Agricultural Biologicals today and tomorrow: potential and regulations

Pete Marshall, Monsanto Canada
CSTA AGM, July __, 2015
Agenda

1. Agricultural biologicals – scope & definitions
2. Market for seed applied biologicals today and tomorrow
3. Regulation – Biopesticides, Biostimulants & Biofertilizers
Seed Company Interest

- Expanding market for Biologicals – innovation & rapid developments
- Increasing focus on agricultural biologicals
  - Biopesticides, biostimulants and biofertilizers
- Potential to resolve existing and developing problems
- Societal and consumer direction
- Complement classical chemical pesticides for seedling protection and chemical fertilizers for growth

Safeguard the investment in the seed
The seed package

Yield, quality & value

Seed treatment

Seed base

unlock potential

coating

chemistry

biological

priming, disinfection etc

germplasm

quality
1. Agricultural biologicals
scope & definitions

• what are they?
• how are they defined in different
countries and regions?
• application as seed applied technologies?
Agricultural biologicals

Bio-pesticides
- Micro-organisms (bacteria, fungi, viruses)
- Plant-extracts (botanicals)
- Plant growth regulators
- Semio-chemicals (pheromones)
  - Weed control
  - Insect control
  - Disease control

Bio-stimulants
- Micro-organisms (bacteria, fungi)
- Seaweed extracts
- Humic & amino acids and other complex organics
  - Yield enhancers
  - Improving nutrient uptake
  - Tolerance to & recovery from abiotic stress

Bio-fertilizers
- Micro-organisms (bacteria, fungi) – inoculants
- Organic fertilizers
- Soil improvers
  - Nutrition
  - Nutrition availability
## Ag Biologicals – seed applied

<table>
<thead>
<tr>
<th>Biological agent</th>
<th>Examples</th>
<th>Type of use</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Biological group</strong></td>
<td></td>
<td><strong>Bio-pesticides</strong></td>
</tr>
<tr>
<td><strong>Microbials</strong></td>
<td>Bacteria, fungi, viruses</td>
<td>✓</td>
</tr>
<tr>
<td><strong>Biochemicals/botanicals</strong></td>
<td>Natural products, plant extracts</td>
<td>✓</td>
</tr>
<tr>
<td><strong>Semiochemicals</strong></td>
<td>Pheromones</td>
<td>✓</td>
</tr>
<tr>
<td><strong>Macrobials</strong></td>
<td>Beneficial insects &amp; nematodes</td>
<td>✓</td>
</tr>
<tr>
<td><strong>Others</strong></td>
<td>Cyclic peptides, RNA</td>
<td>?</td>
</tr>
</tbody>
</table>

### Biopesticides inconsistency of definition

<table>
<thead>
<tr>
<th>OECD Biopesticides</th>
<th>Microbials: bacteria, algae, fungi, protozoa, viruses</th>
<th>Pheromones &amp; semiochemicals</th>
<th>Plant extracts/botanicals</th>
<th>Macrobials/Invertebrates such as insects and nematodes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Canada Biopesticide defined</strong></td>
<td><strong>Microbial pesticides:</strong> naturally occurring or genetically altered microorganisms</td>
<td>pheromones and other, semiochemicals: straight chain lepidopteran pheromones; other pheromones</td>
<td>Not regulated as biopesticides</td>
<td></td>
</tr>
<tr>
<td><strong>USA Biopesticide defined</strong></td>
<td>“microbials” microorganisms such as bacteria, fungi (includes genetically engineered microbes)</td>
<td>“Biochemical” naturally occurring substances that control by non-toxic mechanisms such as plant extracts and pheromones;(includes semio-chemicals)</td>
<td>Not regulated as biopesticides</td>
<td>Plant-incorporated protectants (PiPs) substances that plants produce from genetic material added to the plant</td>
</tr>
<tr>
<td><strong>EU Biopesticide not defined</strong></td>
<td>“micro-organisms” any microbiological entity capable of replication or of transferring genetic material</td>
<td>“semio-chemicals”</td>
<td>“botanicals”</td>
<td>Not regulated as biopesticides</td>
</tr>
</tbody>
</table>
## Biostimulants: a problem of definition

<table>
<thead>
<tr>
<th>OECD</th>
<th>No definition</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Canada</strong></td>
<td>Plant signaling compounds&lt;br&gt;&quot;substances other than fertilizers, manufactured, sold or represented for use in the improvement of the physical condition of the soil or to aid plant growth or crop yields&quot;.</td>
</tr>
<tr>
<td><strong>EU</strong></td>
<td>biostimulants&lt;br&gt;stimulate natural processes to benefit nutrient uptake, nutrient efficiency, tolerance to abiotic stress, and crop quality</td>
</tr>
<tr>
<td><strong>Germany</strong></td>
<td>plant strengtheners&lt;br&gt;maintain plant health in general; or protect plants against on-parasitic impairments, e.g. to reduce water evaporation, anti-freezing agents.</td>
</tr>
<tr>
<td><strong>USA</strong></td>
<td>No category of biostimulants&lt;br&gt;“biostimulants” proposed as new subcategories of “Beneficial Substances” in AAPFCO categories</td>
</tr>
<tr>
<td><strong>Australia</strong></td>
<td>No category found</td>
</tr>
</tbody>
</table>

Detail of these and other authorities’ definition is provided in the Annex of background slide.
## Biofertilizers

<table>
<thead>
<tr>
<th>Country</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Canada</strong></td>
<td>CFIA Fertilizer Safety Office has conducted full safety assessment on the following microbes (non-GMO strains of these microbes are now exempt from Full Safety Data requirement for Product registration): Rhizobial group (<em>Rhizobium</em> spp., <em>Bradyrhizobium</em> spp., <em>Mesorhizobium</em> spp., <em>Sinorhizobium</em> spp.), <em>Bacillus subtilis</em> and Vascular Arbuscular Mycorrhizae (VAM).</td>
</tr>
</tbody>
</table>
| **OECD** | Industrial products based on culturable micro-organisms that were isolated from the soil or rhizosphere of plants and which have been proven capable of modifying and improving plant development through a collection of different modes of action.  
| **EU** | The formulated product containing one or more micro-organisms that enhance nutrient status (and the growth and yield of plants) by either replacing soil nutrients and/or by making nutrients more available to plants and/or by increasing plant access to nutrients.  
| **India** | product containing carrier based (solid or liquid) living micro-organisms which are agriculturally useful in terms of nitrogen fixation, phosphorus solubilisation or nutrient mobilisation, to increase the productivity of the soil and/or crop |
| **USA** | 7 categories of micro-organisms are considered as biofertilisers: Rhihizobia (fast & slow growing), N-fixing bacteria, phosphorus solubilising bacteria (action on organic or inorganic P), Silenium solubilising bacteria; multi-strain consortia |

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Biofertilizers: types

**Symbiotic biofertilizers:** Micro-organisms living inside cells in specialised root structure or nodules
- **Rhizobia:** nitrogen fixing symbiosis with leguminous plants
- **Mycorrhiza:** improved uptake of water, nitrogen, phosphorus, micronutrients

**Free-living (non-symbiotic) biofertilizers**
- **Nitrogen** nutrition
- **Phosphorus** nutrition – solubilisation or mineralisation
- **Phytohormone** mediated mechanisms of plant growth promotion – particularly root and root hair development
  Auxins, Gibberellins, Cytokininins, Polyamines etc

**“Helper” bacteria**
e.g. bacteria which improve a plant-microbe interaction (3-way interaction)
2. Market for seed applied biologicals
Trends in food markets driving agricultural biologicals

**Food chain**
- Demand for safe and “sustainably-sourced” food
- Stronger focus on food quality, healthy nutrition and well-being
- Year-round demand increases global trade of fresh produce
- Increasing regulation and registration requirements for crop protection products
- Global retailers expect sustainable agricultural production
- Rising importance of partnerships along food value chain
- Innovation needed to drive integrated crop solutions

**Growers**
- **Integrated Pest Management** is mandatory in the EU and encouraged by the FAO and OECD
- Pushed to reduce fertilizer and pesticide loss to non-target areas (e.g. water)
- Fewer new pesticide active substances available
- Management of pesticide residues, particularly for vegetables
- Management of pesticide resistance
- Need new technologies to address unsolved problems, e.g. virus control
More drivers for biologicals

- Plant protection issues increase with increasing global trade and global warming
- More regulatory obstacles for plant protection products

The decreasing number of Active Ingredients

![Graph showing the decreasing number of Active Ingredients in development from 1999 to 2012.](image)

Source: PhillipsMcDougal, 2013, R&D trends for chemical crop protection products and the position of the European Market, A consultancy study on behalf of ECPA

The increasing cost of bringing a new chemical Active Ingredient to the market

![Bar chart showing the increasing cost from 1995 to 2005-8.](image)
Market growing strongly

**FIGURE 13** \(^\text{STRONG GROWTH POTENTIAL WITH RISING ENVIRONMENTAL CONCERNS, 2014-2019 ($MILLION)}\)

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**ATTRACTION MARKET OPPORTUNITIES**

- The size of the agricultural microbials market estimated for 2014 is **$2,182.78 million**; a 15.2% increase from 2013.
- Market growth is attributed to the increasing need for enhancing food production through sustainable and cost-effective agricultural solutions.
- Developing economies such as Mexico, China, India, and Brazil are turning out to be emerging markets.
- Portfolio expansion through product launches and acquisitions is projected to be preferred market strategies for gaining market presence in the next five years.

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Growth world wide

**FIGURE 12**  ASIA-PACIFIC PROJECTED TO REGISTER HIGH GROWTH RATE, 2014–2019

*The flags represent five of the fastest-growing country-level markets*

**Note:** The market share provided in the diagram is based on the market size, as estimated in 2013; the CAGR depicts the projected growth rate between 2014 and 2019.

**Source:** Expert Interviews, Government Authorities, Related Research Associations, Government Publications, and MarketsandMarkets Analysis
Microbial market summary

- 2014 market size estimated at $2.18B and projected to be $4.46B by 2019 (15.3% CAGR).
- The bacterial segment accounted for the largest share by microbial type ($1.6B); Bts, rhizobia and other Bacilli accounting for the vast majority. Fungus and other microbes (virus, protozoa) comprised the other two segments.
- The Fruit & Vegetable segment formed the largest market for agricultural microbials and is projected to grow at the highest CAGR (15.5%) over the next 5 years.
- North America accounted for the largest regional market share, estimated at $868M for 2014.
- Emerging markets in Asia Pacific and South America are projected to grow at the highest CAGR, 16.3% and 15.6% respectively.
- Bargaining power of buyers was determined to be moderate to high; attributed to low product differentiation among competitors.
- Entry of large-scale competitors.

Source: Agricultural Microbials Market – 2015 Report from MarketsandMarkets
3. Regulation of ag biologicals
Regulation of biologicals

Biologicals cannot be assumed “safe” until proven

Bio-pesticides
- Existing pesticide regulations
- Some specific requirements
- Stepped data generation & risk assessment
- Preferential treatment

Bio-stimulants
- Inconsistency between countries
- From little regulation to much regulation

Bio-fertilizers
- Existing fertilizer regulations
- Generally clear
## Regulatory for Biologicals varies widely by country

### Canada
- CFIA (supplements): safety assessment only; no efficacy data required (review time: 18-24 months)
- PMRA (pesticides): tiered testing approach for safety and efficacy; pre-consultation is recommended (review time: 18-24 months)

### EU
- Distinct pathways for some categories (e.g. micro-organisms and botanicals as pesticides)
- Similar requirements to US plus some additional testing
- Regulatory review time: 29 months (best case)

### USA
- Well Established Regulatory Framework
- Clearly defined requirements
- Tiered testing approach
- Review time: 18 months

### Latin America
- Brazil (and Argentina) has defined categories and generally follows US or EU approach but with some additional testing. Review time 18 – 36 months
- Other countries often have no specific BLX regulatory framework and try to impose chemical regulations

Source: BCS internal analysis
Regulators encourage biological pesticides

- Agriculture and Agri-Food Canada Pest Management Centre is committed to improving access to biopesticides as part of its Pesticide Risk Reduction Program:
  - http://www.agr.gc.ca/eng/?id=1288727518132
  - http://www.agr.gc.ca/eng/?id=1392136770253 (status report for BioPesticide Projects and Submissions)

- US EPA encourages development of biopesticides because they “have very favorable human health and environmental profiles.”

- Netherlands “Green Deal” applies to ag biologicals
  - Favours biopesticides, biostimulants and biofertilisers
  - e.g. http://www.hdc.org.uk/sites/default/files/Aleid%20Dik.pdf

- UK
  - Microbial pesticides: “The data requirements you need to address are not as extensive as those set for chemical active substances but …”
    - http://www.pesticides.gov.uk/guidance/industries/pesticides/user-areas/biopesticides-home

- EU “low risk substances”
  - EU currently considering definition - None currently approved; Could include microbials

- FAO
  - Encourages biopesticides for “minor uses”
Registration strategy example

Product characteristics
- naturally derived product
- mode of action clearly defined
- claims supported by strong data
  - increased germination
  - improved seedling development
  - stronger roots
  - greater biomass
  - higher chlorophyll density
  - stress tolerance
  - yield
- product categorization and efficacy claims vary depending on local regulatory policies

<table>
<thead>
<tr>
<th>Country</th>
<th>Registration Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA</td>
<td>PGR</td>
</tr>
<tr>
<td>Canada</td>
<td>Fertilizer Supplement</td>
</tr>
<tr>
<td>Argentina</td>
<td>Fertilizer Amendment/ Biostimulant</td>
</tr>
<tr>
<td>Brazil</td>
<td>Biofertilizer</td>
</tr>
<tr>
<td>Chile</td>
<td>PGR or Fertilizer</td>
</tr>
<tr>
<td>Australia</td>
<td>PGR</td>
</tr>
</tbody>
</table>
Thank You!
A new era for seed treatments: agricultural biologicals

Seed treatment based on micro-organisms and natural substances, applied in partnership with chemical treatments

For sustainable market growth:
• drive reputation
• clear and proven efficacy claims
• appropriate registration route
• high quality product
• outstanding product stewardship

Biopesticides
Biostimulants
Biofertilizers

New technologies e.g. RNAi
Annex
BACKGROUND
Biopesticides definitions 1.

**Europe: No category of “biopesticides”, three relevant definitions:**

- **micro-organisms**: specific data requirements (Regulations 283 & 284/2013)
  - “any microbiological entity, including lower fungi and viruses, cellular or non-cellular, capable of replication or of transferring genetic material “
  - Guidance document on taxonomic level of micro-organisms SANCO/10754/2005 rev.5

- **botanicals**: Guidance document
  - SANCO/11470/2012.8, 20 March 2014 'active substances obtained from plant material’.
  - NOT covered: analogues, mimics, natural-identical synthesized molecules and biosimilars

- **semio-chemicals**: Guidance Document in preparation

**USA: Biopesticides** “Pesticides derived from natural materials such as animals, plants, bacteria, and certain minerals”. **Three classes:**

- **Microbial**: microorganisms such as bacteria, fungi (includes genetically engineered microbes)
- **Biochemical**: naturally occurring substances that control by **non-toxic** mechanisms such as plant extracts and pheromones;(includes semio-chemicals)
- **Plant-incorporated protectants (PiPs)**: substances that plants produce from genetic material added to the plant.
  [http://www.epa.gov/pesticides/biopesticides/whatarebiopesticides.htm](http://www.epa.gov/pesticides/biopesticides/whatarebiopesticides.htm)
Biopesticides definitions 2.


- Microbial pesticides, pheromones and other, semio-chemicals, other biopesticides including biochemicals


- “A biological chemical product is an agricultural chemical product where the active constituent comprises or is derived from a living organism (plant, animal, micro-organism, etc.), with or without modification.”
  - includes 'botanicals', 'organics' or 'herbals
- Four major groups:
  - biological chemicals (e.g. pheromones, hormones, growth regulators, enzymes and vitamins)
  - plant and other extracts (e.g. plant extracts, oils)
  - microbial agents (e.g. bacteria, fungi, viruses, protozoa)
  - other living organisms (e.g. microscopic insects, plants and animals plus some organisms that have been genetically modified).

OECD Biological Pesticides

- **microbials** - bacteria, algae, protozoa viruses, fungi
- **pheromones** and semio-chemicals
- **macrobials/invertebrates** such as insects and nematodes
- **plant extracts/botanicals**
Biopesticides definitions 3.

ASEAN  http://asean-agrifood.org/?wpfb_dl=57
- Very similar to OECD. Four categories of BioControl Agents (BCA)
  - Microbial control agents (microbials or MCA),
  - Macro-organisms (macrobials),
  - Semiochemicals (mostly pheromones, kairomones, etc.),
  - Natural products (plant extracts or ‘botanicals’, fermentation and other products)

India  http://www.cibrc.nic.in/guidelines.htm
Two groups of biopesticides
- Microbial biopesticides:
  - Baculoviruses
  - Fungi: Antagonistic, Entomopathogenic
  - Bacteria: Antagonistic, Entomotoxic
- Botanical pesticides/biopesticides
  - Neem based products
  - Herbal plant growth regulators
  - Pyrethrum extract
  - Cymbopogon plant extract
  - Eucalyptus extract containing eucalyptol
Biostimulants definitions 1.

Europe

Plant biostimulants are substance(s) and/or micro-organisms whose function when applied to plants or the rhizosphere is to stimulate natural processes to benefit nutrient uptake, nutrient efficiency, tolerance to abiotic stress, and crop quality independently of their nutrient content.*

- “plant conditioners” is proposed as a synonym, referring to the capacity of biostimulants to enhance nutrition efficacy and/or stress response (supported by European Biostimulants Industry Council http://www.biostimulants.eu/)

EU: Germany:

Plant strengtheners are substances and mixtures, including microorganisms, which are exclusively intended to maintain plant health in general (as long as they are not plant protection products) or are intended to protect plants against non-parasitic impairments, for example, products for reducing water evaporation or anti-freezing agents.


- Products whose priority lies in providing plants with nutrients and trace elements and promoting growth should rather be classified as plant growth improvers or soil improvers. Product groups are subject to the Act on fertilizers

Biostimulants
 definitions 2.

Poland  Law on fertilizers and Fertilisation, 2007
“growth stimulators” are in the category of plant conditioners
“plant conditioners” have a positive impact on plant growth or other metabolic processes of plants in other ways than plant nutrients”

Australia: no category found

USA: No clear definition.
The Biostimulants Coalition agreed with AAPFCO* to address “biostimulants” with new subcategory definitions within “Beneficial Substances”, e.g. a specific fulvic acid definition could be developed that would be defined and placed under the Beneficial Substances category.

Each subcategory material would have to go through a similar process.

- **Beneficial Substance**: any substance or compound other than primary, secondary, and micro plant nutrients that can be demonstrated by scientific research to be beneficial to one or more species of plants, when applied exogenously. (AAPFCO 2007)

http://www.biostimulantcoalition.org/

* Each State in the United States, Puerto Rico and Canada has its own fertilizer regulatory program. The Association of American Plant Food Control Officials (AAPFCO) strives to gain uniformity among each of these entities without compromising the needs of the consumers, protection of the environment or fair competition among the industry. http://www.aapfco.org/
Biostimulants definitions 3.

**Austria: Fertilizer Law**
Micro-organisms can be placed on the market as biostimulants and combined with nutrients as fertilizers.

**Bulgaria**
Microbial fertilizers – material, principal function of which is providing a nutrient to plants.
Biologically active substances – plant substances, produced in small quantities in the plants themselves and/or chemical synthesis products, stimulating or suppressing course of physiological processes, serving growth and plant development not containing nutrient elements.
Soil improvers – materials added to soil with principal function of improvement of physical and/or chemical properties and/or biological activity of soil.”

**Czech Republic**
Supplementary soil substance/Supplementary plant substance if they fulfill following definition of Act on fertilizers: Supplementary soil substance means a substance without any effective amount of nutrients that affects soil biologically, chemically or physically and improves soil condition or it increases the fertilizer efficiency. Supplementary plant substance means a substance without any effective amount of nutrients that otherwise favorably affects the development of cultivated plants or the quality of plant products.”

**Hungary**
Microbiological preparation: means yield enhancing substances containing micro organisms (bacteria, fungi, algae) improving soil fertility and exempt from agents infectious for man or influencing the natural micro flora of the soil adversely.”

## Biofertilizers

**definitions 1.**

<table>
<thead>
<tr>
<th>Country</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Spain</strong></td>
<td>No reference in national legislation to plant beneficial microbes&lt;br&gt;Andalucia: biofertilizers for use in organic production&lt;br&gt;– a group of organisms that are applied to soil or seeds to improve plant nutrition (rhizobium, mycorrhiza, Azotobacter etc)&lt;br&gt;▶ preparations derived from biological fermentation containing groups of nutrients that as used basically as foliar fertilizers</td>
</tr>
<tr>
<td><strong>Italy</strong></td>
<td>Mycorrhizal fungi inocula are included within “products with action on the soil”</td>
</tr>
<tr>
<td><strong>India</strong></td>
<td>Biofertilizers fall under the order for the control of fertilizers, 1985&lt;br&gt;“product containing carrier based (solid or liquid) living micro-organisms which are agriculturally useful in terms of nitrogen fixation, phosphorus solubilisation or nutrient mobilisation, to increase the productivity of the soil and/or crop”&lt;br&gt;Five groups of micro-organisms&lt;br&gt;▶ Rhizobium, Azobacter, Azospirillum, phosphate-solubilising bacteria, mycorrhizal bacteria</td>
</tr>
<tr>
<td><strong>China</strong></td>
<td>7 categories of micro-organisms are considered as biofertilizers&lt;br&gt;▶ Rhihizobia (split into fast or slow growing), N-fixing bacteria, phosphorus solubilising bacteria (split based on action on organic or inorganic P), Si solubilising bacteria; multi-strain consortia</td>
</tr>
</tbody>
</table>

Malusa, E; Vassilev, N (2014) propose that a biofertilizer could be defined as:

The formulated product containing one or more micro-organisms that enhance nutrient status (and the growth and yield of plants) by either replacing soil nutrients and/or by making nutrients more available to plants and/or by increasing plant access to nutrients.

They also propose that only microbial based fertilizers should be included in the category of biofertilizers:

- Stimulatory compounds or additives are included in the product increase the efficiency of inoculation, e.g. humic acids or other organic fractions.

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4108841/
Growth reflected by industry association attention

IBMA
International Biocontrol Manufacturers’ Association
http://www.ibma-global.org/

BPIA
BioPesticides Industry Alliance
http://www.biopesticideindustryalliance.org/

EBIC
European Biostimulants Council
http://www.biostimulants.eu/

Biostimulant Coalition
http://www.biostimulantcoalition.org/

CropLife International https://croplife.org/
BioControl Agents Project Team

International Seed Federation http://www.worldseed.org/isf/home.html
Biological Seed Treatments Working Group

Also the conference and market survey industries, e.g.
• Informa “Biostimulant” conference 2015, and two webinars
• AGROW Biopesticides 2013
• AGROW Biostimulants 2015
• ASDReports N America Bio-fertilizer market 2015
• ASDReports N American Biostimulants market 2015
• World Seed Congress editions of “Seed World” and “Cultivar”