Biologicals for IPM Programs

Pam Marrone, PhD

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Boost yield and quality
Manage resistance
Harvest flexibility
Worker-friendly
Fewer New Chemicals – Higher Cost

Graph 1: # of Chemicals Screened to Find One Product ('000)
- 1990: 10
- 1995: 20
- 2000: 45
- 2009: 150

Graph 2: Cost to Discover & Develop a Synthetic Chemical ($Mil)
- 1956: $1.2
- 1964: $4.1
- 1969: $20
- 1984: $45
- 2000: $85
- 2003: $105
- 2010: $256
- 2016: $280

Source: CropLife

Graph 3: # of New Chemical Leads vs. Product Launches
- Source: Ag Chem New Compound Review (Vol 28) 2010
Biologials Outpace Chemicals Growth

Agrichemicals
- Global regulatory restrictions
- Pest resistance
- Slow growth
- $\sim$280 mil, 12 yrs to develop 1 chemical pesticide

Biopesticides
- Higher yields/quality
- No residues
- No resistance
- Worker safety
- Low cost to develop (<$10 mil, 4 yrs)

Source: Blended numbers and CAGRs from BCC Research, marketsandmarkets, Agropages and Phillips McDougall

NASDAQ: MBII
Many, many companies are going into biostimulants, but fewer venture into biopesticides because of the higher technical and regulatory barriers to entry.
Biopesticide Categories

**Microbials**
- Fungi, Bacteria, Viruses, and Protozoa

**Biochemicals**
- Plant Extracts, Pheromones, Soaps, and Fatty Acids

A 70 year history of safe use of biopesticides
Faster and less expensive EPA registration than synthetic chemicals

Smart. Natural. Solutions.
Biopesticide Pollution Prevention Division (BPPD)

Tiered Data requirements; Start with Tier I:

- Rat Acute Studies - Oral, Inhalation, Intravenous, Dermal; Rabbit Eye; Guinea pig skin sensitization
- Product chemistry, 5-batch analysis
- Microbiology/QC: no human pathogens
- Ecological effects (non-target birds, fish, *Daphnia*, honeybees, lacewings, ladybeetles, parasitic wasps)
- Endangered species review
- Exemption from tolerance petition (for food use)

*California requires efficacy data!*
Organic Labels

National Organic Program (NOP) seal for organic pesticides (active & inert ingredients)

Organic Materials Review Institute (non-profit) seal: list of approved pesticides and fertilizers [NOT REQUIRED – optional listing!]

Organic seal for FOOD (National Organic Program Regulations – how crops are grown and food is processed)

CCOF: Legal agreement with USDA’s NOP to certify organic farms and processors
Successful Pesticides from Natural Products

None of these are biopesticides; they are registered as chemicals

Abamectin (Avid®, Agrimek®) Syngenta

“Toxic mode of action”

Tebufenozide (Mimic®, Confirm®) Gowan

Not nature-identical
(modified from natural molting inhibitor)

Azoxystrobin (Quadris®, Abound®) Syngenta

Not nature-identical
(modified from original mushroom compound)

Spinosyn/Spinosads (Conserve®, SpinTor®, Success®, Tracer®, Entrust® (organic formulation) – Dow Agro

“Toxic mode of action”

Pyrethrins (Pyganic®) MGK

(Can be used in organic)

“Toxic mode of action”

Smart. Natural. Solutions.
Biologica Is Used Across All Production Systems and IPM Programs

1. **Organic**
   - Biopesticide rotations and tank mixes

2. **No Residues for Export**
   - Early sprays & last spray before harvest

3. **Conventional**
   - In the tank with chemicals to enhance control, reduce resistance

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**Grower ROI Drives Adoption (Examples)**

1. **Organic**
   - $1400/Acre Increase
   - >9X ROI

2. **No Residues for Export**
   - 1000 lb/Acre Increase (+12%)
   - >4X ROI

3. **Conventional**
   - 6 bushel/Acre Increase
   - 2.8X ROI
   - 10 lb/Acre Increase
   - Better Grade
Discovery: Sourcing and Isolation of Microorganisms

Soil and other types of samples collected from unique habitats and niches

Individual fungal, bacterial, and actinomycete colonies picked from primary plate

Water extracts of fermentation broths are used for bioassays

- Bacteria
- Fungi
- Actinomycetes

39% 37% 24%
# Primary Screen Testing

<table>
<thead>
<tr>
<th>Insecticide</th>
<th>Fungicide</th>
<th>Herbicide</th>
<th>Nematicide</th>
<th>Algaecide</th>
<th>Bactericide</th>
<th>Biostimulants</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lygus</strong></td>
<td><strong>Botrytis cinerea</strong></td>
<td>Crabgrass</td>
<td>Meloidogyne</td>
<td>Chlamydomonas</td>
<td>Xanthomonas campestris</td>
<td>Tomatoes, Corn, Radish, Soy &amp;</td>
</tr>
<tr>
<td><strong>Beet armyworm</strong></td>
<td><strong>Phytophthora capsici</strong></td>
<td>Lettuce</td>
<td>spp.</td>
<td>reinhardtii</td>
<td>Pseudomonas syringae</td>
<td>Others</td>
</tr>
<tr>
<td><strong>Corn rootworm</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Smart. Natural. Solutions.*
Determining What Causes the Pesticidal Activity

- Characterize/identify pesticidal compounds produced by the microbes or plants
- Eliminate strains with harmful compounds
- Develop analytical assays based on bioactive chemistry for Quality Control in manufacturing
Product and Process Development

- Develop user-friendly formulations (lab & pilot facilities)
- Develop and scale manufacturing processes (lab, pilot & mfg facilities)
- Conduct field trials
- Develop data for the regulatory submission
Marrone Bio Innovations Ag Products

REGALIA®
The industry's first effective plant-extracted fungicide; Increases yields/quality on multiple crops

HAVEN®
Reduces sun & water stress, increasing yields & quality

GRANDEVO®
First broad spectrum microbial insecticide since Bt (50+ yrs); Novel chemistry & mode of action

VENERATE®
New species of insecticidal bacteria with novel compounds as potent as the best chemicals

MAJESTENE®
Reduces broad spectrum of root-feeding nematodes to increase yields/quality

Solutions to meet broad range of grower needs

MBI also distributes biological products that don’t have a distribution channel in the U.S.

Smart. Natural. Solutions.
Our Near-term Pipeline

**MBI-014 Bioherbicide (New species of bacteria produces systemic compounds)**
- Controls glyphosate-resistant & other herbicide-resistant weeds (e.g. palmer amaranth) with novel mode of action (Addresses the #1 need of organic farmers – weed control)

**MBI-110 Biofungicide (Discovered in MBI’s screen)**
- Controls difficult plant diseases such as white mold, Fusarium Race 4 & downy mildews where there are fewer chemical and biological alternatives

**MBI-601 Biofumigant (Novel genus & species of volatile gas-producing fungus)**
- Alternative for methyl bromide and other chemical fumigants that are heavily restricted or being phased out
- Could be deployed for post harvest mold control on fruits and grains

Submit to EPA

Targeting 2017 Soft Launch
## Microbial Insecticides/Acaricides

<table>
<thead>
<tr>
<th>Active</th>
<th>Type</th>
<th>Pests Controlled</th>
<th>Product Examples</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacillus thuringiensis spp. aizawai</td>
<td>Microbial, Bacteria</td>
<td>Diamondback moth, armyworm</td>
<td>XenTari®, Agree®</td>
<td>Valent Bio., Certis USA</td>
</tr>
<tr>
<td>Bacillus thuringiensis spp. kurstaki</td>
<td>Microbial, Bacteria</td>
<td>A broad range of caterpillars</td>
<td>Dipel®, Deliver®, Foray®, Biobit®, Javelin®</td>
<td>Valent Bio., Certis USA</td>
</tr>
<tr>
<td>Chromobacterium subtsugae</td>
<td>Microbial, Non-living Bacteria</td>
<td>Broad range of sucking &amp; chewing insects, mites &amp; flies</td>
<td>Grandevo®</td>
<td>Marrone Bio Innovations</td>
</tr>
<tr>
<td>Burkholderia rinojensis</td>
<td>Microbial, Dead Bacteria</td>
<td>Broad range of sucking &amp; chewing insects, mites &amp; Flies</td>
<td>Venerate®</td>
<td>Marrone Bio Innovations</td>
</tr>
<tr>
<td>Metarrhizium anisopliae</td>
<td>Microbial, Fungus</td>
<td>Thrips, mites, whiteflies</td>
<td>Met52®, GreenGuard®, Green Muscle®</td>
<td>Novozymes, BASF</td>
</tr>
<tr>
<td>Apopka 97 strain of Isaria fumosorosea</td>
<td>Microbial, Fungus</td>
<td>A broad range of sucking insects, mites &amp; black vine weevil</td>
<td>PFR97®</td>
<td>Certis USA</td>
</tr>
</tbody>
</table>
# Plant-extracted & Oil Bioinsecticides

<table>
<thead>
<tr>
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<th>Pests Controlled</th>
<th>Product Examples</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neem oil</td>
<td>Biochemical, Soaps/Fatty Acids</td>
<td>A broad range of sucking insects</td>
<td>Trilogy®</td>
<td>Certis USA</td>
</tr>
<tr>
<td>Azadiractin</td>
<td>Plant Extract</td>
<td>A broad range of sucking &amp; chewing insects</td>
<td>Aza-direct® (and others)</td>
<td>Gowan (and others)</td>
</tr>
<tr>
<td><em>Chenopodium ambrosioides</em></td>
<td>Terpenes (synthetically made) from Plant Extract</td>
<td>Sucking insects and mites</td>
<td>Requiem® (Not organic)</td>
<td>Bayer Crop Science</td>
</tr>
<tr>
<td>Citrus oil solution</td>
<td>Plant extract</td>
<td>A broad range of sucking insects</td>
<td>Oroboost®</td>
<td>OroAgri</td>
</tr>
<tr>
<td>Crop Oils</td>
<td>Paraffinic Oil</td>
<td>Sucking insects</td>
<td>Stylet Oil®, Supreme Oil and others</td>
<td>Many</td>
</tr>
</tbody>
</table>
## Microbial Biofungicides

<table>
<thead>
<tr>
<th>Active</th>
<th>Type</th>
<th>Examples</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Trichoderma harzianum T-22</strong></td>
<td>Microbial, Fungi</td>
<td>RootShield® WP, PlantShield® HC</td>
<td>Bioworks</td>
</tr>
<tr>
<td><strong>Gliocladium virens</strong></td>
<td>Microbial, Fungi</td>
<td>SoilGard®</td>
<td>Certis USA</td>
</tr>
<tr>
<td><strong>Trichoderma asperellum &amp; Trichoderma gamsii</strong></td>
<td>Microbial, Fungi</td>
<td>BIO-TAM 2.0®</td>
<td>Isagro (Marrone Bio)</td>
</tr>
<tr>
<td><strong>Bacillus subtilis 713</strong></td>
<td>Microbial, Bacteria</td>
<td>Serenade®, Cease®</td>
<td>Bayer</td>
</tr>
<tr>
<td><strong>Bacillus amyloliquefaciens D747</strong></td>
<td>Microbial, Bacteria</td>
<td>DoubleNickel® 55</td>
<td>Certis USA</td>
</tr>
<tr>
<td><strong>Bacillus pumilus 2808</strong></td>
<td>Microbial, Bacteria</td>
<td>Sonata®</td>
<td>Bayer (Wilbur Ellis)</td>
</tr>
<tr>
<td><strong>Streptomyces lydicus</strong></td>
<td>Microbial, Actinomycete</td>
<td>Actinovate®, ActinoGrow®</td>
<td>Novozymes (Valent)</td>
</tr>
<tr>
<td><strong>Bacillus amyloliquefaciens F727</strong></td>
<td>Microbial, Bacteria</td>
<td>Stargas™, Amplitude™</td>
<td>Marrone Bio Innovations</td>
</tr>
<tr>
<td><strong>Bacillus mycoides isolate J</strong></td>
<td>Microbial, Bacteria</td>
<td>LifeGard™ WG</td>
<td>Certis USA</td>
</tr>
</tbody>
</table>
# Non-Microbial Biofungicides

<table>
<thead>
<tr>
<th>Active</th>
<th>Type</th>
<th>Examples</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extract of <em>Reynoutria sachalinensis</em> (knotweed)</td>
<td>Biochemical, Plant Extract</td>
<td>Regalia®</td>
<td>Marrone Bio Innovations</td>
</tr>
<tr>
<td>Potassium bicarbonate</td>
<td>Biochemical</td>
<td>Kaligreen®, Milstop®</td>
<td>Otsuka (Brandt), Bioworks</td>
</tr>
<tr>
<td>Paraffin oil</td>
<td>Biochemical</td>
<td>Stylet Oil®, Purespray</td>
<td>JMS, Petro Canada</td>
</tr>
<tr>
<td>Tea tree oil</td>
<td>Biochemical, Plant Extract</td>
<td>Timorex Gold®</td>
<td>Stockton</td>
</tr>
<tr>
<td>Active</td>
<td>Type</td>
<td>Product Examples</td>
<td>Manufacturer</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>-------------------------------</td>
<td>---------------------------</td>
<td>-------------------------------</td>
</tr>
<tr>
<td><em>Purpureocillium lilacinus</em></td>
<td>Microbial, Fungi</td>
<td>MeloCon®</td>
<td>Bayer Crop Science</td>
</tr>
<tr>
<td>Saponins of <em>Quillaja saponaria</em></td>
<td>Biochemical, Plant Extract</td>
<td>Nema-Q®</td>
<td>Brandt</td>
</tr>
<tr>
<td><em>Pasteuria nishizawai</em></td>
<td>Microbial, Bacteria</td>
<td>Clariva® (Seed treatment)</td>
<td>Syngenta</td>
</tr>
<tr>
<td><em>Myrothecium verrucaria</em></td>
<td>Microbial, Fungi</td>
<td>DiTera®</td>
<td>Valent BioSciences</td>
</tr>
<tr>
<td><em>Bacillus firmus</em></td>
<td>Microbial, Bacteria</td>
<td>Votivo® (Seed treatment)</td>
<td>Bayer Crop Science</td>
</tr>
<tr>
<td><em>Burkholderia rinojensis</em></td>
<td>Microbial, Killed Bacteria</td>
<td>Majestene®</td>
<td>Marrone Bio Innovations</td>
</tr>
</tbody>
</table>
Biopesticides – Best Uses and Benefits

- Integrated solutions to improve overall pest control
- Can Increase Yield
- Can Enhance Plant Health/Quality
- Reduce Development of Resistance
- Manage Residues for Export (MRLs) (Zero Pre-harvest Interval)
- For Fast Re-entry (Short REIs) (Labor Management)
- Enhance Beneficials
- Reduce Pollution, Runoff
Biopesticides – NOT IF They Work, But HOW to Make Them Work

- Increasing receptivity to biologicals, but unsure how to use them.
- More education & training on how the products work and how to integrate them into IPM programs; understand their unique modes of action.
- Support from University Extension – fair and realistic field trials consistent with labels, include BOTH: a) stand alone and b) integrated into tank-mix and alternation programs.
- On-farm demonstrations – block of the biopesticide in the program compared to chemical-only program.

NOT to be used when all else fails.

“I tried everything but the kitchen sink so I thought I would try a biopesticide.”
How to Maximize Your Biopesticide’s Effectiveness – Some Variables

- Water pH
- Water hardness
- Water volume/dilution
- Spray droplet size
- Adjuvant effect
- Impact on beneficials
- Impact on pollinators
- Tank-mix partners
- Application timing
- Application interval

We have to read the labels!
Biopesticides Can Help Meet the Challenges of Sustainable Agriculture

Integrated Pest Management
Biopesticides + Conventional Crop Protection Products
1. Increased efficacy
2. Higher yield
3. Reduced chemical load

Meeting the Challenges of Sustainable Agriculture
1. Increase Productivity
2. Promote Food Quality
3. Minimize Impact

Additional Benefits
1. Resistance Management
2. Harvest & Labor Management
3. Residue Management
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