



Natural Products

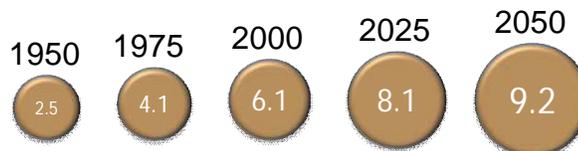
For Pest Management

## Biopesticides as Environmentally Friendly Alternatives

Pam Marrone, PhD  
CEO and Founder



## Global Trends Favor Ag Inputs



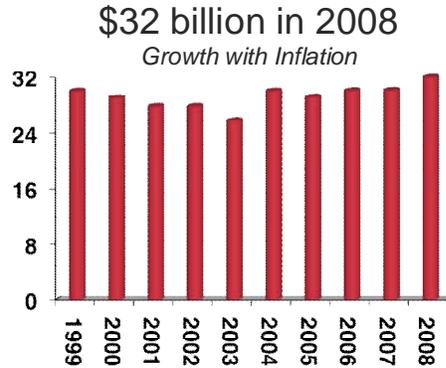
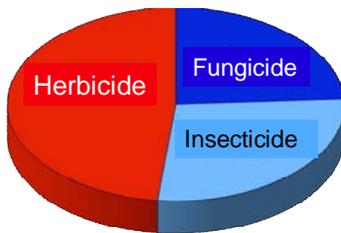
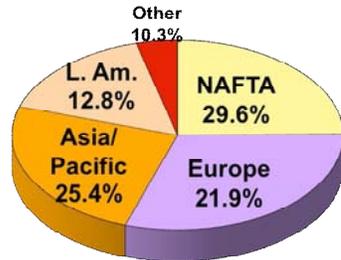
World population growth (billion) (UN)



**Number of people fed by one US farmer (Farm Bureau)**

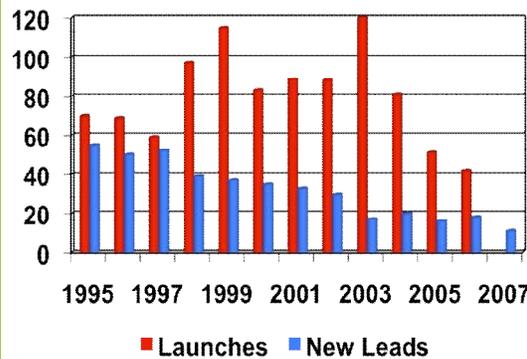
*Sustainable farm practices, emission reductions, less reliance on fossil fuels and environmental responsibility are necessities*

## Global Chemical Pesticide Market is Mature

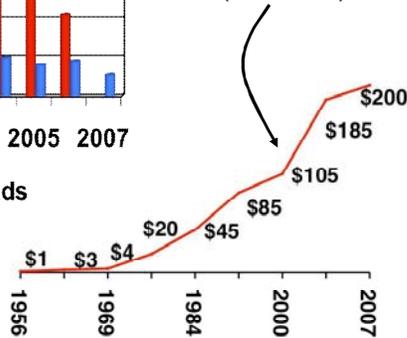


- Government phase-outs
- Pest resistance
- Export residue restrictions
- Transgenic (GM) crops
- Public concern
- Lack of new products

## Fewer New Chemicals, At Higher Cost



Cost to Develop New Synthetic Chemicals (\$Million)

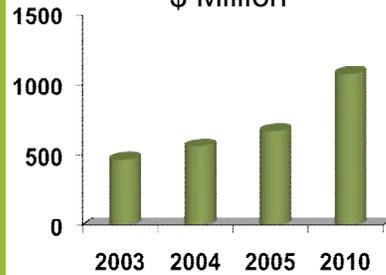


Source: Ag Chem New Compound Review (Vol 25) 2007

## Biopesticides \$1 billion by 2010

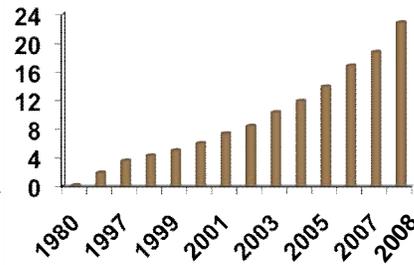


Global Biopesticides  
\$ Million



Source: BCC Research

US Organic Food  
\$ Billion



Source: Organic Trade Association

***But most biopesticides are used in conventional ag!***



## Why Biopesticides?

- v Natural world is underexplored for discovery of new pesticides
- v >50% pharmaceuticals vs. 11% pesticides derived from plants and microbes
  - Aspirin – Pain
  - Taxol - Anti-tumor
  - Quinine, Artemisinin - Anti-malaria
  - Penicillin, streptomycin, etc. – Antibiotics
  - Digitalis - Cardiotonic
- v Consumers driving market to natural products



## But Just Because it is Natural Does Not Mean it is Safe

**But natural products registered as biopesticides  
have a 50 year history of safe use, starting with Bt**

- ✓ All registered biopesticides are exempt from tolerance (can use right up to harvest)
- ✓ Most have >5000 mg/kg rat oral, dermal, inhalation
- ✓ Most have 4-hour (EPA's minimum) re-entry period
- ✓ Do not contaminate ground and surface water
- ✓ Are not ozone disruptors; do not emit VOCs
- ✓ Do not persist in the environment
- ✓ Use the safest (=food grade) inerts

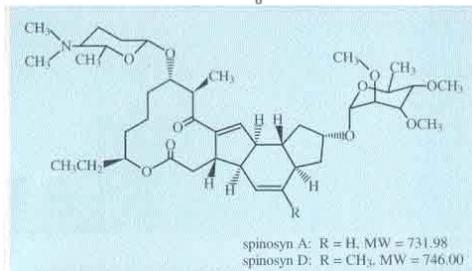
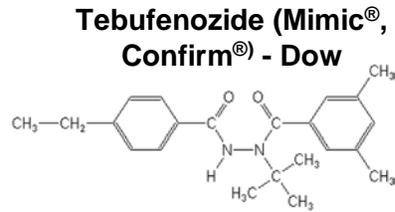
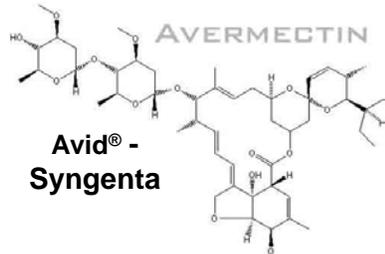


## What are Biopesticides?

- EPA term for certain types of natural products used to control pests, plant diseases and weeds
- NOT all natural products are biopesticides
- Some natural products are registered by the EPA as chemical pesticides (if they act on nervous system of the pest)

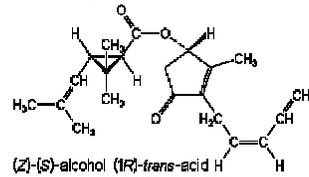


## Successful Insecticides from Natural Products - NOT Biopesticides



**Spinosad (Entrust®, Conserve®, SpinTor®, Success®, Tracer®) – Dow Agro**

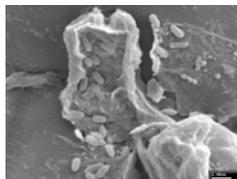
## Pyrethrins



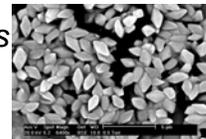
## What are Biopesticides?

### MICROBIALS (e.g., bacteria, virus, fungus)

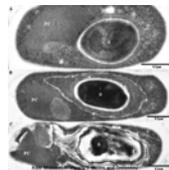
**Bacteria:** e.g., *Bacillus*, *Pseudomonas fluorescens*



*Bacillus thuringiensis*  
(Bioinsecticide)



*Bacillus subtilis*  
on powdery mildew spore  
(Biofungicide)

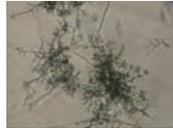


## What are Biopesticides?

### MICROBIALS (e.g., bacteria, viruses, fungi)



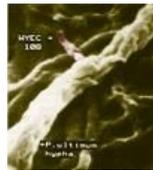
Fungi: e.g., *Trichoderma*,  
*Gliocladium* for root diseases



*Beauveria* for insect  
control



Actinomycetes: e.g., *Streptomyces*

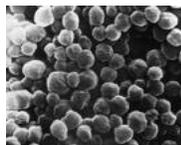


*Streptomyces lydicus*  
Biofungicide

## What are Biopesticides?

### MICROBIALS (e.g., bacteria, virus, fungus)

Virus: e.g., NPV, GV



Gypsy moth killed by  
nuclear polyhydrosis  
virus



Codling  
moth  
granulosis  
virus

## What are Biopesticides?

**BIOCHEMICALS** (e.g. plant extracts (antifeedants, pheromones, fatty acids, potassium bicarbonate, plant growth regulators)



Many insecticide products from the seeds of the neem tree



Kaligreen®, Milstop®  
bicarbonates



Fatty acids



Mating disruption pheromones are heavily used in western fruit and nut production

## Biopesticide Registration US EPA and CAL-DPR

EPA: Biopesticides & Pollution Prevention  
Division

- ✓ GM crops (PIPs=Plant Incorporated Protectants)
- ✓ Microbials (e.g., bacteria, virus, etc.)
- ✓ Biochemical (e.g. plant extracts, pheromones, fatty acids) **NON TOXIC MODE OF ACTION TO THE PEST** (suffocation, desiccation, antifeedant, mating disruption – No insect nerve toxins)



## US EPA and CAL-DPR Biopesticide Registration

Tiered Data requirements; Start with Tier I:

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

*California requires efficacy data!*



## 25-B Exempt Products

Some products don't require EPA registration because they are used in food or considered safer – e.g. :

- ✓ Clove, cedar, cinnamon, peppermint, wintergreen, castor, thyme, lemongrass, citronella, sesame, soybean cottonseed, linseed, garlic oil; Sodium lauryl sulfate
- ✓ Some of these 25-B pesticide products have dubious efficacy

**36 states regulate 25-B products (but not CA)**



## Organics Demystified



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



Organic Materials Review Institute (non-profit) seal: list of approved pesticides and fertilizers



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

## Pesticides - Lawns and Landscapes

- ✓ U.S. households with a yard/garden spent \$13.6 bil 2008 on fertilizers and insect & weed controls.
- ✓ 55% of all U.S. households with a yard/garden (45 mil), purchased one or more types of insect & weed control in 2007.
- ✓ Currently 12 mil U.S. households use all-natural organic gardening methods.
- ✓ ~17 mil households say they **definitely** will use all-natural/organic gardening methods in the future.
- ✓ Another 22 mil say they **probably** will use all natural/organic gardening methods in the future.



National Gardening Assoc. Survey

## Environmentally Friendly Gardening

- ✓ 57% of all U.S. households said it's important that lawns & landscapes be maintained in an environmentally friendly way
- ✓ But only 21% of households scored high on environmentally friendly landscapes and lawns
- ✓ Only 3% were **extremely knowledgeable** about how to maintain their lawns & landscapes in an environmentally friendly way
- ✓ 70% said they were **somewhat, not very, or not at all** knowledgeable.

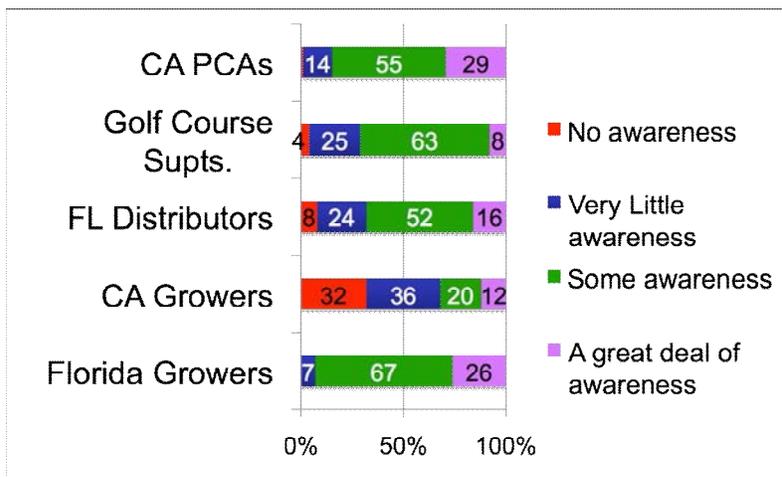


## Why People Use or Don't Use Environmentally Friendly Methods

- ✓ Top 5 reasons to **USE** are:
- ✓ Better for the environment (73%)
- ✓ Reduce risk of exposure to chemicals (59%)
- ✓ Reduce water pollution through fertilizer runoff (54%)
- ✓ Fits with my way of life/philosophy of living (43 %)
- ✓ Better (nutritionally) for my family and me (40%)
  
- ✓ Top 5 reasons **NOT** to use
- ✓ Too expensive (41%)
- ✓ Don't think it works (30%)
- ✓ Need more info about how to garden organically (25%)
- ✓ Never considered/thought about these methods (24%)
- ✓ Can't find the right products to buy (24%)



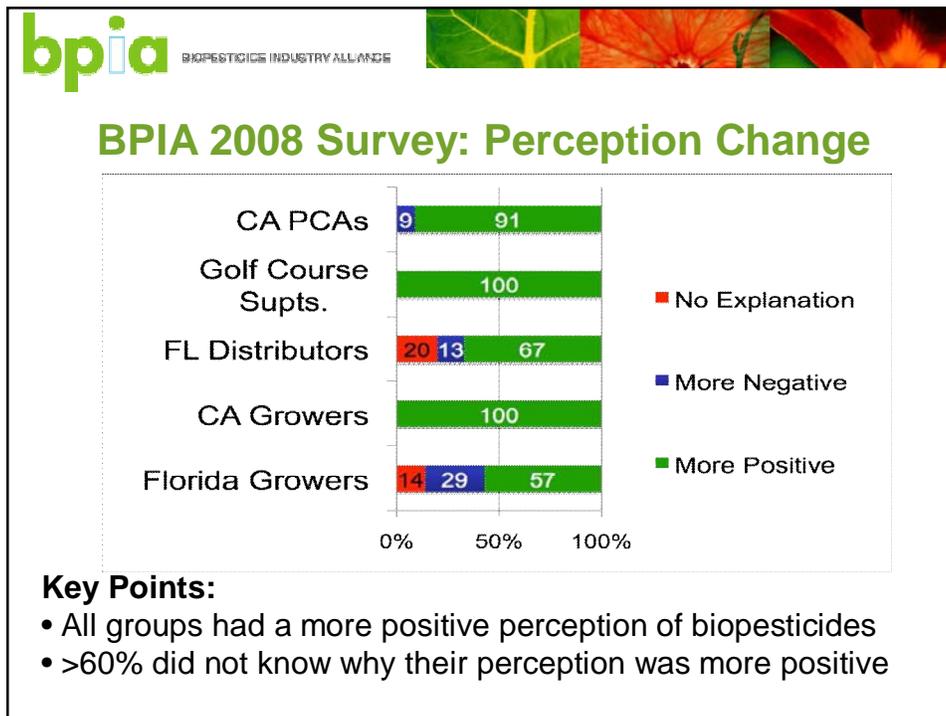
## Awareness of Biopesticides (2008)



## Main Reasons Biopesticides ARE Used (2008)

	CA Pest Control Advisors (n=69)	Golf Course Supts. (n=40)	Florida Distributors (n=26)	CA Growers (n=30)	Florida Growers (n=30)
Environmentally Safe	48%	63%	54%	60%	64%
All Other Replies	35%		27%	16%	11%
Operator Safety	12%	42%	8%	4%	21%
Safe/Benefits Insects	14%		8%	12%	36%
Public Perception	22%	8%	15%	20%	4%
More Natural/Safe	16%	4%	8%	24%	14%
Crop Safety	17%		12%	4%	25%
Organic Farming	25%		12%	16%	4%
Product Effective	13%	13%	15%	8%	4%
Don't Know	3%	25%	4%	8%	4%
Target Specific	9%				7%
Economic Benefits	3%		4%		4%

Main Reasons Biopesticides <u>ARE NOT USED</u>					
	CA Pest Control Advisors	Golf Course Supts.	FL Distributors	CA Growers	FL Growers
	(n=69)	(n=40)	(n=26)	(n=30)	(n=30)
Not as Effective	52%	42%	73%	68%	39%
Higher Cost	36%	42%	31%	44%	43%
Lack of Awareness	39%	38%	18%	32%	43%
Don't Know	6%	17%	8%	24%	7%
Lack of Research	4%	21%	12%	8%	4%
Limited Availability	6%	8%	8%	4%	18%
Too specific	7%	17%	4%		7%
All Other Replies	26%		12%		
Old Habits	3%		7%	4%	14%
Works Too Slowly	12%		4%		11%
Public Perception			4%	4%	



## Issues Impeding Biopesticide Adoption



- Perception of weaker efficacy - “snake oils” & 25-B products?
- Highly competitive marketplace
- Customer avoids risk - no reason to change
- End users lack knowledge and understanding of biopesticides
- Complex selling channel
- Capital intensive - small companies do not have funds for all the required field and demo trials and customer education



## When to Use Biopesticides



- ✓ Use them for Resistance Management
- ✓ In Rotations and Alternations; Tank mixes
- ✓ Use them early season - low pest pressure
- ✓ Use them late season – before harvest; manage residues
- ✓ Use them to save labor costs - short re-entry intervals get you back in the site sooner
- ✓ Reduce risk to people, pets, water, air





## What We Do

We discover, develop, and market **effective** and **environmentally responsible** natural products (biopesticides) that fill unmet needs for weed, pest & plant disease management.

- ✓ **Products that lower the cost and increase yields in organic farming**
- ✓ **Products that improve yields and quality in conventional ag compared to chemical-only systems**

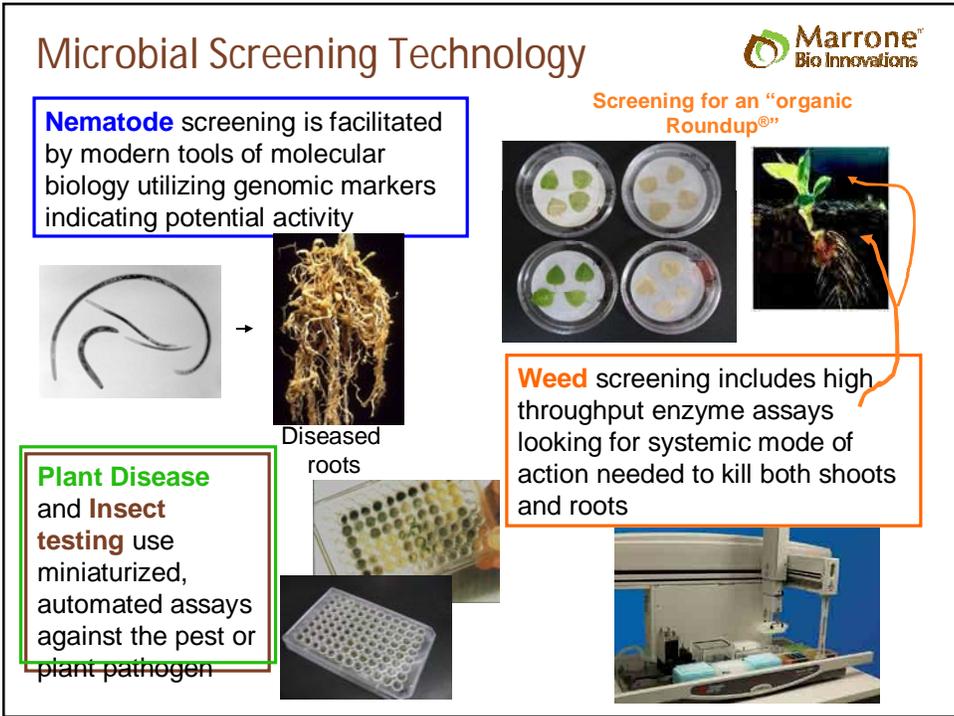
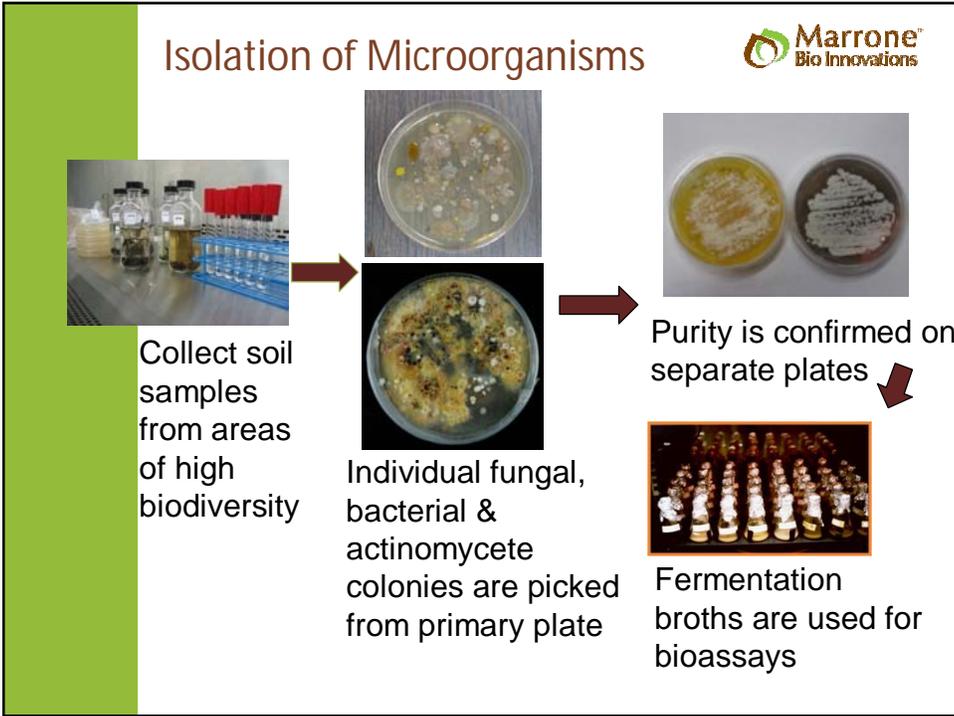


## Two Pronged Approach

*Internal and Externally Sourced Products*

- 1) We have our own microbial natural product discovery screening
- 2) To accelerate revenues, we in-license proprietary technology & products (plant extracts and microbes) on an exclusive basis

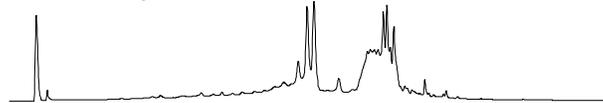




## Natural Product Chemistry



- ✓ Identify pesticidal compounds produced by the microbes (HPLC w/ diode array detection, LCMS and NMR)
- ✓ Eliminate strains with harmful compounds
- ✓ Develop analytical assays based on bioactive chemistry for QC



## Fermentation and Formulation



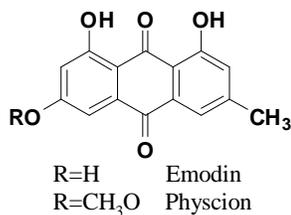
- ✓ Optimize processes
- ✓ Scale up - pilot & manufacturing
- ✓ Field trials
- ✓ Toxicology & Registration

Develop user-friendly formulations (wettable powder, WDG, liquid suspension, RTUs) & packaging

## Regalia® for Plant Disease Control



- ✓ Source: Extract from edible knotweed *Reynoutria spp.*
- ✓ Effective control of mildews, blights, rusts.
- ✓ EPA registration as biochemical biopesticide.
- ✓ Hundreds of field trials prove performance.
- ✓ Novel mode of action: **Induced Systemic Resistance** – increase of “good” plant compounds.



## New Microbial Insecticide



- ✓ Licensed from Lab of Phyllis A.W. Martin (USDA ARS). Isolated from forest soil. Patent pending.
- ✓ New species of *Chromobacterium (substugae)*.
- ✓ Must be ingested for activity. Death in 1-3 days.
- ✓ Activity is from >30 synergistic compounds (identification in progress).
- ✓ Broad spectrum control of sucking and chewing insects
- ✓ Nontoxic to rats (>5000 mg/kgs)
- ✓ Non pathogenic.
- ✓ Submission to the EPA ~3<sup>rd</sup> Q 2009.



## Insect Toxicity Summary



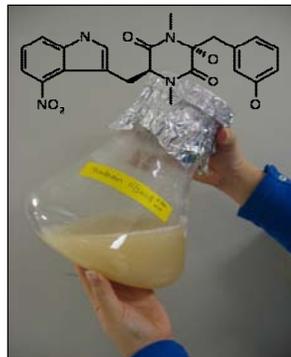
Insect Stage	Stage	Mortality	Sublethal?
CO Potato beetle	Adult	No	Feeding Inhibition
CO Potato beetle	Larva	Yes	"
<i>Diabrotica</i> spp.	Adult/Larva	Yes	-
<i>Plutella xylostella</i>	Larva	Yes	-
Gypsy moth	Larva	No	Feeding Inhibition
Sw. pot. whitefly	Adult	Yes	-
Sw. pot. whitefly	Nymph	Yes	-
S. green stinkbug	Adult	Yes	-
<i>Culex pipiens</i>	Larva	No	None seen
<i>Spodoptera exigua</i>	Larva	Yes	Feeding Inhibition
Lygus bug	Nymph	Yes	"

## Selective Rice Bioherbicide



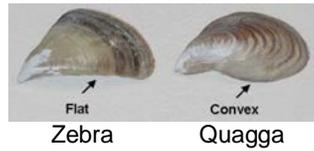
- ✓ Broad spectrum control; excellent on sedges
- ✓ *Streptomyces* compound produced by fermentation; nontoxic, non-pathogenic to rats
- ✓ EPA submission in 2009

No effect on rice





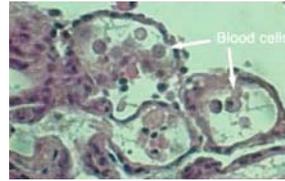
*Invasive Mussels = \$ billions in economic & environmental damage*



Zebra/Quagga mussels clog pipes



*Pseudomonas fluorescens* (dead) bacteria kill Mussels

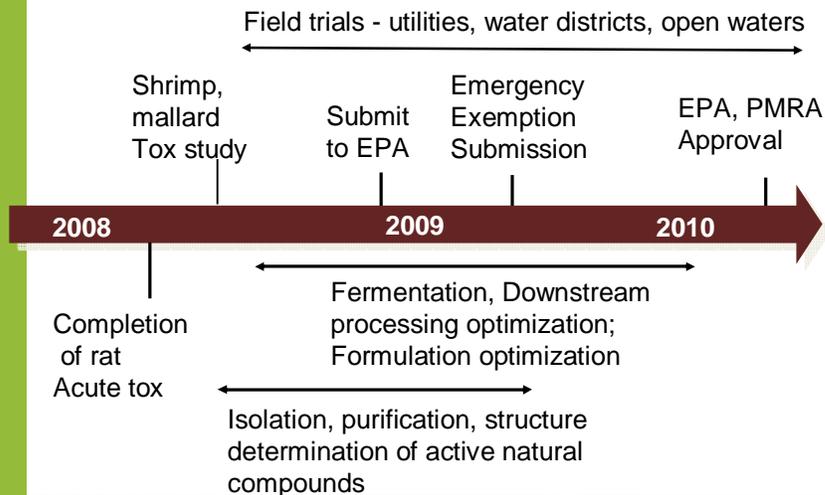


Ruptured gut cells



*Replacement for chlorine; the only biological for open waters. Discovered by NYSM – MBI is exclusive partner*

## Development Timeline



Field Development –  
Lower CO River - Davis Dam  
(US Bureau of Reclamation)



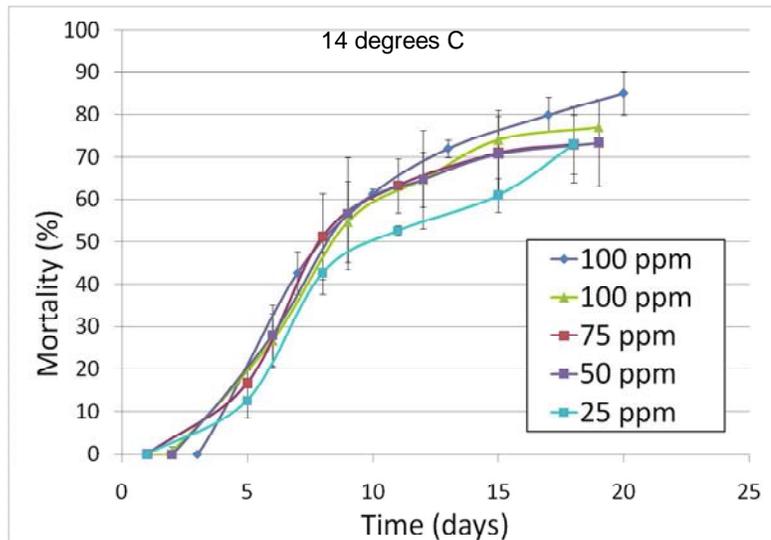
**Quagga Mussels**

- ✓ Biobox trials (Now)
- ✓ Domestic Water Pipe (Summer)  
10 inches diameter x 100 ft  
(ca. 415 gal)
- ✓ Spill Gate Enclosure (Future)  
50 x 50 x 1 foot with barrier  
(20,000 gal)



Davis Dam Biobox Rate Tests

*New Formulation/Application – one 6 hr treatment*



## Biopesticides – Summary Comments

- v Biopesticides are becoming mainstream - most are used in conventional systems
- v But perceptions persist about efficacy/cost
- v Integrate Biopesticides AND Conventionals
- v It's **NOT** Biopesticides **vs.** Conventionals
- v There is still a large need for end-user education on biopesticides – what they are, how they work, when best to use them



**Pam Marrone, Founder/CEO**

[pmarrone@marronebio.com](mailto:pmarrone@marronebio.com)

**1-530-750-2800 (office)**

[www.marronebio.com](http://www.marronebio.com)

