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BIOPESTICIDES ARE HERE – are you ready?

NAICC – New Orleans – January 31, 2014
Marja Koivunen
Novozymes Biologicals, Inc.
OVERVIEW

1. What are biopesticides?

2. Organic vs biopesticides

3. Regulatory requirements

4. Product examples

5. Future – implications to CROs?
Biopesticides – what are they?

Biopesticide: EPA’s name for low risk natural products that control weeds and pests, based on biological or naturally derived chemistry
EPA: BIOPESTICIDES & POLLUTION PREVENTION DIVISION (BPPD)

- Microbials (bacteria, fungi, virus, etc.)

- Biochemicals (plant extracts, pheromones, PGRs, soaps and fatty acids) Have to have a nontoxic mode of action to the pest!

- Pesticidal compounds produced by GM crops (PIPs=Plant Incorporated Protectants)
Non-toxic substances can be *lethal*
QUIZ

Do Biopesticides need EPA and CalDPR registration?  YES

Are the REGISTRATION requirements same for Biopesticides and Chemical Pesticides?  NO

Are all biopesticides approved for use in organic farming?  NO
2. ORGANIC VS BIOPESTICIDES
PESTICIDES FOR ORGANIC PRODUCTION

Regulated by USDA National Organic Program (NOP)

For Organic Production

National Organic Program (NOP) seal for organic pesticides

Organic Materials Review Institute (non-profit) seal: list of approved pesticides and fertilizers [optional listing!]

NOVOZYMES COMPANY CONFIDENTIAL
Allowed Nonsynthetic (Natural) Pesticide Active Ingredients

A substance that is derived from mineral, plant, or animal matter and does not undergo a synthetic process as defined in section 6502(21) of the Act (7 U.S.C. 6502(21)).

- Pyrethrum
- Bacteria (e.g. *Bt*)
- Spinosad
- Neem oil / Azadirachtin
- Diatomaceous earth

- Plant oils
- Gibberellic acid
- Limonene
- Mined minerals

Other natural substances allowed if not explicitly prohibited

Electronic Code of Federal Regulations http://www.ecfr.gov/cgi-bin/text-idx?c=ecfr&sid=6f623e1de5457587ccdfec12bc34ed1c&rgn=div5&view=text&node=7:3.1.1.9.32&idno=7
Allowed Synthetic Active Ingredients on the National List, § 205.601

Commonly used substances

- Insecticidal soaps
- Horticultural oils
- Pheromones
- Elemental sulfur
- Copper sulfate / fixed coppers
- Lime sulfur
- Hydrated lime
- Potassium bicarbonate
- Ferric phosphate

Sanitizers

- Chlorine materials
- Alcohol (ethanol, isopropanol)
- Peracetic acid
- Ozone
- Hydrogen peroxide

NOTE: Many substances have annotations which restrict their use.

A complete list of allowed synthetic substances is available at § 205.601
Biopesticides that are exempt from registration

So-called 25b products don’t require EPA registration because their ingredients are widely used in food and considered safe

- Clove, cedar, cinnamon, peppermint, wintergreen, castor, thyme, lemongrass, citronella, sesame, soybean, cottonseed, linseed, garlic oil; Sodium lauryl sulfate

- Note that both active and inert ingredients in these products have to be from the EPA 25b list

36 states regulate 25-b products
3 REGULATORY REQUIREMENTS

BIOPESTICIDES
DATA REQUIREMENTS - EPA

Data requirements:
- Product chemistry, batch analysis
- Microbiology/strain ID, no mammalian pathogenicity, no contaminants
- Acute toxicity
- Primary dermal & eye irritation
- Ecological effects (non-target birds, fish, invertebrates, insects, plants)

Time requirements:
- Non-crop use – 12 months (PRIA)
- Crop use – 18 months (PRIA)

FIFRA 40 CFR Part 158 - Data Requirements for Pesticides
Biopesticide:
Cost to Develop = $3-15 million

Synthetic Chemical Pesticide:
Cost to Develop = $250-300 million

Submit Registration
Start Field Testing
Approval

Years
1 2 3

Start Field Testing
Submit Registration
Approval

Years
1 2 3 4 5 6 7 8 9 10

Slide from a presentation by P. Marrone
NOVOZYMES COMPANY CONFIDENTIAL
BIOPESTICIDES VS CHEMICALS

Differences:
1. Registered through different branches at EPA
2. Biopesticide development is faster and cheaper:
   • NO residue, e-fate or chronic tox/health effect data needed for registration
   • Usually only Tier I mammalian toxicity testing needed (GLP)

Similarities:
1. No efficacy data required for EPA submission
2. Local efficacy data is required for CalDPR submission
Examples of Biopesticides

There are currently about 250 biopesticide AIs registered through EPA; about 1/3 of them are microbial biopesticides.

- **Fungi & Bacteria**
- **Plant extracts**
- **Soaps/fatty acids**
- **Insect Pheromones and PGRs**
MICROBIAL BIOPESTICIDES
• Taegro® contains spores of a unique, patented strain of *Bacillus subtilis* var. *amyloliquefaciens* FZB24

• protects vegetables and vine crops against diseases such as Botrytis, Downy Mildew, Powdery Mildew, Bacterial Spot etc.

• used as foliar, soil or seed treatment

• available as a dry spore formulation

*Bacillus subtilis* is a Gram-positive, rod-shaped, nonpathogenic soil bacterium
MET 52® EC – microbial bioinsecticide

Entomopathogenic fungus *Metarhizium anisopliae* strain F52
- Mode of action: fungus penetrates the cuticle and infects the insect pest – insect dies of fungal infection

Simplified Life Cycle of *Metarhizium anisopliae*

- Met52 EC (AKA OD) - spores are suspended in an emulsifiable oil
  - Foliar and drench applications
- Met52 G - Granular spores are on the surface of sterile rice granules
  - Formulation suitable potting media/soil incorporation
- Insect targets: *thrips, mites, whiteflies, ticks and weevil larvae*

**KEY BENEFITS**
- Well-suited for inclusion in an IPM (Integrated Pest Management) program
  - Multiple insect pest targets
  - Competitive efficacy with chemical insecticides
  - No known resistance, valuable tool for insecticide resistance management
  - Compatibility with many beneficial insects and other insecticides
Complex mode of action enhances resistance management ...
GRANDEVO is naturally derived from a newly discovered bacterium, commonly known as Achromacil™, which produces a number of compounds that contribute to the creation of complex modes of action, resulting in a potent biopesticide that is highly active against labeled insects and mites. Control of pests is achieved by unique combinations of repellency, oral toxicity, reduced egg hatch, and reduced fecundity (ability of pest to reproduce). Grandevo has also been shown to maintain populations of most beneficials and introduced biological controls.

http://www.marronebioinnovations.com/products/brand/grandevo/

C. subtusgue grown on growth medium was active against multiple insects, including:

- Colorado potato beetle (*Leptinotarsa decemlineata*) larvae
- Western corn rootworm (*Diabrotica virgifera*) adults
- Southern corn rootworm (*Diabrotica undecimpunctata*) larvae and adults
- Sweet potato whitefly (*Bemisia tabaci*) larvae and adults
- Southern green stink bug (*Nezara viridula*) larvae and adults

Dr. Martin and her coworkers at USDA isolated a purple-pigmented bacterium (PRAA4-1) from forest soil in Maryland. This motile, gram-negative bacterium was identified as *Chromobacterium subtusgue* sp nov.
MeloCon® WG is a biological nematicide that contains a naturally occurring fungus, *Paecilomyces lilacinus*, that is a highly effective parasite of all stages of development of common plant-infecting nematodes, especially the eggs and infectious juveniles.

Formulated as a water dispersable granule, MeloCon® is applied through conventional methods, including chemigation. The product is approved by the National Organic Program.

MeloCon® WG is for use against the following pests:
- Root-knot nematode (*Meloidogyne* spp.)
- Burrowing nematode (*Radopholus similis*)
- Cyst nematode (*Heterodera* spp. and *Globodera* spp.)
- Reniform nematode (*Rotylenchulus reniformis*)
- False root-knot nematode (*Nacobbus* spp.)
- Spiral nematode (*Helicotylenchus* spp.)
- Sting nematode (*Belonolaimus* spp.)
- Root lesion nematode (*Pratylenchus* spp.)

Penetration of nematode egg by hyphae (arrows)
PRODUCT EXAMPLES

BIOCHEMICAL BIOPESTICIDES
NEMA-Q™

Control plant parasitic nematodes in turfgrass the natural way with NEMA-Q, a new 100% natural, bio-pesticide that is OMRI Listed for organic production.

Active Ingredient:
*Saponins of Quillaja saponaria ...................................................... 8.6%
Other Ingredients: ................................................................. 91.4%
Total: .................................................................................. 100.0%
*bidesmosidic derivatives of quillajic acid substituted with a trisaccharide at C-3 and an oligosaccharide in C-28
Source: Extract from knotweed: *Reynoutria sp.*
- Mode of action: ISR (Induced Systemic Resistance); active compounds induce the plant’s immune system to fight against infection – boosts phytoalexins, phenolics and other beneficial compounds
- Effective control of mildews, blights, rusts
- Yield increase due to plant health effects
- EPA registration as biochemical biopesticide

Regalia is approved for organic production and is OMRI listed.
Active compound is ammoniated soap of fatty acids (22%)  
Application rate: 
Mix 1 part into 5 parts of water – use 2.5 – 7.5 gal/1000 sq ft
CheckMate® NOW Puffer® is a state-of-the-art delivery system that automatically dispenses pheromone for mating disruption of Navel orangeworm for the entire growing season.

The features and benefits for this product are as follows:

Will not harm beneficial insects
No re-entry restrictions
No pesticide residues
Helps manage insect resistance to pesticides
No impact on production schedules
Lowest labor costs
Consistent delivery of pheromone in all temperatures/conditions
Season-long mating disruption
TAKE HOME MESSAGE TO CROs
Growth of Biopesticide Market

Biopesticide Growth Outpaces Chemical Growth
(15% Bio vs. 5% Chem.)

Biopesticide Advantages

- No chemical residues
- Manage pest resistance
- Short REI/PHI; Spray in AM, return to field in PM
- Environmentally safe
- Work well in IPM programs
- Can be approved for organic production

Most biopesticides are used in conventional farming as part of pest/plant disease management programs

Graph from a presentation by P. Marrone
Important (non-GMO) Biopesticide Companies in the US

• AgraQuest/Bayer Crop Science
• Arysta LifeScience
• Becker Underwood/BASF
• BioSafe Systems
• BioWorks
• Monterey Ag Resources/Brandt
• Certis
• EcoSMART
• JH Biotech
• Marrone Bio Innovations
• MGK
• Natural Industries/Novozymes
• Nufarm
• Novozymes
• SePRO
• SipcamAdvan
• Suterra
• Valent BioSciences

Following companies have recently made acquisitions, alliances or licensing and pipeline deals with biopesticide companies:

Amvac
BASF
Bayer
DuPont
FMC
Monsanto
Scotts
Syngenta

There are >30 new biopesticide actives waiting to be registered by EPA
Biopesticide products require non-GLP efficacy field studies for label development and CA registration – study protocols often involve multiple (weekly) applications

- In fungicide trials, start applications before disease symptoms become visible
- Foliar applications need good coverage (high GPA) – adjuvant?
- Pay attention to use restrictions pertaining application timing and compatibility in rotations/tank mixes (e.g. no fungicides with fungal biopesticides)
- Since biopesticides are exempt from food tolerance, no GLP residue studies are needed for EPA registration
- Ecotox (GLP) studies are required for EPA registration
Summary

Biopesticides are derived from nature

Biopesticide market is growing: product selection and sales are increasing and more companies are involved in Biopesticide discovery and development

EPA recognizes three types of Biopesticides: microbials, biochemicals and PIPs (GM crops)

If pesticide claims are made in the organic/biopesticide/conventional pesticide label, the product has to be registered through EPA unless it is a so-called 25b exempt product

Biopesticides are registered through the EPA Biopesticide and Pollution Prevention Branch

Biopesticides against human health pests follow slightly different registration guidelines
Summary

No GLP residue, environmental fate or chronic toxicity/exposure data are required for EPA Biopesticide registration

Product development and EPA registration is faster and cheaper for Biopesticides than for Conventional Chemical pesticides

Biopesticides are used increasingly in IPM programs in conventional agriculture as rotation or tank mix partners for resistance and residue management

Biopesticide use patterns may be different from those of conventional chemical pesticides

Pay attention to use instructions: compatibility with conventional chemistries should be verified before use
The BioAg Alliance

The BioAg Alliance:
A Transformational Alliance Between World Leaders in Agricultural Innovation and Microbiology

THANK YOU

QUESTIONS?

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