Biopesticides and development in new products
crops

30 – 40 %
lost
before harvest

>10 %
after harvest
Food and Agriculture Organisation of the United Nations

FAO promotes biological pest control agents and IPM/IVM

“Pro-actively favouring registration of less hazardous products where such alternatives are viable and available”
Multiple modes of action

- Kill host
- Competition
- Stimulate plant defenses
- Confer plant resistance
What is driving the markets

Who wants the products?

Why?

What do the products offer?
DRIVERS for farmers and growers

- Efficacy – killing target pest
- Efficacy - yield and quality improvement
- Host specificity
- Use in IPM programmes
- Useful for resistance management
- Useful for residue management
- Growers - crop management
- Worker safety
- Favourable environmental footprint
- Use in organic production
Natural forces already manage pest populations

1 cabbage aphid + 1 year = 250 million tonnes

Information and photo: courtesy of D. Chandler, Warwick Crop Centre and eplantswholesale.com.au respectively
Sustainable crop production and protection

Biology
Ecology
Population management
### Plant Protection Product Registration EU - timelines

<table>
<thead>
<tr>
<th>1107/2009</th>
<th>Year 1</th>
<th>Year 2</th>
<th>Year 3</th>
<th>Year 4</th>
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<tr>
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<td>1 1 1 2 1 1 2 1</td>
<td>1 1 1 2 1 1 2 1</td>
<td>1 1 1 2 1 1 2 1</td>
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<tr>
<td>A.S. Dossier Submission</td>
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<tr>
<td>Completeness check</td>
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<tr>
<td>Rapporteur evaluation</td>
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<tr>
<td>DAR completed</td>
<td></td>
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<tr>
<td>EFSA comment on DAR</td>
<td></td>
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<tr>
<td>EFSA peer review</td>
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<tr>
<td>Standing committee vote</td>
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<tr>
<td>Positive List (Annex I)</td>
<td></td>
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<tr>
<td>Application - zonal product</td>
<td></td>
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<tr>
<td>Zonal evaluation</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Country evaluation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Product approval</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

- Orange boxes indicate first the SANTE vote then it takes 6 months to be ratified
- Purple box indicates when product can be sold
- This is a broad schematic – there can be some variability depending on a.s.
- There can be some extra time added e.g. during active substance review if an expert consultation if needed
Aspects of risk

EU
Precautionary principle

USA
Generally Regarded As Safe (GRAS)*
EU biopesticide actives trebled to $>120$ 2000-2015
Global biopesticide market increased over 200% 2000-2012.

Global market 2019 value over $6 billion.
Examples of nematode based ‘biopesticide’ products

<table>
<thead>
<tr>
<th>Active Substance</th>
<th>Product Name</th>
<th>Type of product</th>
<th>Target(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Steinernema feltiae</em></td>
<td>Nemasys</td>
<td>Entomopathogenic nematode</td>
<td>Sciartids, leafminer, WFT</td>
</tr>
<tr>
<td><em>Steinernema kraussei</em></td>
<td>Nemasys L</td>
<td>Entomopathogenic nematode</td>
<td>Vine weevil</td>
</tr>
<tr>
<td><em>Heterorhabditis megidis</em></td>
<td>Nemasys H</td>
<td>Entomopathogenic nematode</td>
<td>Vine weevil</td>
</tr>
<tr>
<td><em>Heterorhabditis megidis</em></td>
<td>Lavanem</td>
<td>Entomopathogenic nematode</td>
<td>Vine weevil</td>
</tr>
<tr>
<td><em>Heterorhabditis megidis</em></td>
<td>Nemasys H</td>
<td>Entomopathogenic nematode</td>
<td>Grubs</td>
</tr>
<tr>
<td><em>Steinernema carpocasae</em></td>
<td>Nemasys C</td>
<td>Entomopathogenic nematode</td>
<td>Codling moth</td>
</tr>
<tr>
<td><em>Steinernema carpocasae</em></td>
<td>Nemasys C</td>
<td>Entomopathogenic nematode</td>
<td><em>Hylobius</em> sp., Lepidoptera</td>
</tr>
<tr>
<td><em>Steinernema carpocapsae</em></td>
<td>Capsanem</td>
<td>Entomopathogenic nematode</td>
<td>Lepidoptera</td>
</tr>
<tr>
<td><em>Phasmarhabditis hermaphrodita</em></td>
<td>Nemaslug</td>
<td>Slug parasitic nematode</td>
<td>Molluscs</td>
</tr>
</tbody>
</table>
Micro-organism biopesticides

Cydia pomonella granulosis virus  Pasteuria penetrans
Trichoderma harzianum  FUSARIAUM OXYSPORUM
Isaria fumosoroseus  Bacillus firmus
Clonostachys rosea  Coniothyrium minitans
Bacillus thuringiensis  Bacillus subtilis
Gliocladium catenulatum  Lecanicillium lecanii
Metarhizium anisopliae  Ampelomyces quisqualis
Trichoderma asperellum  Beauveria bassiana
# Microorganism bioinsecticides/nematicides examples

<table>
<thead>
<tr>
<th>Active Substance</th>
<th>Product Name</th>
<th>Target(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Adoxophyes orana</em> gv</td>
<td>Capex</td>
<td>Summer fruit tortrix</td>
</tr>
<tr>
<td><em>Bacillus firmis</em> strain I-1582</td>
<td>Flocter</td>
<td>Free-living nematodes</td>
</tr>
<tr>
<td><em>Bacillus thuringiensis var. israelensis</em> strain AM65-52</td>
<td>Vectobac 12AS</td>
<td>Chironomid larvae</td>
</tr>
<tr>
<td><em>Bacillus thuringiensis var kurstaki</em> strain ABST351</td>
<td>DiPel DF</td>
<td>Lepidoptera pests</td>
</tr>
<tr>
<td><em>Bacillus thuringiensis var kurstaki</em> strain EG2348</td>
<td>Lepinnox Plus</td>
<td>Lepidoptera pests</td>
</tr>
<tr>
<td><em>Beauveria bassiana</em> strain ATCC74040</td>
<td>Naturalis-L</td>
<td>Whitefly, thrips, spidermite</td>
</tr>
<tr>
<td><em>Cydia pomonella</em> Granulosis Virus</td>
<td>Carpovirusine</td>
<td>Codling moth</td>
</tr>
<tr>
<td><em>Cydia pomonella</em> Granulosis Virus</td>
<td>Cyd-X and</td>
<td>Codling moth</td>
</tr>
<tr>
<td></td>
<td>Cyd-X Extra</td>
<td></td>
</tr>
<tr>
<td><em>Lecanicillium muscarium</em> strain V-6*</td>
<td>Mycotal</td>
<td>Whitefly, thrips, scale</td>
</tr>
<tr>
<td><em>Metarhizium anisopliae</em> strain F52</td>
<td>Met 52 Granular</td>
<td>Black vine weevil</td>
</tr>
</tbody>
</table>
What are botanicals?

From the EU Botanical Guidance document (rev. 8)
A 'botanical' active substance: obtained by subjecting plants or parts of plants to a process such as pressing, milling, crushing, distillation and/or extractions. The process may include further concentration, purification and/or blending, provided that the chemical nature of the components is not intentionally modified/ altered by chemical and/or microbial processes.

The plants are live or dried plants or parts of plants, including fruits and seeds but excluding genetically modified plants.
# Botanicals examples

<table>
<thead>
<tr>
<th>Active Substance</th>
<th>Product Name</th>
<th>Type of product</th>
<th>Target(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maltodextrin</td>
<td>Eradicoat</td>
<td>Biorational</td>
<td>Mites, aphids, whitefly</td>
</tr>
<tr>
<td>Maltodextrin</td>
<td>Majestik</td>
<td>Biorational</td>
<td>Mites, aphids, whitefly</td>
</tr>
<tr>
<td>Fatty Acids</td>
<td>Savona</td>
<td>Fatty Acids</td>
<td>Whitefly, thrips, mite, aphids</td>
</tr>
<tr>
<td>Garlic concentrate</td>
<td>Eagle Green Care</td>
<td>Botanical</td>
<td>Free living nematodes</td>
</tr>
<tr>
<td>Cold pressed orange oil</td>
<td>Prev-AM</td>
<td>Botanical</td>
<td>Insects &amp; fungi</td>
</tr>
</tbody>
</table>
Pheromones - semio-chemicals

Semio-chemicals “... chemicals emitted by plants, animals, and other organisms - and synthetic analogues of such substances - that evoke a behavioural or physiological response in individuals of the same or other species”

Pheromones are semio-chemicals that modify the behaviour of other individuals of the same species

Straight-chained lepidopteran pheromones (SCLPs) ... unbranched aliphatics having a chain of 9-18 carbons, containing < 3 double bonds, ending in an alcohol, acetate or aldehyde functional group. This structural definition encompasses the majority of known pheromones produced by insects in the order Lepidoptera, which includes butterflies and moths.
Control strategies using semio-chemicals

**Mating disruption**
- Pheromones are released to interfere with the ability of male insects to locate females of the same species,
- Disrupting mating and controlling the damage to crops inflicted by the hatching larvae.

**Lure and Kill**
- Again a simple concept: bring the insects to the insecticide
- Key is to attract females

**Mass Trapping**
- Simple Concept: trap as many insects as you can
- Key is to attract and trap females
- Kairomones becoming increasingly important
Technology innovation areas

Active substances

Production

Formulations

Delivery
<table>
<thead>
<tr>
<th>Activity</th>
<th>$ Millions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research and Development</td>
<td>3 - 5</td>
</tr>
<tr>
<td>Formulation</td>
<td>1 - 2</td>
</tr>
<tr>
<td>Development</td>
<td>2-3 (USA)</td>
</tr>
<tr>
<td></td>
<td>20 - 30 (ROW)</td>
</tr>
<tr>
<td>Registration</td>
<td>1 (USA)</td>
</tr>
<tr>
<td></td>
<td>3 - 10 (ROW)</td>
</tr>
<tr>
<td>Product launch</td>
<td>0.1 - 20</td>
</tr>
<tr>
<td></td>
<td>(over &gt; 50 global)</td>
</tr>
</tbody>
</table>

**EU registration – about 5 years**
Research

Macro-organisms

EPN

Micro-organism

Fungi

Bact.

Phage

Virus

Semio-chems

Botanical

Crop Protection

Very knowledge intensive

Agro-ecosystem

Monitoring

Crop botany
Microbial production systems

Solid state
Mainly fungi

All fermentation material
May be +/- metabolites - involved in activity
Metabolites in product. Increased complexity for MoA?

Spores only
No metabolites present
Metabolites only in situ (field) expression. Role in MoA?

Liquid state
Mainly bacteria

All fermentation material
May be +/- metabolites - involved in activity
Metabolites in product. Increased complexity for MoA?

Spores only
No metabolites present
Metabolites only in situ (field) expression. Role in MoA?

In vivo production
# Microbial innovations

<table>
<thead>
<tr>
<th></th>
<th>Cells</th>
<th>Media</th>
<th>Secondary compounds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common species</td>
<td>±</td>
<td>±</td>
<td>±</td>
</tr>
<tr>
<td>Product formulation - inert</td>
<td>±</td>
<td>±</td>
<td>±</td>
</tr>
<tr>
<td>New species</td>
<td>±</td>
<td>±</td>
<td>±</td>
</tr>
<tr>
<td>New MoA - endophytes</td>
<td>±</td>
<td>±</td>
<td>±</td>
</tr>
<tr>
<td>Split fermentation - solid</td>
<td>±</td>
<td>±</td>
<td>±</td>
</tr>
<tr>
<td>Split fermentation - solid + liquid</td>
<td>±</td>
<td>±</td>
<td>±</td>
</tr>
<tr>
<td>Split fermentation - liquid + liquid</td>
<td>±</td>
<td>±</td>
<td>±</td>
</tr>
<tr>
<td>Product formulation - storage</td>
<td>±</td>
<td>±</td>
<td>±</td>
</tr>
<tr>
<td>Product formulation - persistence on leaf</td>
<td>±</td>
<td>±</td>
<td>±</td>
</tr>
<tr>
<td>Product formulation - synergists</td>
<td>±</td>
<td>±</td>
<td>±</td>
</tr>
<tr>
<td>Co-packs - adjuvants</td>
<td>±</td>
<td>±</td>
<td>±</td>
</tr>
<tr>
<td>Additives</td>
<td>±</td>
<td>±</td>
<td>±</td>
</tr>
<tr>
<td>Technical features of active substances</td>
<td>$ Millions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>--------------------------------------------------------</td>
<td>------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No/low risk, no metabolites</td>
<td>1 - 5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low risk + metabolite</td>
<td>&gt; 5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Microbial metabolite (no micro-organism)</td>
<td>5-10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High risk metabolite (no micro-organism)</td>
<td>15-20</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Biopesticide delivery

Improved delivery systems (formulation, application, etc.) will not save an underperforming biopesticide but...

...performance of a biopesticide, as with a chemical pesticide, may be reduced substantially by a poor delivery system.

• Tank agitation is important.
• Nozzle choice and calibration
• Nozzle wear
• Tank and sprayline cleaning...

Information courtesy of Andrew Chapple
Business innovation areas

- Biocontrol producers and distributors
- Knowledge transfer
- Streamlined regulation
Biopesticide industries – smarter approaches?

Start-up

SME

Multi-national

Very knowledge intensive
Consequences?

Know-how
Diluted

Systems
Standardise

Variability
Quality?
Knowledge intensive – communication to farmers?

Crop protection

- Fungi
- Bacteria
- Virus
- Macro-organisms
- Insects
- EPN
- Synthetic Chemical pesticides
- Botanical
- Biorationale
- Semio-chems
- Monitoring
- Agro-ecosystem
- Crop botany
Regulatory innovation

Proportional

Relevant

Quicker

Cost effective
Recipe for success?

Employ systems biologists
Embrace variability
Good technology transfer
Maintain innovation
Directed by technology
Reflections

- Research investment
- Innovation
- Harmonised regulation
- Global grower demand
- Better advocacy
- Better technology transfer
Thank you for your attention