AN ANALYSIS OF THE BIOPESTICIDE MARKET NOW AND WHERE IT IS GOING

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Keywords: biopesticides, plant-incorporated protectants, open innovation, integrated pest management

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Introduction

Biopesticide use began in the late 1800s with fungal spores used to control insect pests. One of the first documented cases of biopesticide use was by Agostine Bassi, who in 1835 demonstrated that spores of the white-muscadine fungus (*Beauveria bassiana*) could protect silkworms from disease. Since then, biopesticide use has continued uninterrupted through modern agricultural history, but to date it has been a small market compared to conventional crop protection. The major attribute that differentiates biopesticides from synthetic pesticides is the mode of action. While most, if not all, synthetic insecticides are neurotoxic to pests, many biopesticides have other modes of action including mating disruption, anti-feeding, suffocation, and desiccation. The U.S. Environmental Protection Agency (EPA) identifies three classes of biopesticides: microbial, biochemical, and plant-incorporated-protectants (PIPs) (www.epa.gov). We classify predatory insects as a fourth category as their functions in agriculture are fundamentally similar. Microbial pesticides are whole microorganisms, including bacteria, fungi, viruses, and others, that act as pesticides. The core of the definition for this class of biopesticides is the use of whole, live organisms for biocontrol. Biochemical pesticides are either microbial extracts or natural products from other sources like plant extracts or yeast fermentation products that control pests by non-toxic mechanisms like those described above. These are typically small molecules and can include semiochemicals (hormone mimics) and attractants for use in traps. PIPs are pesticides that the plant produces itself from genetic material inserted into the plant. PIPs can result from transgenic events as well as through non-transgenic approaches like direct genome editing and the seed treatment-based method pioneered by Morflora (www.morflora.com). Our fourth category is the application of predatory insects for crop protection. Using insects like ladybugs that predate on pests like aphids is a familiar application of predatory insects for biocontrol.

The prototype biopesticides all come from *Bacillus thuringensis* (Bt), a bacterial species that produces a toxin (called the Bt toxin) which disrupts the insect gut when ingested. Biopesticide products derived from the Bt bacterium and its toxin include microbial, biochemical, and PIP varieties. Currently, approximately 75% of all biopesticide use consists of Bt-based products. The live microbe form is an effective microbial pesticide, purified toxin from this strain is the world's most widely used biochemical biopesticide, and the DNA encoding the Bt toxin makes a powerful PIP as well. This microorganism dominates the current biopesticide landscape, but emerging approaches are poised to capture additional market share going forward, thanks in large part to emerging resistance to Bt-based biopesticide products.

Biopesticides are gaining popularity as lower environmental impact alternatives to conventional synthetic pesticides. Attributes like low-to-no re-entry intervals following applications and less restrictive (sometimes non-existent) maximum residue limits are enticing growers to trade portions of their synthetic crop protection portfolios for biocontrol options. Especially popular are integrated pest management (IPM) strategies that employ a combination of synthetic and biological crop protection products in order to achieve synergies of action and lowered overall use. In these strategies, properly timed applications of biological products can decrease a grower's total need for synthetic pesticides. This sets up a unique growth situation for biopesticides. Part of the market's growth comes from gaining market share previously held by synthetic crop protection. Additional growth of biopesticides is due to new applications for biocontrol that are not possible with synthetic crop protection.

Dissecting the biopesticide market today

Today, biopesticides make up a small fraction of the total global crop protection market at approximately $3 billion in value worldwide (Olson *et al.* 2013). Biopesticides today hold just 5% of the total crop protection market. This segment of the industry is growing, however, with a compound annual growth rate (CAGR) of 8.64%, a rate we expect to continue through at least 2023 (See Figure 1), at which point we expect the market to reach more than $4.5 billion, or more than 7% of the total crop protection market. In performing this market

DOI: 10.1564/v26_oct_04

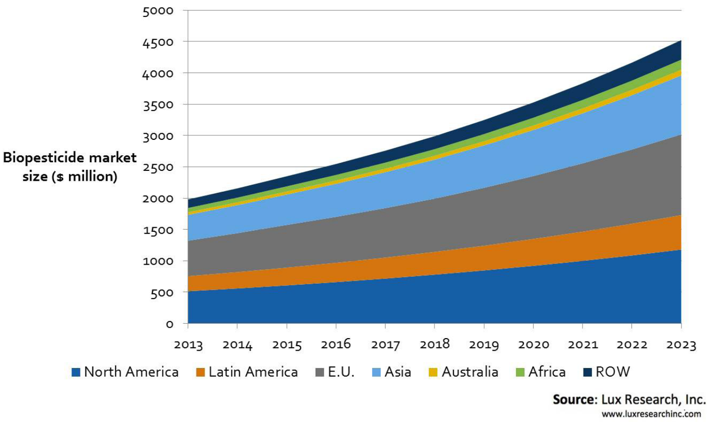

Figure 1. The biopesticide market is approximately $3 billion today, and will rise above $4.5 billion by 2023.

size analysis, we assumed that biopesticides would continue to gain crop protection market share, taking dollars from the conventional crop protection market. We also assumed that growth would be regional, with Europe and Latin America projected to grow most quickly in the coming three years, driven by tightening regulatory restrictions and rapidly emerging insect resistance, respectively. Africa is poised for significant growth, but in a more extended timeframe. North America, which already accounts for a large proportion of the market, will continue to grow at a slower rate than Europe.

Powerful factors work in opposition to shift the biopesticide market going forward

As is the case for any emerging technology approach, various factors alternately drive and inhibit the growth of biopesticides. Regulatory pressures are one of the strongest single drivers for biopesticide development. The European ban on neonicotinoid pesticides from 2013 to 2015 may well drive many of the region's growers to seek biopesticide alternatives for protecting their crops. Ease-of-handling attributes like low-to-no re-entry intervals and post-harvest intervals also drive adoption of biopesticides, mainly by serving as a stark alternative to existing synthetic options and their use restrictions. Additionally, the aforementioned emerging resistance in insects is driving interest in biological alternatives. As conventional synthetic options become ineffective due to developing resistance, growers are more and more willing to try biological options.

The exceedingly high costs associated with developing synthetic crop protection chemistries are another driver for biopesticide development; based on our interviews with tech developers, a novel synthetic typically requires $250 million and nine years for development and regulatory approval while a biopesticide needs less than $10 million and four years for the same process. As a less expensive and quicker development process, biopesticide R&D is more attractive to start-ups and small companies with limited research budgets. As a direct result, start-ups in the biopesticide space have proliferated, creating a competitive and cutting-edge arena for innovations. More novel biopesticide ingredients have been released in recent months than synthetic pesticides.

Competing with established, powerful synthetic pesticides will prove too much for many smaller developers, both in terms of demonstrating the efficacy of biopesticides and, more importantly, in convincing growers to convert from their tried-and-trusted methods to new and relatively unproven products. Additionally, regulatory approval pathways are uncertain for some classes of biopesticides, especially those derived from genetic materials or crop pathogens; this adds to the challenge of approval and commercialization, inhibiting biopesticide innovation and development. Finally, the majority of biocontrol options require frequent, repetitive applications for optimal efficacy. The added labor and expense of these applications is often a deterrent, inhibiting the growth of biopesticides.

Biopesticides to 2020 and beyond

Myriad examples of emerging technologies replacing incumbent approaches exist in other industries, with e-books rapidly taking market share from ink-and-paper publishing and camera-equipped smartphones unseating standalone digital cameras rather quickly after introduction. Likewise in agriculture there is a history of new technologies taking market share from well-accepted approaches. Even chemical pest control was once an emerging technology, replacing prior practices of culling infected and/or infested plants to minimize pest damage. Crop varieties that carry their own PIPs have taken market share from pure spray-applied crop protection strategies as well, as was the case for first-generation Bt crops.

Unseating incumbent technologies is one of the most critical stumbling blocks for many emerging technologies, and biopesticides are already struggling to do so; in the more than 250 year history of crop protection, biopesticides have only managed to wrest 5% of the market from their synthetic counterparts. Taking further market share from conventional crop protection approaches will be a key part of biopesticides having success going forward. A very risk-averse group, growers are typically slow to shift from one technology approach to another. Regardless of the reticence throughout the agriculture industry to shift to new technologies, incumbents are regularly unseated by compelling new approaches, and biopesticides will continue to collect market share through switching.

In a prior analysis of the entire crop protection technology space, we assembled a taxonomy to organize the currently available technologies and those in development. The major categories of classification we identified were targets, sources, and delivery attributes (see Figure 2). Based on our prior studies of start-up activity in the space, we identified two target areas that developers have focused on to date: pests and diseases. Going forward, we expect that start-up activities will target abiotic stressors as another key area of focus, with protection from drought and excess heat being in very high demand. Promising biocontrol approaches in development abound. The U.S. recently approved SolviNix, developed by BioProdex, a first-of-kind bioherbicide that uses a live plant virus as its active ingredient (Tobacco mild green mosaic tobamovirus strain U2 (TMGMV U2)) (bioprodex.com). Additionally, efforts to use RNA interference (RNAi) for crop protection are taking off. Major companies and start-

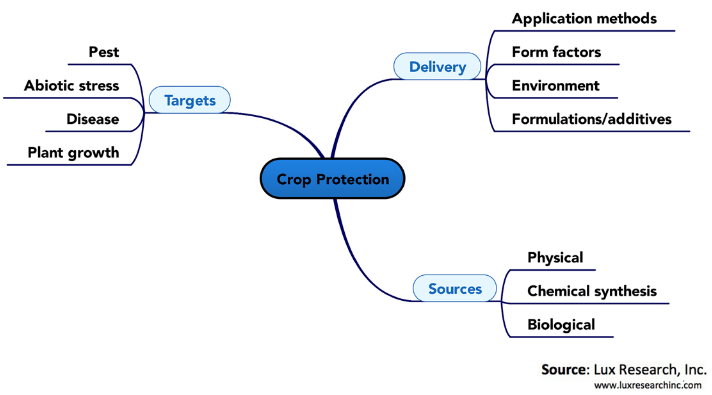

Figure 2. Crop protection targets like pests and disease have historically been a focus of crop protection development efforts; biopesticide developers are targeting abiotic stresses as a key area of focus.

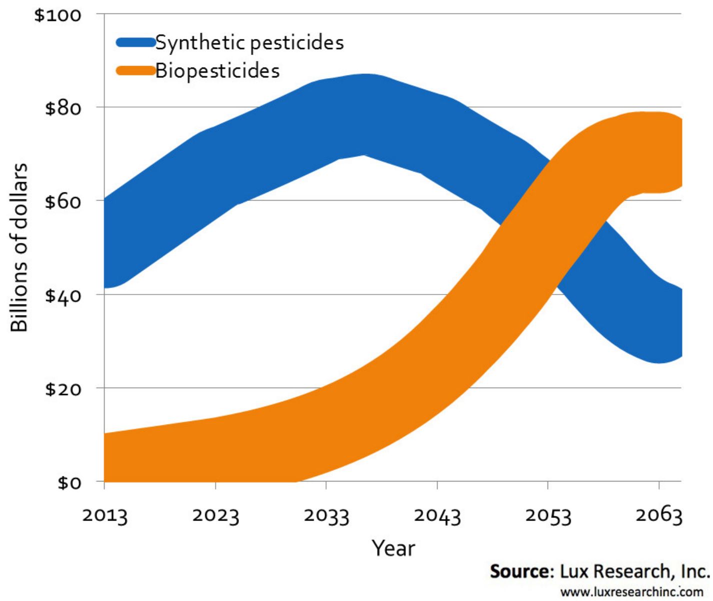

Figure 3. The biopesticide market will continue to grow as synthetic pesticides reach their apex and begin to contract; there is a high degree of uncertainty in this projection, demonstrated by the thickness of the lines.

ups alike are endeavoring to create sprayable RNAi products as well as RNAi-based PIPs for biological crop protection; in this category, Monsanto's Bio-Direct development platform is one of the most press-covered to date, and start-up APSE's work on low-cost, high-purity RNA production holds promise as well (www.apsellc.com).

Recent major business deals in the biopesticide space demonstrate the confidence that major agribusiness and chemical companies have in the potential growth of the industry. Since 2012, multiple acquisitions, licensing agreements, and partnerships with values well into the hundreds of millions of dollars show the depth and breadth of investment large companies are making in biopesticide development (see Table 1). Well-established technologies from other industries will have roles to play in biopesticides, adding to the attractiveness of this technology space for large companies. Fermentation, for example, which has been a core technology for pharmaceutical production, will be a critical production method for biopesticides as well, as many of the small-molecule biologicals will be most cost-effective when produced through fermentation. Specialty chemical companies and pharmaceutical companies alike will have opportunities to gain additional value from underutilized fermentation capacity by producing biocontrol products.

Going forward, we believe the biopesticide market will grow, even as the synthetic pesticide market continues to grow (see Figure 3). The figure shows theoretical projections for the future of both biopesticides and synthetic crop protection agents, using wide lines to indicate the significant degree of uncertainty inherent in such long-range projections. We anticipate that the synthetic crop protection market will peak while the biopesticide market continues to grow. Between the late 2040s and the early 2050s, we project that biopesticides will equalize with synthetics in terms of market size. Significant uncertainties in the rates of uptake, especially in geographies like Africa and Southeast Asia account for a major portion of the flexibility in those projections.

Table 1. Recent development deals in biopesticides demonstrate significant interest in the space from major companies.

Company	Type of deal	Target	Value
Bayer CropScience	Acquisition	AgraQuest	$425 M
	Partnership	Flagship Ventures	Not disclosed
Monsanto	Development partnership	Novozymes	$300 M +
	Start-up founding	Preceres LLC	Not disclosed
BASF	Acquisition	Becker Underwood	$1.02 B
Syngenta	Acquisition	DevGen	$526 M
	Acquisition	Pasteuria	$113 M
DuPont	License	Marrone Bio Innovations	Not disclosed
	Acquisition	Taxon Biosciences	Not disclosed
	Development partnership	Hexima	Not disclosed
Platform Specialty Products	Acquisition	Arysta LifeScience	$3.5 B
Dow AgroSciences	Development partnership	Radiant Genomics	Not disclosed
Sumitomo Chemical (Valent BioSciences)	Development partnership	Evolva	Not disclosed

Conclusions

While we cannot predict the growth of the biopesticide market to the dollar, we are confident in our assessment that the industry will continue to grow in the future. Major global factors may impact that growth, including shifts in regulations and increasing development of resistance in pest organisms. The ban on neonicotinoid pesticide use in Europe is an excellent example of such a situation. The two-year ban will expire at the end of 2015, though the path forward remains unclear. Growers have turned in two directions to replace the banned active ingredients: toward older, more toxic chemistries like organophosphates and pyrethroids, and toward biological alternatives. Other future legal actions affecting growers' abilities to use established crop protection chemistries will likely contribute to increased market share for biologicals as well.

Large agribusinesses and crop protection companies have been moving into the space, both through the open innovation deals mentioned in Table 1 and through internal R&D efforts. For these major players, biopesticides represent an opportunity as well as a threat to their core businesses. While a portion of biopesticide use adds to the total market size, a significant majority comes from market share shifted away from synthetic products. Large agribusinesses will approach the biological space as a means of supplementing their existing synthetic portfolios, thereby mitigating much of the risk of cannibalizing core business for new business. Meanwhile, chemical companies and pharmaceutical companies with fermentation capacity and expertise will enter the space to increase the profitability of otherwise underutilized fermentation capacity.

Whereas synthetic crop protection has been dominated by fewer than ten massive companies, biopesticide developers number in the hundreds, with more than 50 companies combining for just 60% of the total market. Large companies expecting few competitors in this new space will need to adjust their strategies to account for the universe of small-scale developers. In some cases, those would-be competitors can make great partners. The combination of chemistry, biology, agronomy, and physiology needed to excel in biopesticide development and commercialization makes the space ripe for successful partnering. Companies like Dow AgroSciences and Valent BioSciences have made early moves in this direction, partnering with Radiant Genomics and Evolva, respectively. Both larger companies bring biopesticide screening and production expertise, while the smaller partners bring genetics capabilities for identifying promising candidates. Monsanto and Novozymes have come together in the BioAg Alliance with similar stated goals (portal.luxresearchinc.com). Partnerships like these will serve to shorten development timelines, allowing biopesticide development efforts to bear fruit more rapidly and giving growers more biological options from which to choose.

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As a Research Analyst at Lux Research, *Sara Olson* leads the Agro Innovation Intelligence practice, identifying and assessing key opportunities for profit and technological advances within a broad range of agricultural topics including, among others, genetically modified crops, fertilizer and pesticide optimization, precision ag developments, and marker-assisted selection in crops.

Sara received her PhD in Biochemistry from Texas A&M University after completing her BS in Biology at the same institution. Her research focused on quantitative functional genomics of crop plants with implications for advancing nitrogen use efficiency, drought tolerance, and biomass generation in both food and fuel-generation applications.

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