Biopesticides: integrating and optimising biologicals with chemicals
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”
“On the basis of Regulation (EC) No 1107/2009 and of this Directive, implementation of the principles of integrated pest management is obligatory and the subsidiarity principle applies to the way the principles for integrated pest management are implemented. Member States should describe in their National Action Plan how they ensure the implementation of the principles of integrated pest management, with priority given wherever possible to non-chemical methods of plant protection and pest and crop management.”

‘integrated pest management’ means careful consideration of all available plant protection methods and subsequent integration of appropriate measures that discourage the development of populations of harmful organisms and keep the use of plant protection products and other forms of intervention to levels that are economically and ecologically justified and reduce or minimise risks to human health and the environment. ‘Integrated pest management’ emphasises the growth of a healthy crop with the least possible disruption to agro-ecosystems and encourages natural pest control mechanisms.

‘non-chemical methods’ means alternative methods to chemical pesticides for plant protection and pest management, based on agronomic techniques such as those referred to in point 1 of Annex III, or physical, mechanical or biological pest control methods.
Alternative plant protection products

- Micro-organisms
- Botanicals
- DNA
- Semio-chemicals
- Biorationales?

Low Risk substances
Global biopesticide market increased over 200% 2000-2012

Global market 2019 value over $6 billion
Biocontrol investment

Syngenta, Novozymes Ink Deal To Commercialize Taegro

American Vanguard Invests in TyraTech Natural Product Technologies

From: Biopesticideindustryalliance.com
## Biopesticides – USA products

<table>
<thead>
<tr>
<th></th>
<th>Insecticide</th>
<th>Fungicide</th>
<th>Herbicide</th>
<th>Nematicide</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microorganism Bt</td>
<td>44</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Microorganism non-Bt</td>
<td>18</td>
<td>41</td>
<td>5</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Botanical</td>
<td>8</td>
<td>6</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Semio-chemical + pheromones</td>
<td>56</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Other</td>
<td>25</td>
<td>8</td>
<td>3</td>
<td>0</td>
<td>21</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>151</strong></td>
<td><strong>55</strong></td>
<td><strong>9</strong></td>
<td><strong>5</strong></td>
<td><strong>23</strong></td>
</tr>
</tbody>
</table>
## Biopesticides – EU active substances

### Updated Jan 2013

<table>
<thead>
<tr>
<th></th>
<th>Insecticide</th>
<th>Fungicide</th>
<th>Herbicide</th>
<th>Nematicide</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microorganism Bt</td>
<td>4</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>Microorganism non-Bt</td>
<td>12 (2)</td>
<td>15 (10)</td>
<td>0</td>
<td>1 (2)</td>
<td>0</td>
</tr>
<tr>
<td>Botanical</td>
<td>5 (4)</td>
<td>0 (4)</td>
<td>1</td>
<td>0</td>
<td>6 (1)</td>
</tr>
<tr>
<td>Semio-chemical</td>
<td>29</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>52 (6)</strong></td>
<td><strong>16 (14)</strong></td>
<td><strong>2</strong></td>
<td><strong>1 (2)</strong></td>
<td><strong>8 (3)</strong></td>
</tr>
</tbody>
</table>

### Updated October 2015*

<table>
<thead>
<tr>
<th></th>
<th>Insect</th>
<th>Fungi</th>
<th>Weeds</th>
<th>Nematodes</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Micro-organism Bt</td>
<td>9</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Micro-organism non-Bt</td>
<td>11 (2)</td>
<td>24 (9)</td>
<td>-</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Botanical</td>
<td>5 (2)</td>
<td>7</td>
<td>1</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Semio-chemical</td>
<td>28 (2)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Other</td>
<td>8</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
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<tr>
<td><strong>Total</strong></td>
<td><strong>61 (6)</strong></td>
<td><strong>32 (9)</strong></td>
<td><strong>2</strong></td>
<td><strong>3</strong></td>
<td><strong>7</strong></td>
</tr>
</tbody>
</table>

* Definition of biopesticide not fixed so approximate numbers only

Figures in bracket = pending

79 (25) = 104

106 (15) = 121
EU biopesticide actives trebled to >120 2000-2015
EU plant protection products – pending registration*

* October 2016
DRIVERS

• 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
Very knowledge intensive
Reductionist principles

Holistic principles

Systems biology

Complex
Multiple modes of action

Kill host

Competition

Stimulate plant defenses

Confer plant resistance

Endophytes – MoA?
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.
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.
Micro-organism biopesticides

*Cydia pomonella* granulosis virus  
*Pasteuria penetrans*

*Trichoderma harzianum*  
*Fusarium oxysporum*

*Isaria fumosoroseus*  
*Bacillus firmus*

*Clonostachys rosea*  
*Coniothyrium mimitans*

*Bacillus thuringiensis*

*Gliocladium catenulatum*  
*Bacillus subtilis*

*Lecanicillium lecanii*

*Metarhizium anisopliae*

*Trichoderma asperellum*

*Ampelomyces quisqualis*

*Beauveria bassiana*
Microorganisms - multiple modes of action

*Trichoderma* spp.

*Bacillus subtilis*

*Baculoviruses*

*Metarhizium* spp.

*Beauveria* spp.
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>
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</tbody>
</table>
## Biofungicides – UK

<table>
<thead>
<tr>
<th>Active Substance</th>
<th>Product Name</th>
<th>Target(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Ampelomyces quisqualis</em> strain M10</td>
<td>AQ10</td>
<td>Powdery mildew</td>
</tr>
<tr>
<td><em>Bacillus subtilis</em> strain QST713</td>
<td>Serenade ASO</td>
<td><em>Botrytis</em> spp.</td>
</tr>
<tr>
<td><em>Candida oleophila</em> strain O</td>
<td>Nexy1</td>
<td>Post harvest diseases</td>
</tr>
<tr>
<td><em>Coniothyrium mimitans</em> strain CON/M/91-08</td>
<td>Contans WG</td>
<td><em>Sclerotinia</em> spp.</td>
</tr>
<tr>
<td><em>Gliocladium catenulatum</em> strain J1446 (new species name <em>Clonostachys rosea</em>)</td>
<td>Prestop</td>
<td>Botrytis, soft rots</td>
</tr>
<tr>
<td><em>Lecanicillium muscarium</em> strain V-6*</td>
<td>Mycotal</td>
<td>Whitefly, thrips, scale</td>
</tr>
<tr>
<td><em>Peniophora gigantea</em></td>
<td>PG Suspension</td>
<td>PGR</td>
</tr>
<tr>
<td><em>Streptomyces griseoviridis</em> strain K61</td>
<td>Mycostop*</td>
<td>Soft rots</td>
</tr>
<tr>
<td><em>Trichoderma atroviridae</em> strain T34</td>
<td>T34</td>
<td><em>Fusarium</em> sp. on dianthus</td>
</tr>
<tr>
<td><em>Trichoderma harzianum</em> strain T22</td>
<td>Trianum P</td>
<td>Root diseases</td>
</tr>
</tbody>
</table>

* Not yet marketed in UK
Technology innovation areas

- Active substances
- Production
- Formulations
- Delivery
Society requires regulation

Consumer safety
Operator and worker safety
Environmental safety
Crop safety
Assure product quality
### 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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<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>
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<tr>
<td>EFSA comment on DAR</td>
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<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>
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<tr>
<td>Application - zonal product</td>
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<td>Zonal evaluation</td>
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<td>Country evaluation</td>
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<tr>
<td>Product approval</td>
<td></td>
<td></td>
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<td></td>
</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
Regulatory groupings

Out of scope
- Entomopathogenic nematodes
- Root symbionts

Registered PPP
- Microorganism
- Semio-chemicals
- Botanicals
- Biorationals
  - (acetic acid
    - fatty acids
    - Paraffinic oils)

Basic substances
- Not PPP but may be used for plant protection
Regulatory status?

- Plant strengthener
- Biostimulant
- Growth stimulant
- Biological inoculant

Label claims and packet contents ≠ out of scope
Biostimulants

There are proposed changes to the fertiliser regulations which potentially clarifies the boundary between ‘fertiliser’ biostimulants and PPP*

Of particular relevance for many microorganisms - from the Fertiliser Regulation:

(15) Certain substances, mixtures and micro-organisms, commonly referred to as plant biostimulants, are not as such nutrients, but nevertheless stimulate plants' nutrition processes. Where such products aim solely at improving the plants' nutrient use efficiency, tolerance to abiotic stress, or crop quality traits, they are by nature more similar to fertilising products than to most categories of plant protection products. Such products should therefore be eligible for CE marking under this Regulation and excluded from the scope of Regulation (EC) No 1107/2009 of the European Parliament and of the Council21. Regulation (EC) No 1107/2009 should therefore be amended accordingly.

(16) Products with one or more functions, one of which is covered by the scope of Regulation (EC) No 1107/2009, should remain under the control tailored for such products and provided for by that Regulation. Where such products also have the function of a fertilising product, it would be misleading to provide for their CE marking under this Regulation, since the making available on the market of a plant protection product is contingent on a product authorisation valid in the Member State in question.

* To note this fertiliser CE mark regulation is not yet ratified however, it is unlikely that there will be substantial changes now
And from the Fertiliser Regulation Annexes: Biostimulants are now defined as follows:

**PFC : PLANT BIOSTIMULANT**
1. A plant biostimulant shall be a CE marked fertilising product stimulating plant nutrition processes independently of the product's nutrient content with the sole aim of improving one or more of the following characteristics of the plant:
   (a) nutrient use efficiency, (b) tolerance to abiotic stress, or (c) crop quality traits.

Further:
**PFC 6(A): Microbial plant biostimulant**
1. A microbial plant biostimulant shall consist solely of a micro-organism or a consortium of microorganisms referred to in Component Material Category 7 of Annex II.

And:
**CMC 7: MICRO-ORGANISMS**
A CE marked fertilising product may contain micro-organisms, including dead or empty-cell microorganisms and non-harmful residual elements of the media on which they were produced, which have undergone no other processing than drying or freeze-drying and are listed in the table below:

- *Azotobacter spp.*
- *Mycorrhizal fungi*
- *Rhizobium spp.*
- *Azospirillum spp.*
Why do we not get the results we wanted or expected for biopesticides?
What is efficacy?

IPM?

Advantages?

Interactions?

Effects expected?
Results from multiple trials
Typical results?

Number of pests (out of 100)

- Mean
- Trial 1
- Trial 2
- Trial 3
- Trial 4
- Trial 5

Legend:
- Untreated
- Standard
- Test 1 l/ha
- Test 2 l/ha
- Test 4 l/ha
- Standard+test
Efficacy will be by POPULATION MANAGEMENT based on:

Biological characteristics of products

Relationship between dose and effect

Modes of action
Summary 2

Biological systems:

Biopesticides multiply variance in the system, variation in outcome is the PRODUCT of the natural variation in the target population AND biopesticide population.
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
Where do particles go?

- Concentration of particles in suspension (\(X \times 10^Y\) conidia / litre)
- Droplet size spectrum
- Size of particles – will they fit into a droplet?
Knowledge intensive – communication to farmers?

Crop protection

- Synthetic Chemical pesticides
- EPN
- Insects
- Macro-organisms
- Micro-organism
- Bacteria
- Fungi
- Virus
- Botanical
- Biorationale
- Semio-chems
- Agro-ecosystem
- Monitoring
Sustainable crop production and protection

Biology
Ecology
Population management
Recipe for success?

Employ systems biologists

Embrace variability

Good technology transfer

Maintain innovation

Directed by technology
Thank you for your attention