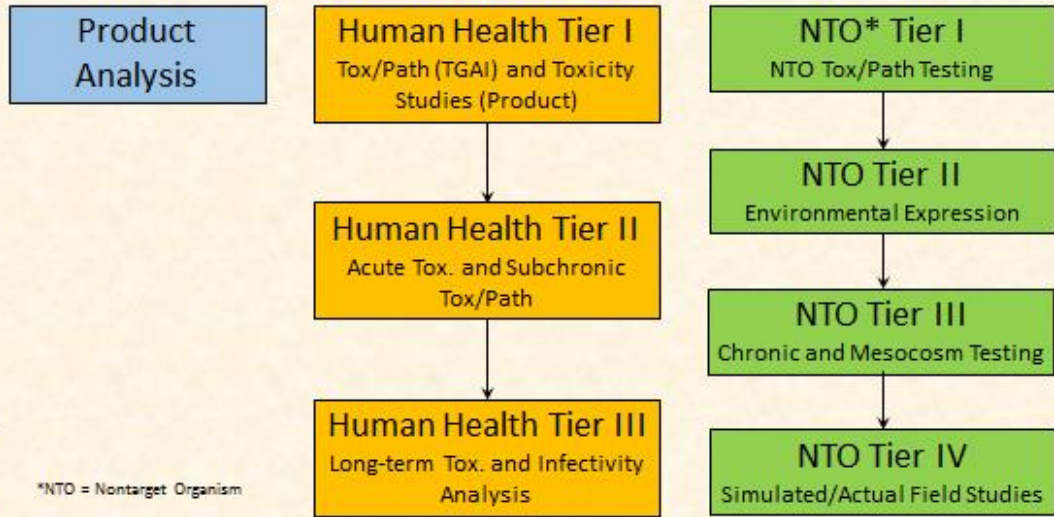


Pesticide Data Requirements

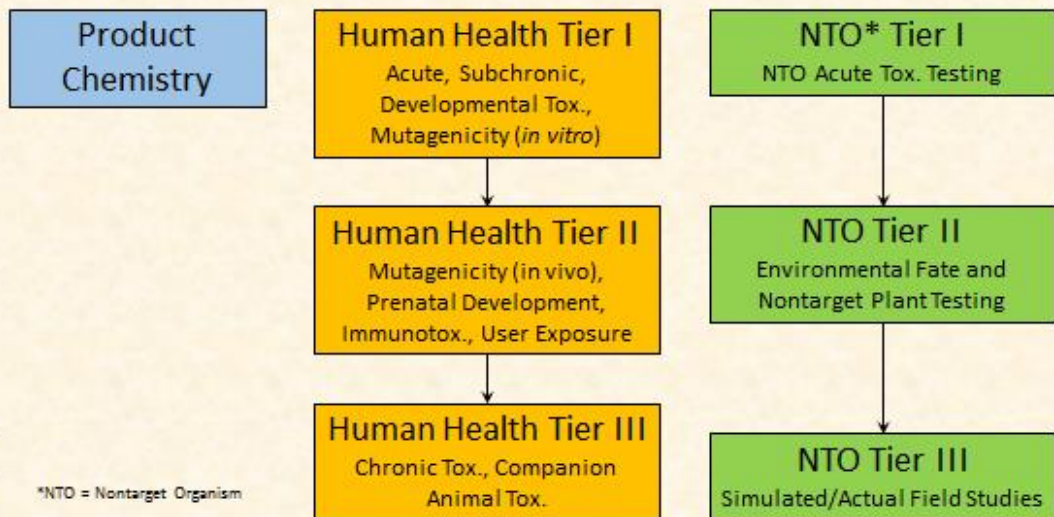
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 - Environmental fate
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Microbial Pesticide Data Requirements



Biochemical Pesticide Data Requirements



How To Satisfy Data Requirements

- Conduct a study in accordance with EPA guidelines
- Cite a study from the literature
- Cite existing data from similar active ingredients/products (“bridging” rationale or studies may be needed)
- Provide a scientific rationale to address the requirement
 - Cite scientific literature or other sources of data
 - Physical and/or biological characterization of the active ingredient and product formulation
 - Lack of exposure
- Many data requirements can often be addressed by means other than conducting a guideline study



Conclusions

- In the U.S., biopesticides includes microbial and biochemical pesticides (also PIPs)
- Many biopesticides have niche uses
- EPA recognizes the benefits of biopesticides, including that they generally have a low risk profile
- EPA’s approach to regulation of biopesticides is aimed at facilitating and streamlining their registration
 - Lower registration fees; shorter time frames
 - Reduced, more targeted data requirements
 - Pre-registration consultations provide a.i.- and product-specific advice on data requirements
- <https://www.epa.gov/pesticides/biopesticides>



Presentation 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)



The Ctgb approach to the registration of highly specific biocontrol products

Jacobijn van Etten

OECD, June 26th 2017

ctgb

Highly specific biocontrol

- Less risk
- Fit for IPM
- Contribute to diversity of modes of action
- Small markets
- Relative high burden of development and regulatory cost

ctgb

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Highly specific biocontrol

- Highly desirable,
- in line with EU and national politics, consumer wishes, grower needs

Increase feasibility

- Orphan drug law?
- New procedure for tiny uses?

ctgb



Ctgb experience niche products

Three examples:

- Dutch trig
- Mild Pepino Mosaik virus VC1 and VX1
- Semiochemicals (SemiosNET)

ctgb



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Dutch Trig

- protective agent based on *Verticillium albo-atrum* to prevent the Dutch elm disease.
- injected into the trunk of the tree using a special tree-injection-device
- no exposure
- no studies required for fate, ecotox and human tox
- sound justification for the waivers

ctgb



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Mild Pepino Mosaik virus VC1 and VX1

- an inoculant that induces resistance to prevent the infection by virulent PepMV in tomatoes in greenhouses
- Ctgb RMS of substances
- Full data package for human tox
- proposed use of direct rubbing of leaves of plants within a greenhouse
- exposure to the environment is not relevant.

ctgb



Mild Pepino Mosaik virus VC1 and VX1

- The host range of PepMV is mainly restricted to plant species of the Solanaceae family
- Question: we had to justify that the (plant!) virus could not be transmitted to humans and animals

ctgb



Semiochemicals

- Feromones generally effective at very low rates, often comparable to levels that occur naturally
- New guidance makes it possible to do a very limited evaluation
- non-testing strategies if the applicant can provide a justified rationale
- read-across

SemiosNET

- SCLP group
- Highly specific; very limited assessment

ctgb



Lessons highly specific products

- Explain the mode of action: exposure, extrapolation
- Understand biology: GreenTEAM
- Be pragmatic where possible, justified with sound science and/or long term experience
- Do we need new procedures for tiny uses (specific, low risk)?

ctgb



Experience from the Green Deal

Aim:

- To stimulate sustainable growth by collaboration between all stakeholders
- To resolve obstacles in the authorisation process
- To have more “green” products available for Dutch growers

ctgb



Experience from the Green Deal

Activities

- Pilot assessments of biopesticides
- Adapt organisation of Ctgb (GreenTEAM for intake and assessment)
- Contribute to harmonisation in EU

ctgb



Results Green Deal

- Decision taken on 6 product dossiers, important steps in two substance dossiers
- A successful workshop on human toxicology “micro-organisms in PPP’s” >> guidance by COM
- A harmonizing workshop on efficacy for biopesticides organised together with EPPO and NPPO>> New EPPO guidance (sept 2017)
- Evaluation manual Biopesticides

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Lessons learned Green Deal

- A Pre Submission Meeting is important to clarify possibilities and difficulties
- High quality dossiers support speedy assessments
- A specialised “greenTEAM” of assessors for intake and assessment
- Efficacy assessment should be in line with nature of products
- Tailor made solutions for dossiers

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How to get your business case right?

for green innovation

outside 1107/2009

- Biostimulants
- Basic substances
- Illegal use

within 1107/2009

- Low Risk
- Specific guidances for biopesticides
- New procedural solutions needed??

ctgb



Concerns

- 1107/2009 should enable green innovation
- Large differences in regulatory requirements of biostimulants and low risk products

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Solutions (?)

- 120 days for zonal low risk product dossiers
 - > criteria are clear
 - > development of guidance
- Highly specific biopesticides with low risk profile (tiny uses) might ask for different requirements
- Enforcement of non-authorized products

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