Green Chemistry and Sustainable Agriculture
The Role of Biopesticides

Green Chemistry and Sustainable Agriculture: The Role of Biopesticides

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Introduction

As a society we are receiving clear signals that some chemicals routinely used in conventional agriculture are associated with alarming health and environmental effects. From human to ecological health impacts, there are growing concerns about how we farm. In contrast, 'Sustainable Agriculture' describes a robust and balanced agricultural system to which many increasingly aspire. There are many unknowns in the details of how such an agricultural system would work, what inputs would supply it, and what technologies to employ in the transition. We do know, however, that Green Chemistry innovations will be key to transitioning to a more sustainable agricultural system.

Even with this most basic awareness, there is a lack of clarity about where we stand on the path towards change – are we close to replacing some of the most egregious agricultural chemicals or is the technology gap still wide? What are Green Chemistry's strengths and what are its weaknesses in approaching these issues? Are there technologies available that could benefit from clear demonstration of market demand? How can we be sure that these new chemicals are safe?

PART I: GREEN CHEMISTRY AND AGRICULTURE

A. Goals and focus of this project

Advancing Green Chemistry (AGC) set out to "scope" the field of green chemistry and evaluate the capacity of green chemistry to facilitate a shift to sustainable agriculture. We asked the following questions:

- How does green chemistry currently connect with agriculture?
- What are the leading areas of green chemistry innovation that are relevant to sustainable agriculture?
- What is involved in developing replacements for ubiquitous chemicals of concern used in agriculture?
- What are the opportunities and obstacles to green chemistry innovations in agriculture and what are some strategic suggestions for moving them forward?

AGC did a year-long survey of the field of green chemistry to find initial answers to these questions. What we discovered was that, in short, the sector within green chemistry that self-identifies as being applicable to sustainable agriculture is very much in the minority. There have been two significant efforts in the past to connect these fields- in 2003 a book, "Agricultural Applications in Green Chemistry" contained papers from a symposium on the subject; and, in 2007, A CHEMRAWN XII conference "The Role of Chemistry in Sustainable Agriculture and Human Wellbeing in Africa". Interaction between green chemists and the field of conventional agriculture, however, is trending upward fast, as pressure to develop biofuels and biomaterials is mounting. The missing link in this relationship is that most green chemists developing bio-based materials are not demanding feedstocks that have been sustainably produced. Closing this loop of awareness and interaction is a challenge to place before the field of green chemistry.

Though green chemistry applications for sustainable agriculture are relatively few, there is a specific area within green chemistry that has direct implications for sustainable agriculture: the field of biopesticides. We have chosen to focus this project on biopesticides because the field is the most likely source for alternatives to some of the pesticides of greatest concern. Several Presidential Green Chemistry Challenge Awards have been given for innovations in biopesticides. Also, the area of biopesticides is a) a rapidly growing market, b) raises both optimism and concerns, and c) is a critical new issue area for anyone concerned with agriculture. A chief conclusion of this study, however, is that as it grows in scale, the field of biopesticides is ripe for green chemistry's broad, principles-based approach to stainability.

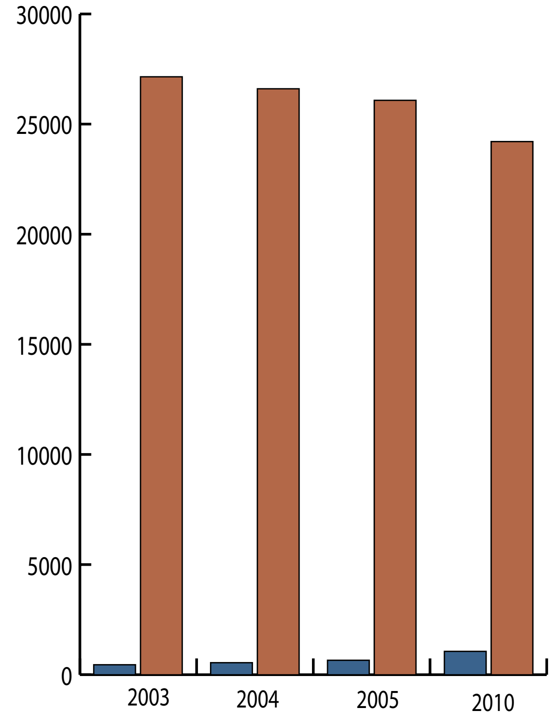
Context

The market for biopesticides is expanding rapidly: growing at some 10% per year, by 2010

More than 80% of biopesticides are used by producers employing conventional farming practices.

global sales are expected to hit the $1 billion mark and make up 4.2% percent of the overall pesticides market. Much of this rapid growth is due to the fact that, perhaps surprisingly, more than 80 % of biopesticides are used, not by organic farmers, but by producers employing conventional farming practices. Orchard crops hold the largest share of total biopesticides use at 55%. It is hard to get current data on overall pesticide use; tracking this data is not in the purview of the USDA, and the EPA last reported on pesticide use data in 2001. Expert estimates, however, hold that overall pesticide use has been declining at a rate of some 1.3% per year over the last decade. This decline is attributed to increased concerns about health and environmental effects, the rise in organic agriculture, and the emergence of alternatives, including biopesticides. In fact, as we shall discuss, the banning of particular pesticides in some cases has been a direct driver of the discovery (and in some cases the rediscovery and development) of biopesticide alternatives.

Global biopesticides and synthetic pesticides market, 2003-2010



source: BCC Research

Methodology

Over the course of a year, Advancing Green Chemistry consulting staff surveyed publicly available literature and information and conducted a series of interviews. Experts consulted included: specialists in green chemistry and sustainable agriculture, environment and health, as well as in biopesticides, ranging from those directly involved in scientific research and product development, to regulation and industry representatives. AGC staff interviewed 23 experts, the list of which is included at the end of the accompanying manuscript.

B. How Green Chemistry links with Sustainable Agriculture

Green chemistry and sustainable agriculture are both revolutionary fields with significant overlap, though the connections are not fully developed nor appreciated. Sustainable agriculture encompasses a wide variety of farming techniques and practitioners. Broadly speaking sustainable agriculture seeks to achieve three goals: farm profitability; community prosperity; and environmental stewardship. The latter includes: protecting and improving soil quality, reducing dependence on non-renewable resources, such as fuel, synthetic fertilizers and pesticides and minimizing adverse impacts on safety, wildlife, water quality, and other environmental resources.

Green chemistry is "a set of principles that reduces or eliminates the use or generation of hazardous substances in the design, manufacture and application of chemical products" (see page 11). Green chemistry moves products and processes toward an innovative economy based on renewable feedstocks, where toxicity is deliberately prevented at the molecular level.

Both of these fields envision safe products, healthy people, a clean environment, green jobs, and most importantly, a systemic approach to sustainably producing what we need. No one action or technique, taken out of context, provides the answer; but an interconnected system of sustainable technologies and approaches will move us closer to our ultimate goals. Green chemistry and sustainable agriculture are inherently intertwined; farmers need green chemists to make safe agricultural chemical inputs. Green chemists need farmers practicing sustainable agriculture to provide truly "green" bio-based raw materials to process into new products. It is a vital circle of creative interdependence – yet very few practitioners in either field are aware of this fact.

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There are three ways in which green chemistry connects with sustainable agriculture: as a consumer of agricultural products, as a source for remediation technologies, and as a producer of inputs.

First, green chemistry is a consumer of agricultural inputs: biofeedstocks and biocatalysis are central to Green Chemistry. In its founding principles green chemistry encourages the use of bio-based materials – specifically, chemists should, whenever possible, use raw materials and feedstocks that are renewable. Renewable feedstocks can come from specifically grown agricultural crops or from agricultural waste products. Green chemists are creating biocatalysts to be employed in the conversion of agricultural materials into high value products, including novel carbohydrates, polysaccharides, enzymes, fuels, and chemicals.

Green chemistry's explicit encouragement of the use of biofeedstocks and biocatalysts provides a direct link to agriculture. What is less explicit, however, in the green chemistry literature is whether biofeedstocks themselves should be produced in a way that is sustainable. One of the goals to emerge from this project is to promote this focus within the Green Chemistry community.

Second, green chemistry intersects with agriculture through applications for site remediation. Traditional farming practices leave unwanted chemicals in the environment—in the soil, water and air. Green Chemists are tackling the challenge of removing pollutants without, in the process, creating more toxic waste. For example, Green Chemists at Carnegie Mellon University have developed TAML® catalysts that can be safely used to remove specific chemicals, including pesticide residues (including atrazine and alachlor), from water. Such GC innovations should not be viewed as a panacea for continued use of these chemicals, but they give communities a valuable tool with which to deal with contamination and to help farmers deal with the transition to more organic methods, and to more generally manage the use of recycled water.

Green Chemistry connects with sustainable agriculture as a consumer of agricultural products, as a source for remediation technologies, and as a producer of inputs.

Third, and the focus of this paper: green chemistry is necessary to generate greener inputs for agricultural production. Green chemistry alternatives are vital to sustainably producing agricultural goods without continued dependence on toxic pesticides and chemicals of concern. One central question of the health and environmental communities is how close are we to replacing pesticides/chemicals of concern with greener alternatives? Promising work is underway in green chemistry; new pesticides are being designed and produced that can be more benign and/or more targeted. Biopesticides - derived from plant or microbial "pesticides" - is an area in which there is a lot of movement and potential for Green Chemistry to supplant certain chemicals of concern, and is where we chose to focus this study.

C. What is involved in replacing a ubiquitous chemical of concern?

We discovered no "Manhattan project" underway to replace some of the most ubiquitous and suspect chemical pesticides in agricultural use (though indeed such efforts might be happening undercover). Moreover, it is unlikely that green chemists will discover a single brilliant "green" solution to replace a dangerous ubiquitous chemical. The logic of this is simple: a "green" broad-spectrum pesticide that kills everything it comes into contact with is extremely hazardous (it still kills everything - targets and non-targets). The more narrowly one defines the focus of a pesticide, such that its target is more refined, the more of a specialized niche product it is.

This is indeed what we found: the various services of broad-spectrum pesticides are being addressed and replacements created on a by-use basis. For example- it is very unlikely that there will be one over arching "green" replacement for methyl bromide; rather there will be a variety of replacements developed– one greener alternative to address pests particular to strawberries, another for tomato pests. As safer replacements tend to be more specifically targeted, the market for them is consequently narrower. Small or niche markets sometimes mean that green chemistry solutions are left sitting on the shelf because the costs of manufacturing is too high and demand for a solution is too low.

D. Biopesticides: definition, categories

In very general terms, according to the US EPA, biopesticides are pesticides derived from natural materials such as animals, plants, bacteria, and minerals. The two key categories focused on in this report include biochemical and microbial pesticides (reviewing the third category of biopesticides, transgenic crops, was outside the scope of this report). The subcategories of biochemical pesticides introduced in this report include insect pheromones, plant extracts and oils, plant growth regulators and insect growth regulators. Microbial pesticide subcategories discussed include bacteria, virus, fungus, and other less common microorganisms.

Some common benefits and disadvantages of biopesticides in comparison with conventional pesticides are shown in the table below. While this table presents generalities, each category of biopesticide and each individual product must be analyzed individually to assess the full range of impacts and trade-offs of the particular product on human and environmental health endpoints as well other factors related to grower adoption.

Table 1:
Pros and Cons of Biopesticide Active Ingredients in Comparison with Conventional Pesticides

Benefits	**Disadvantages**
Less toxic	Short shelf life
Biodegrade more quickly	Limited field persistence
More targeted to specific pest	Narrower target range
Specific mode of action	Specific mode of action
Manage rather than eradicate (maintain ecological balance)	Slower acting (slower kill rate)

E. Opportunities and Challenges for Biopesticides

The field of biopesticides is deep, consequently they are a source of both optimism and concern. There is a tremendous amount of work and research occurring in this field, but like other green chemistry solutions, developing safe, effective biopesticide products requires holistic thinking and multi-disciplinary approaches to establishing safety, which is a challenge for the biopesticide industry. Turning lab discoveries into profitable business products is also daunting. This mirrors what other inventors face when implementing green chemistry solutions in other sectors.

Also, it is important to note that biopesticides fall along a spectrum of toxicity. At one end are products that are extremely narrow in focus (e.g. targeting a single species in a specific window of its life cycle). At the opposite end are biopesticide products that are wider in effect (pyrethroids for example, derived from chrysanthemums, affect a relatively wide range of species and can have unintended toxic collateral effects). When highly specified, biopesticides can be almost utterly benign in their human and environmental effects. When their impact is broader, however, biopesticides raise some of the same human and ecosystem impact concerns that conventional pesticides do. Table 1 sums up key pros and cons that result from this investigation into biopesticides.

Overview: General Pros and Cons of Biopesticide Active Ingredients in Comparison with Conventional Pesticides

Generally speaking, there are distinct benefits to using biopesticides in comparison with conventional chemical pesticides. These advantages also bring with them their own unique disadvantages as can be seen in Table 1. In sum, biopesticides tend to be less toxic, more quickly biodegradable, and more targeted to the specific pest (US EPA Pesticides, 2008). With a narrower target range of pests, they also tend to have a more specific mode of action (Clemson HGIC, 2007). Biopesticides are often designed to control a pest population to a manageable level rather than completely eradicate a target pest (Lewis and others, 1997). These technical differences translate into benefits to humans and ecosystems including increased food safety, worker safety, and reduced concerns for development of pest resistance to existing control tools.

There are also some general challenges with use of biopesticides. They tend to be more slow-acting (Clemson HGIC, 2007) and may be very specific to the life cycle of the pest. Other attributes such as persistence in the environment have both a benefit and challenge that must be balanced. For example, a biopesticide that degrades very quickly in the environment (benefit) may also have a short shelf life or limited field persistence (Clemson HGIC, 2007) requiring multiple applications. Having a narrow target range and very specific mode of action can be seen as both a benefit and a challenge (Clemson HGIC, 2007). While one benefit of specificity is lower impact on non-target species, one challenge is that control of the dominant pests on a given crop may require more than one product and may be more costly. Also as noted, biopesticides fall on a continuum of breadth of specificity: some active ingredients are highly specific to a particular organism at a particular window of opportunity; others have a broader mode of action.

Discussion: Opportunities and Challenges of Biopesticides

Biopesticides, generally speaking, are targeted and can be non-toxic.

Some attributes of biopesticides can be seen as both benefits and disadvantages. For example, the specificity of many biopesticides minimizes the negative impact on non-target organisms because they are designed to target a specific pest. The benefits of this can be profound: by focusing on an individual pest, biopesticides are generally much less toxic than conventional pesticides. However, as noted above, some biopesticide products are broader spectrum actors and consequently can have negative impacts on non-target species. These broader systemic impacts could be better understood – and anticipated – if the right questions are asked.

Broader questions of hazard are sometimes poorly understood.

Many chemistry research institutions do not investigate chemicals for hazard in its broadest sense. This is true in both the agricultural and industrial chemical sectors. For example, the USDA has several research labs across the United States that focus on discovering new products, pesticides and more, sourced from nature. The typical process is: the USDA does the basic research and, when promising chemicals are identified, USDA licenses them to universities or industry for further research into the applications of the chemical. But USDA does not investigate whether or not the chemicals they license are hazardous to human health and the environment. There are missing skills sets in the product discovery and development process. Broader questions of human and ecological health – both for the active ingredient and the inert ingredients in which the active ingredient is suspended – often are not systematically addressed.

Multi-disciplinary teams are essential for moving from active ingredient to product.

Biopesticide products are typically developed across disciplines – from entomology, microbiology, mycology, and biochemistry to entrepreneurship and investor education. Moving from the discovery of an active ingredient to a product requires even more multi-disciplinary teamwork. A university lab may do the basic research, then a company may license the patent and develop a way to produce the active ingredients and yet another company may develop the product formulation. But as noted above, there is a need for a broader set of perspectives present in the design and launch of a biopesticide product – most profoundly, this process should include environmental health scientists and green chemists.

Some good ideas sitting on the shelf require a technological "push".

Sometimes promising green chemistry discoveries sit neglected on the shelf. For example, a particular microbial biopesticide that can control nematodes on par with methyl bromide was discovered by academic and USDA researchers some fifty years ago but never was commercialized due to high production costs. This discovery was launched as the product Pasteuria thanks to a newly discovered, highly efficient way to grow the Pasteuria microbes (see page 25). There are no doubt other similarly orphaned technologies waiting to be rediscovered and developed into products.

Banning bad actor chemicals is a powerful driver.

Forcing toxic chemicals out of the marketplace provides incentives for developing green chemistry solutions and makes these solutions commercially viable. As a result several new biopesticide technologies for managing pests formally treated with these more toxic pesticides have come to market. Without the bans, the research funding for alternatives and the market space for new products would not have been allocated. For example, the severe restriction of Azinphos-methyl and the ban on methyl parathion made it essential to develop safer alternatives for controlling the Codling Moth (see page 40).

Biopesticides offer growers both opportunities – and challenges.

Biopesticide solutions often require the grower to learn new application techniques and new ways of thinking about pest management. As noted, biopesticides are often highly specific and have very precise modes of action. This specificity can mean that workers can enter fields quickly after use, thus cutting wait times and offering more flexibility to the user. Specificity also means, however, that growers may need to purchase several different kinds of product to meet their pest management needs; this is a potential cost concern for growers. Biopesticides also require new skills and understanding of pests, their life cycles and how to

The Challenge of Commercialization for Niche Products

The USDA Natural Products Research Unit developed and patented an algaecide to prevent musty off-flavor in catfish production from certain blue-green algae (USDA ARS, 2008). It was researched as a more benign alternative to the current synthetic herbicide being used called diuron. Diuron is included in the Pesticide Action Network's "Bad Actor Pesticides" due to concerns of carcinogenicity, reproductive and developmental toxicity, and ground water contamination (PAN, 2008). However, diuron is not banned under US EPA or international regulations.

The US EPA gave the new algaecide an emergency approval (Section 18), which was renewed for several years. It was granted full approval for use in catfish aquaculture in 2008 (Duke, 2008). Since the market is so small, however, the USDA laboratory has not been successful in finding a company willing to bring the technology to market. An EPA ban on diuron would be a galvanizing driver for marketing this diuron alternative. This example highlights economic and regulatory challenges and opportunities impacting commercialization of biopesticides alternatives due to their niche market applications.

use biopesticides to intercede effectively. This is both a challenge but also an opportunity for expanding a new category of skilled labor in the farm sector.

Efficacy is Key

Green chemistry solutions must work. Proving efficacy in comparison to traditional pesticides is one of the chief concerns of the biopesticide industry. The Biopesticide Industry Alliance is beginning to define industry standards. To date, these standards have focused on efficacy. There is an opportunity, however, to encourage this industry to develop standards that reflect green chemistry principles – including inherent human and ecological hazard.

Transparency and Dialogue are Essential

Transparency is essential to public adoption of all green chemistry solutions, including biopesticide products. Negative public reactions to biopesticides have been due to a lack of transparency about inert ingredients used in a product, as well as to negative side effects of some broader spectrum biopesticides on non-target species. These issues can be prevented if products are developed using a green chemistry principles-based approach and if more inclusive public dialogue were employed about these products.

Conclusion

Biopesticides are a set of tools and applications that will help our farmers transition away from highly toxic conventional chemical pesticides into an era of truly sustainable agriculture. Of course biopesticides are only a part of a larger solution; sustainable agriculture is a broad and deep field. But helping farmers move from their current chemical dependency to organic agriculture and beyond requires tools for the transition and tools for a new era. Biopesticides can and will play a significant role in this process.

There remain, however, serious questions about the safety of these products from both a human and ecosystem health standpoint. Current regulations do not go nearly far enough in evaluating systemic broader impacts of biopesticides. By definition, green chemistry is about continuous improvements aimed at reducing or eliminating hazard. Fully defining hazard is difficult. Even products hailed by green chemistry and regulators alike as safer for human health may turn out to have unforeseen negative environmental health impacts- for example, Spinosad, a green chemistry award winning biopesticide, is significantly safer for humans than other treatments but is toxic to bees.

We must encourage pest management solutions and regulations to continuously evolve and ensure that multi-disciplinary teams, including green chemists, environmental health sciences and other sciences, approach these products systemically to both discover and refine them.

The 12 Principles of Green Chemistry

1. **Prevention.** It is better to prevent waste than to treat or clean up waste after it is formed.
2. **Atom Economy.** Synthetic methods should be designed to maximize the incorporation of all materials used in the process into the final product.
3. **Less Hazardous Chemical Synthesis.** Whenever practicable, synthetic methodologies should be designed to use and generate substance that possess little or no toxicity to human health and the environment.
4. **Designing Safer Chemicals.** Chemical products should be designed to preserve efficacy of the function while reducing toxicity.
5. **Safer Solvents and Auxiliaries.** The use of auxiliary substances (solvents, separation agents, etc.) should be made unnecessary whenever possible and, when used, innocuous.
6. **Design for Energy Efficiency.** Energy requirements should be recognized for their environmental and economic impacts and should be minimized. Synthetic methods should be conducted at ambient temperature and pressure.
7. **Use of Renewable Feedstocks.** A raw material or feedstock should be renewable rather than depleting whenever technically and economically practical.
8. **Reduce Derivatives.** Unnecessary derivatization (blocking group, protection/deprotection, temporary modification of physical/chemical processes) should be avoided whenever possible.
9. **Catalysis.** Catalytic reagents (as selective as possible) are superior to stoichiometric reagents.
10. **Design for Degradation.** Chemical products should be designed so that at the end of their function they do not persist in the environment and instead break down into innocuous degradation products.
11. **Real-time Analysis for Pollution Prevention.** Analytical methodologies need to be further developed to allow for real-time in-process monitoring and control prior to the formation of hazardous substances.
12. **Inherently Safer Chemistry for Accident Prevention.** Substances and the form of a substance used in a chemical process should be chosen so as to minimize the potential for chemical accidents, including releases, explosions, and fires.

PART II: CATEGORIZATION OF BIOPESTICIDES

F. Overview of Biopesticide Categories and Formulations

"Biopesticides are certain types of pesticides derived from such natural materials as animals, plants, bacteria, and certain minerals" (US EPA Pesticides, 2008). The EPA separates biopesticides into three major classes based on the type of active ingredient used, namely microbial, biochemical, or plant incorporated protectants (GMOs).

The active ingredient of a microbial pesticide is typically a microorganism such as a bacteria or fungus. A microbial active ingredient can be either the spores or the organism itself. Biochemical pesticides are chemicals either extracted from natural sources or synthesized to have the same structure and function as the naturally occurring chemicals. Biochemical pesticides are distinguished from conventional pesticides both by their structure (source) and by their mode of action (mechanism by which they kill or control pests). Plant incorporated protectants are substances produced by plants from genetic material that has been added to the plant. The resultant plant is commonly known as a transgenic crop or a genetically modified organism. The topic of genetically modified organisms is a broad topic that warrants its own investigation, and will not be covered in this report.

The US EPA has specific definitions that apply to biopesticides in a regulatory context. However, within the agricultural community, common use definitions of the term "biopesticide" can vary significantly. In addition there are related and overlapping terms that can create misunderstandings with terminology. For example, the term "biorational pesticide" also refers to natural organisms or plant-derived products (Krischik, 2008, p. 23).

In addition to being categorized by the active ingredient, biopesticides can be categorized by the target pest, such as insecticides to manage insect populations and fungicides to manage fungus. While the former categorization system is more relevant from a scientific and regulatory perspective, the latter is more relevant in the context of marketing, sales, and grower use of biopesticides. For the purposes of this report, biopesticides have been categorized in a manner similar to that used by the EPA, while allowing some topics that don't align with strict EPA definitions. Additionally, biopesticide categories included in this report that contain active ingredients that are not regulated as biopesticides by the EPA have been noted herein.

Environmental Protection Agency Regulations

Over the past decade, US and other national and international regulatory bodies have passed laws to limit or eliminate the use of some of the most toxic conventional pesticides. Tightening restrictions such as decreased residue limits, longer pre-harvest intervals, and longer worker re-entry intervals are making the use of such conventional products less attractive to growers. As current pest control tools are phased out and others are slated for re-evaluation, growers are seeking alternatives (Hartmeier, 2008). Changing regulations have supported increasing biopesticide use among non-organic growers.

Expedited EPA Registration and Review

Pesticides are regulated by the US EPA under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). The EPA reviews each regulated active ingredient for its potential to harm humans and the environment. The manufacturer must submit data on a broad range of toxicological endpoints. The Office of Pesticide Programs reviews toxicity and exposure information for each active ingredient and target crop combination, and specifies approved use conditions.

Biopesticides are evaluated for the same breadth of toxicological endpoints as conventional products. The US EPA provides a fast-track review and registration for biopesticides by combining lower data requirements with high review priority. "Typically, new biopesticide ingredients are registered in 11 months; conventional pesticides can take 2-3 times longer" (Hall and Menn, 1999).

There is a separate fast-track category called "reduced risk pesticides" which include products that are regulated by the EPA as conventional pesticides but meet certain requirements for lower impact on human and environmental health. Some products in categories discussed in this report, such as insect growth regulators or plant extracts, may be candidates for review as reduced risk pesticides. "For FY95 and FY96 (prior to the passage of FQPA in August 1996) the average total time required to register a new conventional pesticide was thirty-eight months. For reduced-risk pesticides the average total time for registration was only fourteen months. Since passage of FQPA three new AI, reduced-risk pesticides were registered in seventeen, eighteen and seventeen months, somewhat longer than the pre-FQPA average but still substantially shorter than the conventional pesticide times" (US EPA OPP, 2007).

Beyond Regulations: Ecolabels and other Standards

There is a trend to move beyond regulatory requirements to develop more broad scope and restrictive standards. One driver behind this trend is a perception that the current regulations are inadequate. The predominant focus of the EPA pesticide registration process is on human health and safety. There are no adequate regulations to provide meaningful ecosystem-level protection, such as protection of birds, pollinators, and aquatic systems (Benbrook, 2008). Green Chemistry principles and integration of supply chain considerations are not addressed in the current regulatory framework either. In order to provide an additional level of product differentiation in the marketplace, ecolabels are developing in particular markets.

Ecolabels are driven by consumers, and designed to help them differentiate between agricultural products available to purchase. The USDA Organic Certification label is the most widely accepted food label that provides additional restrictions on pesticide use. Ecolabels typically incorporate broad social and ecological considerations including conservation and social responsibility. While some ecolabels incorporate an assessment of the pesticide(s) used in production of the agricultural product, pesticide standards and evaluation are imbedded in the ecolabel. Thus, pesticide information is typically not directly available to the consumer. The ecolabel system for food and agricultural products does not provide the transparency required for most consumers to take an active role in impacting pesticide selection by growers. See the table below for an overview of some of the assessment systems in the marketplace and a comparison of how pesticide evaluation is incorporated into them.

Table 2. Ecolabels Incorporating Pesticide Standards (Consumer Union, 2008; OTA, 2008)

Label	**Organization**	**Pesticide Evaluation**	**Label Applied To**
Certified Organic	USDA	Permitted & Prohibited Pesticides Lists[1]	Agricultural Products
Healthy Grown	Protected Harvest	Pesticide Environmental Assessment System[2]	Agricultural Products
Green Shield	NRDC	Pesticides Prohibited based on human health criteria[3]	Pest Management Services and Professionals
Rainforest Alliance Certified	Rainforest Alliance	Prohibited Pesticides Lists[4]	Food
Fair Trade Certified	Fair Trade USA	Prohibited Pesticides Lists[5]	Food
Food Alliance Certified	Food Alliance	Prohibited Pesticide List	Food

1. Generally natural substances are permitted and synthetic substances are prohibited, with some notable exceptions.

2. Aggregate of 5 toxicity indices: acute mammalian risks to workers, dietary risks to infants and children, acute avian toxicity, acute aquatic organism toxicity, acute toxicity to honey bees

3. Human health criteria include acute mammalian toxicity, carcinogenicity, neurotoxicity, reproductive and developmental toxicity

4. Prohibited materials include pesticides listed by the Pesticide Action Network ("Dirty Dozen" chemicals), the World Health Organization (Class I., A & B chemicals), and the Food and Agriculture Organization ("Prior Informed Consent" chemicals).

5. List of pesticides that are prohibited for use that includes the Pesticide Action Network's (www.panna.org) "dirty dozen" and EPA red lists.

G. Biopesticide Categories

This section defines each key category of biopesticides, offer illustrative examples, and discuss formulation issues and biopesticide products. Categories of biopesticide discussed here are:

a. Biochemical Pesticides
  1. Insect Pheromones
  2. Plant Extracts and Oils
  3. Plant Growth Regulators
  4. Insect Growth Regulators

b. Microbial Pesticides
  1. Bacterial Biopesticides
  2. Fungal Biopesticides
  3. Viral Biopesticides
  4. Other Microbial Biopesticides

c. Biopesticide Formulations

a. Biochemical Pesticides

Biochemical pesticides are the most closely related category to conventional chemical pesticides. Biochemical pesticides are distinguished from conventional pesticides by their non-toxic mode of action toward target organisms (usually species specific) and their natural occurrence (Steinwand, 2008). The active ingredient can be a single molecule or a mixture of molecules, such as a naturally occurring mixture comprising a plant essential oil, or a mixture of very structurally similar molecules called isomers in the case of insect pheromones. While all active ingredients of biochemical pesticides occur in nature, the active ingredient in the product may be a synthetic analogue to the naturally occurring substance. This is often necessary to make a viable product and/or process, such as with insect pheromones. As many of the active ingredients in this category of biopesticides are synthetic, the full range of Green Chemistry principles should be applied to the development of the active ingredient and the biochemical pesticide product.

Not all naturally occurring chemicals are regulated as biopesticides, and some are quite toxic. For example, d-limonene is a component of several citrus essential oils. The concentrated extract of d-limonene is regulated as a conventional insecticide due to its toxic mode of action. In contrast, the oils from which d-limonene may be derived, when used as a pesticide, normally have a non-toxic mode of action and are regulated as biopesticides. "Depending on the product and what it is used against, a classic mode of action for these types of oils is suffocation. Some essential oils work as repellents, and their mode of action would be as a fragrance." (Steinwand, 2008).

In practical terms, a non-toxic mode of action typically means that there is a delay between contact with the substance and death (Mandula, 2008). Some examples of non-toxic modes of action include suffocation or starvation. Distinguishing between biochemical and conventional pesticides can be complex, and is determined by an EPA committee on a case-by-case basis.

Biochemical pesticides typically fall into distinct biologically functional classes, including semiochemicals, plant extracts, natural plant growth regulators, and natural insect growth regulators. These classes of biochemical pesticides are described below with examples provided for each category. There are almost 122 biochemical pesticide active ingredients registered with the EPA, which include 18 floral attractants, 20 plant growth regulators, 6 insect growth regulators, 19 repellents, and 36 pheromones (Steinwand, 2008).

a.1 Insect Pheromones

Insect pheromones are chemicals used by an insect to communicate with other members of the same species. Structurally these chemicals are often very similar to substances used in flavors and fragrances. Pheromones are a subset of a broader category called semiochemicals. A semiochemical is defined as a message-bearing substance produced by a plant or animal, or a synthetic analogue of that substance, which evokes behavioral response in individuals of the same or other species (US EPA BRT, 2002). Semiochemicals are used for various functions including attracting others to a known food source or trail, locating a mate, or sending an alarm. Insect sex pheromones are used in pest management.

The insect pheromones themselves do not kill a target pest. When used for pest management, two common uses are to attract an insect to a trap containing a lethal pesticide or to disrupt mating. With mating disruption, proportionately large concentrations of the sex pheromones are present in the air, thus confusing the males and decreasing their success at locating a female with which to mate. Pheromones can also be used to monitor pest populations as part of larger Integrated Pest Management (IPM) systems, particularly to determine appropriate timing and application of pesticides.

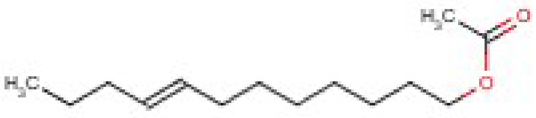
Insect pheromones account for a large percentage of the biochemical pesticides on the market. In mid 2002, EPA had registered 36 pheromones, which comprised over 200 individual products (Ware and Whitacre, 2004). Insect sex pheromones can be used alone to manage pest populations when pest pressure is moderate to low, such as after several years of consecutive use. Other practical uses include, “in survey traps to provide information about population levels, to delineate infestations, to monitor control or eradication programs, and to warn of new pest introductions” (Ware and Whitacre, 2004).

Advantages to the use of insect pheromones include their high species specificity and relatively low toxicity. Sex pheromones tend to be specific to a particular species or even strain of insect, making them one of the most targeted pest management strategies. This specificity thus maintains an ecological balance by leaving undisturbed populations of other insect species and non-target organisms.

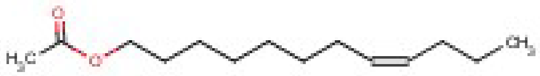
A disadvantage of insect pheromones is that they often must be used in combination with other pest management strategies to achieve the efficacy desired. This is particularly true when pest pressure is high. With high pest pressure, the male is more likely to locate a mate by simply bumping into her rather than by using pheromones to communicate over long distances. However, the combination of pest management strategies typically lowers pest pressure in subsequent years, creating the opportunity for the insect pheromones to be used alone.

Insect Pheromone Example 1:
Macadamia Nut Borer: A combination of three related molecules is used to control the Macadamia Nut Borer in fruit and nut crops. The two acetate molecules are called stereoisomer, differing only in the spatial orientation of their component atoms as indicated by the preceding letter (E and Z below). The third is the corresponding alcohol.

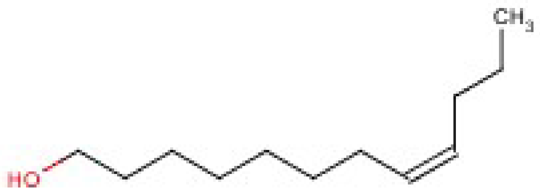
(E) – 8 Dodecen-1-yl acetate (CAS # 38363-29-0)



(Z) – 8 Dodecen-1-yl acetate (CAS # 28079-04-1)



(Z) – 8 Dodecen-1-ol (CAS # 40642-40-8)



Insect Pheromone Example 2:
Mating Disruption of Tortix Species: The blending of mixtures of very similar molecules in particular combinations and ratios can be used as mating disruption for several species of insects, predominantly various tortix species. The main components of the blends are the stereoisomers of Tetradec-11-en-1-yl acetate

Mating Disruption as a Pest Management Tool In California's Wine Industry

Within the last decade the vine mealybug (Planococcus ficus) invaded and spread through California from Mexico, causing significant damage to valuable vineyards. The initial response was to focus on eradication. A pheromone was identified for detection and monitoring of the invasive species. Jocelyn Millar and his lab at University of California at Riverside successfully conducted applied research to synthesize the pheromone molecule and develop and test its use in pheromone-baited monitoring traps. However, as the vine mealybug became established in many of California's grape growing regions, the focus shifted from eradication to control.

Due to its effectiveness in traps, developing the pheromone to control vine mealybug populations using mating disruption was pursued. The key goal of the research was to identify less-toxic insecticides that may be effective alternatives to organophosphates. Two companies got involved in the commercialization of large scale mating disruption products. Kuraray developed the synthesis route and process for large-scale production of the active ingredient, and Suterra developed the pesticide product including selection of inert ingredients, design of the applicator, and product testing and registration. Some of the field-testing was coordinated and conducted in collaboration with Kent Daane and his team at the University of California Berkeley Extension.

The white waxy exterior of the vine mealybug combined with its habit of hiding under the bark can make it particularly challenging to control. Most pesticides require direct contact with the mealybug, and will not be effective against those under the bark. Many of the "softer" insecticides are not able to penetrate the waxy exterior; some insecticides such as soap even slide off the bug. However, pheromones are volatile molecules dispersed through the air and sensed by the insect without requiring penetration (analogous to perfumes being sensed by humans).

Mealy bugs on grape vine. Mealy bugs (Planococcus ficus) on the trunk of a grape vine (Vitis sp.). Female mealy bugs feed on plant sap, normally in roots or other crevices. They attach themselves to the plant and secrete a powdery wax layer used for protection while they suck the plant juices. The males on the other hand, are short-lived as they do not feed at all as adults and only live to fertilize the females. Photo Credit: Jack Clark / AGStockUSA / Science Photo Library

Through field-testing, researchers also discovered unexpected benefits. One was that application of the pheromone seemed to attract higher populations of natural vine mealybug predators to the application area. The higher level of pheromones presumably fooled the parasitoid predators into believing there were more vine mealybugs present. The pheromone-filled air attracted the natural predators to the fields.

A second benefit of the pheromones use over conventional broad-spectrum pesticides was that the ecological balance and natural predator populations where preserved. This specificity can prevent the need for additional pesticides later in the season to control secondary pest population. Secondary pest populations often surge later in the season when broad-spectrum pesticides are used because the pesticides kill natural predators of the primary pest.

The use of the pheromone is not a one for one replacement for organophosphates.

Vine mealybug pheromones are often integrated into pest management systems, particularly for the first several years when pest pressure is high. They can be used stand-alone after several years if pest populations are managed at a low level. When used in systems, they are often combined with neonicotinoids, insect growth regulators, or other biopesticides – some of these other methods have raised concerns about intended impacts on non-target organisms such as bees.

Growers need transparent and comprehensive information to make informed choices between vine mealybug management options. The use of the vine mealybug pheromone is not a one for one replacement for organophosphates. Pheromone use has unique benefits and limitations that must be understood to assess the trade-offs. In addition, new skill sets are required of growers to properly identify and monitor both the pest and its life cycle, as well as to evaluate other tools used in comprehensive insect management systems.

This example demonstrates the complexity of both developing and using biopesticides, from the collaborative development process often required to bring biopesticides to the market, to the need for transparency and education to allow growers to make informed choices, to the niche nature of pheromones and the challenges in designing IPM systems.

and the corresponding alcohol Tetradec-11-1-ol. The specific mixtures of isomers used to control a given species are displayed in Table 3 below. An even greater level of specificity is required to control the various strains of the European corn borer, each requiring a customized blend made by adjusting the ratios of the stereoisomers (US EPA Fact Sheets, 2008).

Table 3: Sex Pheromones for Tortix Species

Insect Species	**Scientific Name**	**Acetate Isomers**	**Alcohol Isomers**
Tea Tortix	Homona magnanima	Z	
Blackheaded fireworm	Rhopobota naevana	Z	
European corn borer	Ostrinia nubilalis	Z and E	
Omnivorous leafroller	Platynota stultana	Z and E	Z and E
Tufted apple moth	Platynota idaeusalis	E	E
Light Brown Apple Moth	Epiphyas postvittana	E	

a.2 Plant Extracts and Oils

Plant extracts and oils are specific chemicals or mixtures of chemical components derived from a plant. This category of biopesticides is much more diverse in composition, target pest, and mode of action than insect pheromones discussed above. Plant extracts and oils are most often used as insecticides, but can also be used as herbicides. The mode of action varies greatly from product to product. Where sex pheromones directly interrupt the reproductive cycle of insects, plant extracts and oils often act less directly and specifically. Some botanical extracts such as floral essences attract insects to traps. Others such as cayenne can be used as deterrents. Others, such as Lemongrass Oil, strip the waxy coating off leaves of weeds to cause dehydration. Others coat the pest causing suffocation, and still others enhance the natural immune system of a crop (systemic acquired resistance).

Products made from plant extracts and oils can be regulated as biopesticides or conventional pesticides depending on their mode of action and level of toxicity. For example, pyrethrum is an extract from a species of chrysanthemum and is commonly used in organic agriculture, yet it can be highly toxic. Pyrethrum quickly paralyzes and kills insects by altering the way that electrical impulses are transmitted by the nervous system; the mode of action is similar to that of DDT. Pyrethrum and a closely related class of synthetic insecticides called pyrethroids are regulated as conventional pesticides. Other notable plant products that are not considered biopesticides include nicotine extracted from tobacco (which is toxic to bees), and rotenone extracted from roots of two genera of the legume family (Ware and Whitacre, 2004). The myth that all products derived from natural sources are safe is in clear contrast with these examples.

Overall among plant extracts and oils there are more exceptions to the general advantages and disadvantages than the generalities discussed for other categories of biopesticides. The higher level of exceptions is due to the diversity of active ingredients in this category.

A disadvantage of plant-based products is that many of them are further on the broad-spectrum end of the specificity continuum than other categories of biopesticides. For example, Lemongrass oil (mentioned above) effectively kills all plant species with a waxy cuticle including weeds and crops. That said they do tend to have relatively low toxicity in comparison with conventional pesticides.

Plant Extract Example 1: Thymol
Thymol is a chemical constituent of thyme essential oil. The thyme oil is a naturally occurring mixture of compounds from the plant Thymus vulgaris. Thymol is used to control the Varroa mite (Varroa destructor), a species that is parasitic to bees. Thymol is volatile and permeates the hive, coming in direct contact with the parasitic mites. The volatilized thymol irritates the mites, causing them to withdraw from the bees and die from starvation.

Plant Extract Example 2: Enzyme Extract
A product that will soon be commercialized by Marrone Organic Innovations is based on an enzyme extracted from Giant Knotweed, an abundant invasive in the US and native to Asia. The extract turns on the natural immune system of the crop, allowing the crop to protect itself more effectively from powdery mildew. Powdery mildew refers to a group of numerous fungi that thrives under humid conditions. The enzyme extract is effective on a range of vegetable, fruit, and fruit tree crops including grapes and cucumber (Nguyen, 2008).

a.3 Plant Growth Regulators

Plant hormones and plant growth regulators are chemicals that alter the growth of a plant or plant part or promote certain biological changes in the plant. Plants produce hormones naturally, while humans apply growth regulators to the plants. Plant growth regulators may be synthetic compounds (e.g. IBA and Cycocel) that mimic naturally occurring plant hormones, or they may be natural hormones that were extracted from plant tissue (e.g. IAA). According to the Florida Department of Agriculture and Consumer Services, "a plant growth regulator is defined as any substance or mixture of substances intended, through physiological action, to accelerate or retard the rate of growth or maturation or for otherwise altering the behavior, of ornamental or crop plants or the produce thereof; but does not include substances intended as plant nutrients, trace elements, nutritional chemicals, plant inoculants, or soil amendments" (Fishel, 2006).

While regulated as pesticides in the US, plant growth regulators do not specifically target any type of pest. Instead they are used to enhance crop yield, crop shelf life, and the appearance of the crop. They do so by affecting flowering; ripening and aging; root growth; distortion and killing of leaves, stems, and other parts; prevention or promotion of stem elongation; color enhancement of fruit; prevention of leafing and/or leaf fall; and many other functions. Some plant growth regulators are regulated as biopesticides while others are regulated as conventional pesticides.

An advantage of plant growth regulators is that very small concentrations of these substances produce major growth changes. Plant growth regulators are typically dosed in parts per million or parts per billion. In order to be effective plant growth regulators must be absorbed by plant tissue, which can be a disadvantage.

Plant growth regulators, moreover, are potent compounds and there are concerns about how their use might have unintended affects on non-target species and ecosystem balance issues. (Lovatt, 2008). Some plant growth regulators are known to be human carcinogens and endocrine disrupters. This category of compound needs much more study by environmental health specialists.

There are 5 main groups of plant growth regulators and several minor groups. Each group has a distinct set of modes of action that effect one or more of the functions listed in the preceding paragraph such as supporting root growth to help with transplanting. See Table 4 for a summary of the associated function(s), practical uses, and examples of the major classes of plant growth regulators.

Table 4: Plant Growth Regulators (Fishel, 2006)

Class	**Function(s)**	**Practical uses**	**Example**
Auxins	Shoot elongation	Thin tree fruit, increase rooting and flower formation	Indole-3-butyric Acid (IBA)[1]
Gibberellins	Stimulate cell division and elongation	Increase stalk length, increase flower and fruit size	Gibberellic Acid (GA_3) [1]
Cytokinins	Stimulate cell division	Prolonging storage life of flowers and vegetables, bud initiation and root growth	Kenetin[1]
Ethylene and Ethylene generators	Ripening	Induce uniform ripening in fruit and vegetables	Ethylene[1]
Growth Inhibitors and retardants	Stops growth (inhibitor) or Slows Growth (retardant)	Promote flower production by shortening internodes (inhibitor); or retards tobacco sucker growth (retardant)	Abscisic Acid[2]

1. Regulated by the US EPA as a biopesticide
2. Regulated by the US EPA as a conventional pesticide

Plant Growth Regulator Example 1 California Citrus:
A combination of three plant growth regulators is used prior to harvest on California citrus crops. 2,4-dichlorophenoxyacetic acid (2,4-D) is used mainly to delay and reduce unwanted fruit drop. Gibberellic acid (GA_3) is used mainly to delay over ripening. Naphthaleneacetic acid (NAA) is used to promote fruit drop of excess fruit (thinning to increase the size of the remaining fruit) and to inhibit the growth of suckers on the trunk (Lovatt, 2008). While GA_3 is regulated as a biopesticide, NAA and 2,4-D are regulated as conventional pesticides. Pesticide 2,4-D in particular is suspected to have endocrine disrupting effects and is a potential carcinogen (PAN, 2008).

Plant Growth Regulator Example 2 Retain:
Valent BioSciences produces a product called Retain that can be used in organic orchards. The active ingredient is aminoethoxyvinylglycine (AVG). AVG blocks the production of ethylene to slow down fruit ripening. It is produced by fermentation of Streptomyces, a soil-borne bacteria. AVG is regulated as a biopesticide by the US EPA.

a.4 Insect Growth Regulators

Insect growth regulators are chemical compounds that alter the growth and development of insects. Thus, they are specific to the control of insect pests. There are three key types of insect growth regulators, each with a distinct mode of action. Juvenile hormone-based insecticides disrupt immature development and the emergence of an adult. Precocenes interfere with normal function of the glands that produce juvenile hormone, thereby indirectly preventing the emergence of a reproductive adult. Chitin synthesis inhibitors limit the ability of the insect to produce a new exoskeleton after molting. Thus, chitin synthesis inhibitors leave the insect unprotected from the elements and from prey, drastically reducing its chances of survival.

The EPA may regulate insect growth regulators as biopesticides or conventional pesticides. For example, while both Neem and its constituent azadirachtin are considered biopesticides, various chitin synthesis inhibitors including benzoylureas, buprofezin and cyromazine are regulated as conventional pesticides. Most insect growth regulators registered as biopesticides are juvenile hormone-based insecticides. More specifically, most registered insect growth regulators are chemicals that are structurally similar to juvenile hormone, commonly known as juvenoids. Juvenoids can be naturally occurring or synthetic. Juvenile hormone-based insecticides have been used predominantly indoors for both household applications such as roaches and mites, and greenhouse applications. Some juvenoids are more stable and are registered for outdoors use on crops as well.

As in plant growth regulators, an advantage of insect growth regulators is that they are effective when applied at very minute quantities. However, they are not species specific and impact arthropods generally including insects, spiders, and crustaceans such as shrimp, lobster and crayfish. This can result in large negative impacts on non-target species populations. As with plant growth regulators, insect growth regulators need further investigation on a case-by-case basis by environmental health specialists.

Insect Growth Regulator Example 1 Neem:
Neem is a naturally derived material from Neem trees (Azadirachta indica) native to India. Neem materials can affect insects, mites, nematodes, fungi, bacteria, and even some viruses. Despite being derived from natural and renewable sources, the use of Neem products raises some concerns due to its relatively broad-spectrum activity. Insect growth regulation is one of multiple functions provided by the constituents of this plant oil. Among the isolated Neem constituents, limonoids (azadirachtin) are effective in insect growth-regulatory activity. Azadirachtin does not directly kill pests, but alters the life-processing behavior in such a manner that the insect can no longer feed, breed or undergo metamorphosis (Elahi, 2008). More specifically, azadirachtin disrupts molting by inhibiting biosynthesis or metabolism of ecdysone, the juvenile molting hormone (Ware and Whitacre, 2004).

Insect Growth Regulator Example 2 S-Methoprene:
S-Methoprene is a juvenile hormone analogue. As such, S-Methoprene interferes with the normal function of insect juvenile hormone, which controls the growth, development, and maturation of insects. The presence of these chemical analogues during larval stages allows the larva to grow and become a pupa, but the pupa never emerges as an adult. S-Methoprene is used both for indoor and outdoor applications including food and nonfood crops. S-Methoprene is effective in controlling a broad range of insects including ticks, mites, spiders, moths, and beetles. A particularly unique application of S-Methoprene is to add it to cattle feed. S-Methoprene passes through the cattle's digestive system without being broken down. The presence of S-Methoprene in the manure is effective at controlling cattle pests known as horn flies. S-Methoprene is not harmful to birds or mammals, but can be toxic to some fish and aquatic invertebrates (US EPA Fact Sheets, 2008).

b. Microbial Pesticides

Microbial pesticides come from naturally occurring or genetically altered bacteria, fungi, algae, viruses or protozoans. They suppress pests either by producing a toxin specific to the pest, causing disease, preventing establishment of other microorganisms through competition, or various other modes of action (Clemson HGIC, 2007). For all crop types, bacterial biopesticides claim about 74% of the market; fungal biopesticides, about 10%; viral biopesticides, 5%; predator biopesticides, 8%; and "other" biopesticides, 3% (Thakore, 2006). At present there are approximately 73 microbial active ingredients that have been registered by the US EPA. The registered microbial biopesticides include 35 bacterial products, 15 fungi, 6 non-viable (genetically engineered) microbial pesticides, 8 plant incorporated protectants, 1 protozoa, 1 yeast, and 6 viruses (Steinwand, 2008).

An Alternative to Methyl Bromide: "Pasteuria" for Nematode Control

Plant parasitic nematodes are one of agriculture's largest challenges. These microscopic worms burrow into the soil and attack plant roots causing damage to crops, causing an estimated $100 billion in worldwide crop damage annually. They have traditionally been controlled by fumigants, notably the problematic chemical methyl bromide. As fumigants are being phased due to negative human and environmental health effects, alternatives such as biological controls are being investigated.

Microbial pesticides have specific advantages over fumigants in the control of nematodes. Nematodes can burrow deep into the soil during fumigant applications to avoid contact. They can then ascend to the level of the plant roots after crops have emerged, at which point fumigants cannot be reapplied due to their toxicity and potential to damage crops. In contrast, many microbial pesticides can be applied to the post-emergent crops for protection throughout the plant life cycle. However, many microbial pesticides depend on the nematode consuming the microbe. This can present a challenge because plant pathogenic nematodes are generally herbivores.

More than 50 years ago, academic and USDA researchers discovered a genus of bacteria called Pasteuria to be a promising alternative for the control of nematodes. A particular advantage of Pasteuria over other biological controls is that it does not need to be eaten by the nematode to be effective. The Pasteuria spores are applied to the soil, and as a nematode passes, they attach to the nematode's outer cuticle. The spores germinate and enter the nematode's body causing death, spreading new spores into the soil. Each strain of the bacteria is specific to a particular species of nematode.

The primary technical challenge for commercialization of Pasteuria was development of an economically viable large-scale manufacturing process. The initial process developed in the laboratory involved growing live nematodes as hosts, growing the bacteria inside the hosts (in vivo), and extracting the spores to formulate the product. This process was too costly to scale up and a technological breakthrough was needed. The technical challenge was recently overcome by finding a way to grow the bacteria outside of a living host (in vitro). A new-patented process allows rapid and effective growth of multiple strains of Pasteuria penetrans in traditional commercial fermentation tanks using easily available growth media (Pasteuria, 2008). This technological advance significantly decreased the cost of production, making the product economically viable.

Microbial biopesticides may be delivered to crops in many forms including live organisms, dead organisms, and spores. The manufacture, regulation and use of microbial biopesticides differ most significantly from conventional chemical pesticides. To be effectively culture the organism, either in the field or during manufacture, requires an understanding of a broad range of ecological considerations. While microbial pesticides control a diverse array of pests, each specific microbial pesticide active ingredient is relatively specific to its target pest.

b.1 Bacterial Biopesticides

Bacterial biopesticides are the most common form of microbial pesticides. They are typically used as insecticides, although they can be used to control unwanted bacteria, fungi or viruses as well. As an insecticide they are generally specific to individual species of moths and butterflies, as well as species of beetles, flies and mosquitoes. To be effective they must come into contact with the target pest, and may require ingestion to be effective.

The mode of action varies depending on the target pest, as seen in Table 5 below. In insects the bacteria disrupt the digestive system by producing an endotoxin that is often specific to the particular insect pest. When used to control pathogenic bacteria or fungus, the bacterial biopesticide colonizes on the plant and crowds out the pathogenic species.

Table 5: Bacterial Biopesticides and their Modes of Action

Example Bacteria	**Primary Categories**	**Target Pest(s)**	**Mode of Action**
Bacillus thuringiensis (Bt)	Insecticide	Butterfly & Moths Lepidoptera	Digestive System
(Bs) Bacillus subtilis	Bactericide	Bacterial & Fungal Pathogens such as Rhizoctonia, Fusarium, Aspergillus, and others	Colonizes on plant root and competes
Pseudomonas fluorescens	Fungicide\ Bactericide	Several fungal, viral, and bacterial diseases such as frost forming bacteria	Crowds out and controls the growth of plant pathogens

Bacterial Biopesticide Example 1 Bacillus thuringiensis:
The most widely used microbial pesticides are subspecies and strains of Bacillus thuringiensis (Bt), accounting for approximately 90% of the biopesticide market (Chattopadhyay and others, 2004). Each strain of this bacterium produces a different mix of proteins and specifically kills one or a few related species of insect larvae. When ingested by insect larvae, Bt releases endotoxins (proteins) that bind to the intestinal lining of the insect midgut. The endotoxin binding creates pores in the intestinal lining, paralyzing the digestive system and causing death. Bt is primarily used to control lepidopteran pests (moths and butterflies), which are some of the most damaging crop pests. However, Bt

can also be used to control a broad range of other pests including specific species of mosquitoes, flies, and beetles. Researchers have identified between 500 and 600 strains of Bt. Approximately 525 insects belonging to various orders have been reported to be infected by Bt toxins (Thakore, 2006). Bt endotoxins are also the most common basis for genetically modified pest resistant crops.

Bacterial Biopesticide Example 2 Pasteuria:
Various species of the genus Pasteuria can be used to control nematodes, microscopic worms that feed on plant roots. The species of bacteria is specific to the species of nematode to be controlled. The spores of the bacteria germinate in the nematode, reproducing and causing death.

b.2 Fungal Biopesticides

Fungal biopesticides can be used to control insects, plant diseases including other fungi or bacteria, nematodes, and weeds. They are often parasitic or produce bioactive metabolites such as enzymes that dissolve plant walls. The mode of action is varied and depends on both the pesticidal fungus and the target pest, as seen in by the examples in Table 6. Beauveria bassiana spores germinate, grow, and proliferate in the insect's body, producing toxins and draining nutrients to cause insect death. Trichoderma is a fungal antagonist that grows into the main tissue of a disease-causing fungus and secretes enzymes that degrade the cell walls of the other fungus, then consumes the contents of the cells of the target fungus and multiplies its own spores.

Muscodor albus, is a candidate to replace the problematic pesticide, methyl bromide in particular applications. As shall be discussed below, muscador albus releases gaseous toxins into the soil which can eradicate soil-borne pests and bacteria affecting major commercial crops.

One advantage of fungal biopesticides in comparison with many of the bacterial and all of the viral biopesticides is that they do not need to be eaten to be effective. However, they are living organisms that often require a narrow range of conditions including moist soil and cool temperatures to proliferate.

Table 6: Fungal Biopesticides and their Modes of Action

Example Fungi	Primary Categories	Target Pest(s)	Mode of Action
Beauveria bassiana	Insecticide	Foliar feeding insects	White muscadine disease
Trichoderma viride/harzianum	Fungicide	Soil borne fungal disease	Mycoparasitic
Muscodor albus	Fumigant	Bacteria and soil-borne pests	Releases volatile toxins

Fungal Biopesticide Example 1 Muscodor Albus:
Muscodor Albus is proposed as a methyl bromide replacement for seed, propagule, soil and post harvest treatments of all food or feed commodities, and for ornamentals and cut flowers. A specific strain of Muscodor albus called QST 20799 is a naturally occurring fungus originally isolated from the bark of a cinnamon tree in Honduras. When hydrated, M. albus Strain QST 20799 produces a number of volatiles, mainly alcohols, acids, and esters, that inhibit and kill certain bacteria and other organisms that cause soil-borne and post harvest diseases. Products containing QST 20799 can be used in fields, greenhouses, and warehouses (US EPA Fact Sheets, 2008).

Fungal Biopesticide Example 2 Aspergillus flavus:
The fungus Aspergillus flavus strain AF36 is used as a fungicide for cotton. Certain strains of A. flavus produce a highly toxic substance called aflatoxin in cotton seeds, which is a liver carcinogen. AF36 is a strain of A. flavus that does not produce aflatoxin. Thus application of the AF36 strain to cotton fields decreases the amount of aflatoxin producing fungus that would otherwise become established, thereby protecting workers and the public (US EPA Fact Sheets, 2008).

b.3 Viral Biopesticides

Baculoviruses (viral biopesticides) are pathogens that attack insects and other arthropods. Unlike other members of this category, they are not considered living organisms, but rather parasitically replicating microscopic elements (US e-CFR, 2008). Baculoviruses are extremely small and are composed primarily of double-stranded DNA required for the virus to establish itself and reproduce. Because this genetic material is easily destroyed by exposure to sunlight or by conditions in the host's gut, an infective baculovirus particle (virion) is protected by protein coat called a polyhedron (D'Amico, 2007). Two main families of baculoviruses include Granulosis virus and Nucleopolyhedrosis virus. They differ in the number and structure of the protective protein coat and are both relatively large and complex in structure in comparison to many other types of viruses.

All types of baculoviruses must be eaten by the host to produce an infection. The resulting infection is typically fatal to the insect host. Each strain of baculovirus is targeted for a specific insect species. The two types of baculovirus differ in the range of target pests, as summarized in Table 7. The Nucleopolyhedrosis viruses have a relatively wide range of target pests among three different insect orders, including butterflies and moths (Lepidoptera), ants, bees, and wasps (Hymenoptera), and flies (Diptera). Target pests for Granulosis viruses are limited to species of Lepidoptera. Baculoviruses develop in the nuclei of the host insect cells. When ingested by the host insect, infectious virus particles are liberated internally and become active. Once in the larval gut, the virus's protein overcoat quickly disintegrates, and the viral DNA proceeds to infect digestive cells. Within a few days, the host larvae become unable to digest food, and so weaken and die (Thakore, 2006).

Baculoviruses are particularly attractive for use as biopesticides due to their high host specificity. Each virus only attacks particular species of insects, and they have been shown to have no negative impacts on plants, mammals, birds, fish, or non-target insects (D'Amico, 2007). This specificity is useful in preservation of natural predators when used in Integrated Pest Management systems. Baculoviruses can also cause sudden and severe outbreaks within the host population for complete control (Sylvar, 2008). Another chief advantage of baculoviruses is that in some cases they replace antibiotics in agricultural use.

Disadvantages of baculoviruses include the need for the virus to be ingested, resulting in lower efficacy, and their traditionally high cost of production. The lower efficacy resulting from the need to be ingested is partially counterbalanced by the mode of action. When the target insect dies, the dead insect host's body is spread on the foliage. The location and form of the infected insect carcass increases the probability the infected carcass will be eaten by another larval host. Historically the production of baculoviruses has required live hosts (in vivo production), making it costly.

Greater Production Complexity (and Potential Costs) Of Developing a Biopesticide

Producing biopesticides, particularly when the objective is to maintain an environment that promotes the growth of a living organism, often requires very stringent control of process conditions. One example is large-scale production of baculovirus isolate.

Traditional in vivo production involved feeding the virus to insect larva. The temperature must be maintained carefully between 20-26 C to keep the larva alive. To produce the highest yield and quality of virus, the virus must be harvested from the larvae at the proper time in the life cycle of the larval species.

For example, in development of the baculovirus Lymantria dispar, the virus multiplies up through the fourth host molting by the host larva, and it then decreases after the fifth molting. To separate the virus from the larval bodies at this critical step, water or another solvent must be added and the mixture blended, and then filtered to isolate the virus (Mishra, 1998). To ensure success and high yield, careful attention must be paid to all processing parameters.

This example of stringent process control requirements for production of baculovirus isolate illustrates the high complexity (and costs) associated with manufacturing.

Table 7: Baculovirus Target Pest and Mode of Action

Virus Type	Primary Categories	Target Pest(s)	Mode of Action
Nucleopolyhedrosis virus (NPV)	Insecticide	Species specific for species of Lepidoptera (88%), Hymenoptera(6%), and Diptera(5%)	Infect digestive cells in larvae gut
Granulosis Virus (GV)	Insecticide	Specific species of Lepidoptera	Infect digestive cells in larvae gut

Viral Biopesticide Example 1, Cydia pomonella Granulosis Virus:
Codling moth is a pest that damages fruit trees such as pears and apples. The Cydia pomonella granulosis virus is applied as a foliar spray onto eggs prior to hatching. The larvae need to ingest the virus prior to entering the fruit. If sprayed on the eggs, the larvae ingest the virus while eating the shells after hatching, get infected, and die. Cydia pomonella granulosis virus is used typically in rotation with other control measures in both organic and conventional agriculture, and can be used in conjunction with mating disruption. It can reduce or eliminate use of organophosphates and pyrethroids for conventional agriculture and protect against pest resistance to Spinosad for organic agriculture. Because it degrades in sunlight, it must be reapplied every 7-10 days.

Viral Biopesticide Example 2, Bacteriophage:
A bacteriophage is a virus that infects bacterial cell walls. If the virus attacks bacteria that cause plant disease, it can be used as a pesticide. One example is a product made by Omnilitics to kill Xanthamonus, a pathogenic bacteria (Braverman, 2008). It can replace conventional products include copper or antibiotics such as streptomycin, a commonly used as plant antibiotic. As with bacteria that cause disease in humans, plant pathogenic bacteria develop resistance to antibiotics, and can contribute to the evolution of highly resistant bacterial strains (“super bugs”) and the cost to develop more potent antibiotics to control them.

b.4: Other Microbial Biopesticides

Various other organisms are also used as biological controls in integrated pest management systems. Protozoa are microscopic single-celled animal-like organisms rarely used as biopesticides. As of 2002 there was only one insecticidal protozoan registered with the EPA. Use of macroscopic predators such as live insect releases is also a common biological control strategy that can be very effective, but must be well managed to prevent ecological imbalances that can result from introducing insects into areas where they may have no natural predators. Macroscopic predators are not regulated as biopesticides, and are outside the scope of this study. Nematodes are microscopic worms that are typically parasitic and commonly used as insecticides. Although the EPA does not regulate them as biopesticides, they are often considered part of this category of control agents.

c. Biopesticide Formulations

A registered biochemical or microbial pesticide contains one or more active ingredients from the categories described above. The active ingredient(s) is primarily responsible for the pesticide claims. In addition to the active ingredient, the product formulation contains one to dozens of other ingredients called "inerts." This term can be misleading, as it implies these components do not have a particular function or that they are benign from a human and environmental health perspective. To the contrary, inerts are very important components required to make an effective product and the toxicity profiles of inerts vary widely. Moreover inert ingredients can have serious potential health and ecosystem impacts and can include endocrine disrupting chemicals, allergens and other chemicals of concern. In the case of biopesticides this is problematic; a company can combine a highly targeted, benign active ingredient in a formulation that includes endocrine disrupting inert ingredients. From an environment and health perspective, this changes what might have been a deep green product into a product of concern. Note that this was possibly what happened in the example of the little brown apple moth pheromone spray used in California.

In pesticide products inerts assist in the effectiveness of the product by ensuring the product contacts the target pest or even insuring the active ingredient is absorbed or eaten so it can harm or kill the target pest. Inerts are included in the product formulation for various reasons including to improve product performance, make the product easier to apply to the crop, help the pesticide spread over the surface or stick to the leaves and soil, help move the pesticide into the insects' body, stabilize the product for longer shelf-life, and help the active ingredient dissolve in water (NPTN, 2000). Solubility in water is important, as water is the most common solvent and carrier in pesticide formulations.

The US EPA classifies inert pesticide ingredients based on their overall toxicity profile for human and environmental health. All inert ingredients allowed in pesticide formulations are classified in one of the following four lists as described in Table 8 below. In general, pesticides used in organic agriculture may only contain inerts from List 4. The entire pesticide product formulation including the identity and relative quantity of each inert ingredient must be disclosed to the EPA during the registration process, and is incorporated into the overall risk assessment performed in order to register the pesticide product.

Controversially, current laws do not require the identity or relative quantity of each inert ingredient to be listed on the pesticide label, or disclosed to the public, unless the inert is determined to be highly toxic. This information is generally regarded as confidential business information or "trade secrets," as in other products such as formulations for cleaning products or fragrances. The label simply lists the additive amount of all inerts as "other" ingredients.

Table 8: EPA Inert Ingredient Lists

Inert Ingredient List	Description
List 1	Inert ingredients of toxicological concern
List 2	Potentially toxic inert ingredients/high priority for testing
List 3	Inerts of unknown toxicity
List 4	Inerts of minimal concern

Conclusion of Biopesticide Categories and Formulations

As we can see, the term biopesticide encompasses a wide diversity of both chemical and microbial active ingredients. Biopesticide formulations also include a broad range of other ingredients required to deliver the product and support performance, commonly referred to by the misleading term "inerts." Given the diversity in composition of biopesticide products, it is not surprising that the efficacy, cost, and impact of these products on human and environmental health also varies greatly from product to product. Understanding the complexity and breadth of the biopesticides industry is an essential foundation to an exploration of major trends, opportunities and challenges for broader adoption of biopesticides.

The Challenges of Product Formulation, Proprietary Ingredients and Community Dialogue:

The Light Brown Apple Moth

The Light Brown Apple Moth (LBAM) is a quarantined pest in California (Hartmeier, PANNA, NRDC); growers must demonstrate their crops are free of LBAM in order to export. Conventional pesticides used against similar species of Lepidoptera have raised public concerns about associated health and environmental issues. USDA officials became interested in employing pheromones since they do not hurt humans or other non-target organisms.

USDA approached the company Suterra to develop a product for LBAM because they have a "micro encapsulation technology" which could act as an effective delivery system for the pheromone. Suterra developed a pheromone spray product called "Checkmate" and subsequently the state began pursuing a wide-spread spraying campaign.

The state severely underestimated public response to the spraying: public perception of the spray was one problem, but a second problem was concern about inert ingredients used in the products. The lack of information offered about the inert ingredients did not help the situation. In the end, responding to public pressure, the state stopped the use of the pheromone spray. Alternatives subsequently considered included Bt and pyrethroids, both known to kill non-target species, as well as sterile release programs and alternative, non-sprayed pheromones.

An article by the Natural Resources Defense Council concludes that Suterra's Checkmate is non-toxic and generally poses little risk to human health and the environment. While they support further research to answer some questions (exposure to particulate pollution, effectiveness of eradication efforts, actual threat posed by LBAM), they believe pheromones have the potential to reduce exposure to more highly toxic chemicals.

Two important lessons from this experience:

- Inert ingredients should be designed according to green chemistry principles and ingredients made public.
- It is vitally important to conduct public dialogues about broad-scale pest management efforts, to discuss options for preventative measures and provide complete information about products being used.

PART III. DISCUSSION – CHALLENGES AND OPPORTUNITIES FOR BIOPESTICIDES

Biopesticides offer powerful tools to create a new generation of sustainable agriculture products. They are the most likely source for alternatives to some of the most problematic chemical pesticides currently in use that are under ever-increasing scrutiny. Biopesticides may also offer solutions to concerns such as pest resistance to traditional chemical pesticides, public concern about side effects of pesticides on the surrounding environment and ultimately, on human health.

The overriding challenge for the biopesticides industry is to live up to the promise that the field holds. As the discussion of specific technologies and products above indicates, there are unanswered questions and un-examined assumptions about them with which those involved must contend. Challenges to biopesticides stem from questions about their efficacy and safety, public and grower confusion about the wide spectrum of biopesticide products on the market, and current market conditions that paradoxically both hinder and favor the field's growth. Specific challenges and opportunities to intervene and advance the promise that biopesticides offer include the following:

Table 9: Challenges and Opportunities

Challenges	**Opportunities**
Efficacy • Do they work?	*Efficacy* • Demonstrations: More field trials, agricultural extension outreach, collaborative R&D
Safety: • For humans • For the environment	*Safety:* • Deeper testing (more inter-disciplinary environmental health science-based testing) • Rapid screening and throughput (borrow techniques from pharmaceutical companies using broader ecological assays) • Wider testing of both Active and Inert ingredients (using cutting edge environmental health sciences)
Transparency: • User education • Public Understanding • Questions about products (both active and inert ingredients)	*Transparency:* • Industry Standards and Ecolabels: better communication on efficacy and safety of products to public, growers, and policy makers • Multi-stakeholder dialogue on choices and trade-offs in pest management techniques and products, including biopesticides

Challenges	**Opportunities**

Market Issues:
• Small producers vs. Economies of scale
• Niche products vs. Broad scale
	Market Issues
	• Shift the playing field:
	  • Phase out pesticides of greatest concern;
	  • Award the innovators
	• Create multi-disciplinary "Pesticide Innovation Teams" to develop and test urgently needed replacements, test across environmental and health endpoints.

Efficacy

Biopesticides have an image problem. As is the case with many "greener" products, biopesticides suffer from user (in this case, grower) doubt about their effectiveness. Many growers do not trust biopesticides to work as well as traditional chemical pesticides, and indeed, in a head-to-head contest, some may not. But as noted throughout this study, biopesticides are not designed to be one-for-one replacements of existing, broad-spectrum, pesticides. They are best used as part of a systemic, integrated pest management strategy, and sometimes require more skill and understanding to use effectively. When used in the manner intended, however, biopesticides can be very effective and can not only help growers control pests, but can restore natural predators, protect workers' health, and provide consumers with chemical-free produce and clean water.

Opportunities to improve and/or promote awareness of the efficacy of biopesticides include *expanding field trials*, and deliberately fostering *research and development collaborations* between developers, growers, and agricultural experts. Biopesticides would benefit from broader and deeper testing of (and reporting on) how well they perform, how best to ensure optimal performance, and how differing conditions affect these outcomes.

Expanding the resources available for field trials is essential. Engaging local agricultural colleges, universities and field extensions in these trials is also very important. Bringing in these partners not only improves the final product, but broadens the base of information resources available to farmers on how to best use them.

Safety

At their best, biopesticides are targeted exclusively on a particular pest, are non-toxic to humans and other species, and are environmentally benign. They allow growers and farm workers to enter fields immediately after usage, saving time, crops and money. Biopesticides can be, at the greenest end of the spectrum, among the least toxic means of managing pests. But this is not always the case. Some biopesticides are more broad-spectrum than others. Some, like pyrethroids, can affect human health in unexpected ways. Others, while benign to humans, can negatively impact non-target organisms, including beneficial insects and

Niche Marketing as an Opportunity for Competitive Differentiation "Bioworks"

Biopesticides are often effective for a particular pest species, crop, or geographical region. The specificity of biopesticides provides an opportunity for companies willing to target their product line to a niche market. Small to medium sized companies are often structured more effectively than large companies to profitably focus resources on a small market. BioWorks Inc. focuses their business on the horticulture specialty agriculture market. Within this market the organization participates in the entire life cycle of the product from discovery, field-testing and manufacture, to sales and distribution.

Developing relationships and maintaining direct contact with growers forms a foundation for the success of this company. Regular contact with growers informs the company of unmet needs and opportunities for product improvements. BioWorks compares their product portfolio to the information gathered from growers to identify potential innovation gaps. They then target product development efforts either through in-house discovery or licensing of technology from universities, government laboratories, or other companies to create an effective product. Innovations or product improvements may include formulating the biopesticide in the same form as the conventional product it is replacing, where possible. Using the same product form as the prior pesticide can facilitate adoption, minimize the cost of grower education, and avoid grower investment in new equipment to accommodate a new product form, but this is not always possible.

BioWorks strength and expertise lies in the commercialization process. This includes ensuring there is a market for the product, that the claims match what the product delivers, and that the appropriate communication happens through the marketing channels to get the product into growers' hands. A strong marketing foundation includes setting the right price, advertising, and educating the sales force and growers. Customers need to know how to obtain the product and use it effectively to ensure the claims the sales person makes are being realized in the field. Through very targeted approaches, a strong connection to their specific market, and investments in education of distributors and users, BioWorks has built a profitable business. This case illustrates how biopesticide companies can position themselves for success within a shifting paradigm.

pollinators. The challenge of establishing the safety of biopesticides lies in their diversity. The wide spectrum of biopesticides available makes generalizations - and regulations - difficult.

The US EPA, under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), regulates conventional pesticides. The EPA reviews each regulated active ingredient for its potential harm to humans and the environment. Manufacturers submit data on a broad range of toxicological endpoints. The Office of Pesticide Programs reviews toxicity and exposure information for each active ingredient and target crop combination, and specifies approved use conditions.

Biopesticides are "fast-tracked" through a US EPA process that accelerates their review and registration by combining lower data requirements with high review priority. Typically, new biopesticide ingredients are registered in 11 months; conventional pesticides can take 2-3 times longer. There is a also a separate fast-track category called "reduced risk pesticides" which include products that are regulated by the EPA as conventional pesticides but meet certain requirements for lower impact on human and environmental health. Some products in categories discussed in this report, such as insect growth regulators or plant extracts, may be candidates for review as reduced risk pesticides.

While accelerating the review process for biopesticides is more efficient in bringing them to market, the predominant focus of the EPA pesticide registration process is on human health and safety. This is a serious *challenge* to biopesticides. Currently there are no adequate regulations to provide meaningful ecosystem-level protection, such as protection of birds, pollinators, and aquatic systems (Benbrook, 2008). While speed to market is an economically important goal, these environment and health data gaps must be addressed. The absence of regulations addressing these issues for biopesticides may lead to serious surprises followed by backlash against them.

Speed to market is a real concern for biopesticide producers and consumers. Registration is a key cost in commercializing any new pesticide product. For biopesticides, the regulatory process can dominate this cost of bringing a new product to market. The toxicological studies that must be performed for data submission to the EPA are very expensive. The testing requirements place a proportionately larger burden on small companies such as many of the biopesticide manufacturers. Separate registration is required for each designated product (e.g. soy or tomatoes). To recoup the costs of registration, most large chemical companies focus on registering pesticide products only for very high volume crops such as wheat and corn. Biopesticides are typically niche products used on lower volume crops such as fruits and vegetables. Thus it is often more difficult for biopesticide companies to recoup the cost and time of the regulatory process. In addition, small biopesticide companies often lack the experience and expertise to navigate the regulatory process.

There are *opportunities* to mitigate the high costs and time investments for biopesticide testing and registration. A *governmental program* that should be expanded is the Interregional

Research Project No. 4 (IR-4). IR-4 is a program funded by the USDA to support registration of products used for specialty crops (low volume crops). The program provides expert assistance to help companies through the regulatory process, and funds grants for research to promote reduced risk and biopesticide development. The IR-4 Project has been a key support to the growth of the Biopesticides Industry Alliance (BPIA). In addition to working with the EPA to register biopesticides, the BPIA has also worked with the EPA to educate growers on these products. An IR-4 grant funded the field research for the development of granulosis virus for controlling the codling moth discussed on page 40.

There are other opportunities to address safety and testing by borrowing from other fields, including the pharmaceutical industry and the environmental health sciences. The pharmaceutical industry uses a variety of "rapid screening" methods to asses both active pharmaceutical ingredients and processing methods. It is possible that some of these methods could be useful in evaluating biopesticides and the manufacturing process.

But as we have discussed, biopesticides also need to *broaden their testing range to include additional ecological and health impacts*. Dovetailing with research underway in the environmental health sciences is absolutely essential. Encouraging cross-science communication and collaboration is very important for all of green chemistry; there are initial efforts underway to link these fields but these need to be systematized and institutionalized.

In addition to testing the active ingredients of biopesticides, *inert* product ingredients require more safety testing. As we saw in the case of the Little Brown Apple Moth in California (page 33), public concern can arise not just about the pheromone used but about the product's inert ingredients as well. Inert ingredients need to not only pass the EPA preferred inputs list, but meet public concerns about newer toxicological issues such as their potential to act as endocrine disruptors and the like. This is a safety issue for the EPA – and as products can be pulled from use because of these concerns – an economic issue for the biopesticide industry.

Transparency

Efficacy and safety testing are only useful if people are aware of the results; there is a need for greater transparency about biopesticide products. The Biopesticide Industry Alliance (BIA) is currently engaged in developing industry standards to enable greater transparency, but it is our understanding that these standards will focus primarily on efficacy. Biopesticides could learn much from experiences in other product areas to develop Ecolabels – information tools based on efficacy but also on more nuanced environment and health information; this presents the greatest *opportunity* to generate better transparency around biopesticides.

Ecolabels are driven by consumers and companies to help differentiate between agricultural products available. The USDA Organic Certification label is the most widely accepted food label that provides additional restrictions on pesticide use. Ecolabels typically incorporate broad social and ecological considerations including conservation and social responsibility.

While some ecolabels incorporate an assessment of the pesticide(s) used in production of the agricultural product, pesticide information is typically not directly available to the consumer. The ecolabel system for food and agricultural products does not provide the transparency required for most consumers to take an active role in impacting pesticide selection by growers. See the Table 2, (page 14) for an overview of some of the assessment systems in the marketplace and a comparison of how pesticide evaluation is incorporated into them.

At their best, Ecolabels serve multiple interests: they help users differentiate among products by safety, efficacy, performance, and the trade offs that exist between these categories. Ecolabels can help evaluate the choices that exist in the efforts to control pests. But Ecolabels must not be static or they become a detriment to innovation – they must constantly respond to and incorporate the latest knowledge and understanding of environment health and efficacy to be relevant and a positive driver toward sustainability.

This leads to our last– but distinctly not least – point about creating greater transparency around biopesticides: there is a profound need for *dialogue* across stakeholder sectors if the promise of biopesticides is to be realized. Too often products are used before their full range of impacts is known, or used without engaging the surrounding community in discussion about what is happening in their back yard. Pest management affects all of us, not just those on the farm; too often food producers and policy makers in coming to decisions on products and processes to manage pests forget this fact. Without dialogue, however, the public remains in the dark and is often reasonably distrustful of what is being sprayed or dusted or sown. In addition, public concerns can sometimes point to unaddressed short-comings in products (as in the example of concerns about inert ingredients) that must be addressed before a product is commercialized and used.

Market Issues

Enhanced testing on efficacy and safety, better transparency and communication on these advances, including industry standards and public dialogue, will do much to help the emerging field of biopesticides both realize its greater promise, and succeed in the market. But biopesticides will continue to fight the battle that most disruptive technologies face in attempting to challenge an entrenched industry: fighting against mature industries' incumbent position, and economies of scale.

The traditional pesticide industry is, by some measures, struggling to maintain its industry dominance as new science continues to build the environment and health case against certain ubiquitous pesticides. But these same industries and companies also enjoy pride of place in commanding cheap inputs and supply chain pull. Many biopesticide companies are quite small in comparison, as noted above, and the costs of market entry are proportionately higher. Some large companies are, as also was mentioned, entering into this field. But tensions remains between large-scale production of broadly applicable, easily applied products and those that are niche-applications, pest and life-cycle specific, and requiring more skill to use.

Regulatory Changes Can Drive Innovation (And Lack of Regulation Can Stymie It)

Pear fruit is an important crop in California, accounting for over 20,000 acres of orchards in 1999. The codling moth is a significant pest in the production of pear fruit, and can cause damage in up to 10-50% of cannery loads when orchards are untreated. A series of conventional pesticides were severely restricted and subsequently phased out between 1998 and 2000, generating incentives to develop more benign alternatives. Azinphos-methyl was the most effective tool for controlling codling moths prior to 1998. Its use was first restricted by the state of California in 1998 and further restricted by the US EPA in 1999. Another pesticide used, methyl parathion, was eliminated in 2000 under the Food Quality Protection Act. These regulatory changes necessitated an immediate transition to alternative pest management strategies for codling moth on pears (UC ANR, 1999).

Extensive research and development has been conducted on two biopesticide alternatives that can be used alone or in conjunction with one another to control codling moths. The first is a pheromone used in mating disruption and the second is a granulosis virus (GV) that infects codling moth larvae. An early technological challenge to develop a reasonably priced pheromone dispenser was overcome by a researcher at the University of California with funding from the pear industry. Product development and field-testing later transitioned to Suterra, a manufacturer of pheromones for pest management.

Rachel Elkins, the Pomology Farm Advisor at the University of California Cooperative Extension, performed field-testing for GV. The funding for her research came from a federal IR-4 grant. She focused on efficacy testing, comparing different treatment conditions and types of applications. She found that a narrow set of conditions resulted in acceptable efficacy, posing challenges to growers. The virus must be ingested by the codling moth at a particular stage early in its life cycle, prior to burrowing into the fruit. The virus is also sensitive to various weather conditions such as being washed off by rain or degraded in sunlight. With these constraints, application timing and knowledge and detection of the pests are critical for success. Due to its short life, GV may require multiple applications, adding labor and fuel costs for growers. To be most effective, GV is typically used in combination with mating disruption or another type of pest management strategy.

This example highlights how regulatory changes can create strong drivers for the technical innovation and grower education required to transition to more benign pesticide alternatives. It also emphasizes that shifting to more sustainable agricultural practices rarely is as simple as a one to one replacement of an existing pesticide, and requires a paradigm shift to holistic system-based approaches to agriculture and pest management. Information and education are keys to the success of these alternatives.

One irrefutable fact is that *phasing out*, or outright banning, pesticides of greatest concern moves markets. Nothing inspires innovation and creativity faster than the knowledge that one's main product is going off-line. This has been true of many pesticides in this study including methyl bromide and methyl parathion. Market disruptions such as these create openings for new technologies and companies to enter with alternatives.

Of course one must be assured that the alternatives are truly benign from an environmental and health perspective. This is where standards and ecolabels would be of tremendous help in allowing users and policy makers to differentiate among products. Additionally, *awards* such as the Green Chemistry Presidential Challenge can also be very helpful in highlighting new technologies and products, but one must be assured that the criteria by which such awards are given meets the very highest environment and health standards.

Another opportunity to shift markets is to create multi-disciplinary *"Pesticide Innovation Teams."* Government and industry could combine resources to invite teams across scientific disciplines, including chemistry, biology and toxicology, to work with partners in industry and policy-making to develop truly sustainable alternatives to some of the most dangerous pesticides in use today. One can imagine such teams working on specific crops or pests, researching and developing all aspects of a product from the active ingredient to the inert ingredients used in formulation. These innovation teams would be working with product development and marketing team members, and conducting outreach and education with interested stakeholders to help both broaden public understanding of biopesticide products and to gather data on public opinions and concerns to return to the design team.

Conclusion

As we said at the outset of this paper, we are not endorsing the field of biopesticides or any specific products as being "green" or as falling under the heading of "Green Chemistry"., However, if designed employing the twelve principles of Green Chemistry, biopesticides could provide a new generation of agricultural pest management products that are sustainable both from an environmental and health perspective. By utilizing Green Chemistry, and addressing the need for confidence in product efficacy and safety, by generating greater transparency about the products, and by moving markets to make way for the greenest solutions, biopesticides could be revolutionary. They could change how people conduct agriculture, how we understand and approach both pests and non-target species, including beneficial organisms. They could change how farm workers do their jobs and live their lives, and protect the health of consumers, communities and ecosystems. There is much to be done to help biopesticides play this transformative role in agriculture, and we as a society need to reflect upon and invest in making these changes happen. Linking Green Chemists and biopesticide producers is an essential first step in ensuring these changes happen.

APPENDIX I: ACKNOWLEDGEMENTS

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