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Biopesticides to drive the next

Green Ag Revolution


As a global leader in biopesticides, AgraQuest is committed to delivering tools to meet the challenges facing the food value chain: Consumers demanding diverse, healthy foods with limited pesticide residues; a population expected to exceed 9 billion by 2050; and increased regulation of crop inputs driven by concerns for the health of the environment, farmers and consumers. We believe the solutions to these challenges can be unlocked through science focused on the natural world – and we’re working everyday to reinvent food production in ways that balance the needs of both humans and the environment.

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1540 Drew Ave., Davis, CA 95618 | +1 (530) 750-0150
Biopesticides: no longer a fringe sector

The increasing thrust towards sustainable agriculture and integrated pest management has led to biopesticides emerging from their status as a fringe sector to being viewed as an intrinsic part of crop protection. Sanjiv Rana presents a comprehensive look at the sector.

The term “emerging sector” has been synonymous with biopesticides for quite a few years. The sector has been variously hailed as the future of crop protection while also derided as a fringe sector selling “snake oils”. But a combination of some fairly recent factors indicates that the sector has become established as an intrinsic part of crop protection and is on the growth curve.

Agrow took the first step of acknowledging its importance by setting up the Agrow Award for Best New Biopesticide a couple of years ago. We now feel that it is time to compile the information in Agrow’s previous coverage and consult the main players in the industry to come out with a comprehensive review of the sector.

One of the reasons that the industry comes across as a bit hazy is the lack of a clear definition of biopesticides. Although the term brings up visions of microbes attacking pests and diseases, the US EPA has quite a wide classification for biopesticides that includes microbial pesticides, plant-incorporated protectants and biochemical pesticides. Biochemicals include growth regulators, pheromones, oils, soaps and minerals. The EPA website itself says that “because it is sometimes difficult to determine whether a substance meets the criteria for classification as a biochemical pesticide, EPA has established a special committee to make such decisions”.

Sumitomo Chemical subsidiary Valent BioSciences prefers to use the term biorationals, which it defines as a broad range of substances typically derived from natural or biological origins and including biological pesticides as well as products used for crop stress management, enhanced plant physiology benefits, and root growth management.

The EPA defines biorational products as any of the following: National Organic Program (NOP) compliant, insect growth regulators, biological control tools, boric acid and diatomaceous earth dusts, insect baits, plant-based, and EPA reduced-risk products.

Quite a few people prefer to include macrobials within the category, which include predatory insects. In order to give a clearer focus to the article, we will be mainly examining microbial pesticides.

**types of microbials**

**Bacteria:** Many spore-forming and non-spore-forming bacteria are known to be effective against a wide spectrum of insects and diseases. More than 90 species of naturally occurring, insect-specific bacteria have been isolated from insects, plants and soil. They are ideal as biopesticides as they can be manufactured by industrial fermentation and can be stored for extended periods. Apart from varieties and subspecies of *Bacillus thuringiensis* (Bt) acting as bioinsecticides, there are: biofungicides such as *B licheniformis*, *B pumilus* and *B subtilis*; and bioematicides such as *Pasteuria nishizawae*.

**Fungi** as microbial products surfaced in the 1980s and 1990s. They may show nematicidal, acaricidal, insecticidal, fungicidal and/or herbicidal properties. Examples: *Paecilomyces fumosoroseus* and *P lilacinus* (bioematicides); *Trichoderma spp* and *Coniothyrium minitans* (biofungicides); *Beauveria bassiana* (bioinsecticide); and *Phytophthora palmivora* (bioherbicide).

**Viruses:** Baculoviruses are a family of naturally occurring viruses known to infect only insects and some related arthropods. Most are so specific in their action that they infect and kill only one or a few species of Lepidoptera larvae. Examples: *Cydia pomonella granulovirus*, *Spodoptera exigua* NPV, *Helicoverpa zea* NPV.

**Nematodes** are used primarily to control insect larvae. Nematodes enter a target pest through bodily openings and release toxic bacteria that kill the hosts. Examples: *Heterorhabditis bacteriophora* and *Steinernema puertoricense* (both bioinsecticides).

**Protozoa** are single-celled eukaryotic organisms, some of which are insect parasites. A key small group of products is based on the protozoan, *Nosema locustae*, which provides grasshopper and cricket control.

**Yeast** microbials include a small group of products to control post-harvest pathogens that promote fruit decay. These can also stimulate natural plant defence mechanisms in plants to help fight off disease. Example: *Candida saitoana*.

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1. [Source: BPIA, Valent BioSciences and Agrow]
**Biopesticides**

**history**

*Bt* was first isolated by Japanese biologist Shigetane Ishiwatari in 1901 while investigating the cause of the sotto disease (sudden-collision disease) that was killing large populations of silkworms. It was rediscovered by Ernst Berliner in 1911 when he isolated a bacterium that had killed a Mediterranean flour moth. He was the one who gave the bacterium its name after the German town Thuringia where the moth was found.

Farmers started to use *Bt* as a pesticide in 1920. France began making commercialised spore-based formulations called Sporine in 1938. More products subsequently entered the market but they had limitations such as: sprays were washed away by rain; degraded by UV light; and all *Bt* strains known at the time were only toxic to lepidopteran pests. Also, insects living within the plant or underground could not be reached by *Bt* sprays.

In 1956, the Pacific Yeast Product Company developed an industrial process known as submerged fermentation, which allowed production of *Bt* on a large scale. In the US, *Bt* was registered as a pesticide in 1961. In 1977, the first subspecies toxic to dipteran insects was found, and the first discovery of strains toxic to species of coleopteran pests followed in 1983. Government and private funding for research on *Bt* began in the 1980s when insects became increasingly resistant to synthetic insecticides, and scientists and environmentalists became aware that the chemicals were harming the environment. The first genetically modified plant containing *Bt*, maize, was registered with the EPA in 1995.

Among other microbials, in 1973, *Heliothis zea* NPV was granted exemption from tolerances and the first viral insecticide, Elcar, received a label in 1975. In 1977, *Bt* var *israelensis* was discovered, and in 1983 *Bt* var *tenebrionis* was found. In 1979, the EPA registered the first insect phenome for use in mass trapping of Japanese beetles.

**timeline**


1994 – US EPA forms the Biopesticides and Pollution Prevention Division within the Office of Pesticide Programs.

1994 – US EPA registers Ecogen’s AQ-10 (*Ampelomyces quisqualis*) - the first biofungicide

1996 - Biopesticide industry group formed (International Biocontrol Manufacturers Association)

1998 - Certis’ *Paecilomyces fumosoroseus*-based bioinsecticide gains provisional EU approval in Belgium.

2000 - US biopesticide group formed to develop industry standards for biopesticides encompassing quality control, efficacy and registration (Biopesticide Industry Alliance - BPIA).

2001 - Certis’s *P fumosoroseus*-based bio-insecticide becomes the first biopesticide to gain full EU approval following its inclusion in Annex 1 of the EU agrochemical registration Directive (91/414).

2001 - EU amends Directive 91/414 specifically to take into account approval applications for biological pest control products. The amendments make up EU Directive 2001/36 and lay down the data requirements that an applicant must include in the dossier for an active ingredient that consists of microorganisms or viruses.

2005 – New EU rules for the evaluation and registration of microbial pesticides in the EU introduce common procedures for member states to follow when approving microbial pesticides.

**pros and cons**

The foremost advantage of biopesticides listed by the EPA is that they are “usually inherently less toxic than conventional pesticides”. Moreover, they are typically target-specific and have little to no impact on non-target organisms. A third benefit listed by the EPA is that biopesticides often are effective in very small quantities and usually decompose quickly, thereby resulting in lower exposures and largely avoiding pollution problems caused by conventional pesticides. A consequent advantage is that biopesticides are generally exempt from tolerance levels and can help growers to manage pesticide residues. Other benefits include shorter re-entry intervals and less chance of resistance developing in the pathogen.

The EPA mentions a caveat, however, that to use biopesticides effectively, users need to know a great deal about managing pests. That has been one of the major constraining factors preventing the technology from being used on a mass scale by itself. That is why the target specificity of bioinsecticides can be a handicap as well because proper identification of a target insect pest is essential and the pest problem must be accurately identified before selection of a biopesticide. The advantage of minimal residues can also be a double-edged sword as the relatively short residual activity compared with conventional pesticides implies the need for them to be applied when the pest is in its most vulnerable life stage, or else, applications may prove ineffective.

Another problem is that as they are composed of living organisms, storage conditions, soil and air temperatures, and use of other chemicals can compromise their efficacy. A shorter shelf life also makes them somewhat more complicated.

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2 (Source: University of California San Diego, BPIA, EPA)
Other factors that have inhibited their popularity include the perception of their being not as effective as conventional pesticides. Their being considered more costly has not helped matters either.

But in overall consideration, the environmental and “green” advantages outweigh the deficiencies, which could eventually be overcome with the enhancement of technology.

global market . . .

The question about the market size of biopesticides is one that draws varied responses. One of the problems encountered in calculations is the lack of a clear definition and how narrow or broad the definition of biopesticides one considers. So, despite the presence of varying figures from some reports, the absence of any industry-accepted market study complicates matters.

There seems to be a broad consensus that biopesticides account for 2.5–3.5% of the global pesticide market. The share increases each year as the sector’s growth has been over double that of the overall crop protection industry. But estimates about the proportion of microbials within this share vary.

After talking to various experts within the industry, we would place the total biopesticide market at around $1,500 million currently. It is expected to grow at a rate of over 15% annually in the coming years so that its current 3.5% share of the total crop protection market would double to over 7% by 2015 and cross $3,000 million.

The greatest use of biopesticides is currently in the US, which accounts for over 40% of the total. Europe comes in next with around a quarter of all sales, followed by Asia at around 20%. Latin America accounts for some 10%.

microbial pesticide market . . .

The current size of the global microbial pesticide market is around $900 million. The US accounts for some 30% of sales, with Asia and Australasia using much more of microbials than other regions, making up some 30% of sales. Europe follows next with 20%, with the remaining 20% being used in Latin America and the rest of the world.

UK consultancy CPL Business Consultants provides some interesting details about regional markets. Within the US, the proportion of the market taken up by Bt-based products has declined from an estimated 90% in the 1990s to around 55%. This has partly been due to a steady down-turn in Bt use for caterpillar control and to some extent to increased sales of new products.

In the Asia/Australasia region, China is the largest microbial biopesticide market, followed by India and Japan. The proportion of the market taken up by Bt-based products is estimated to be 55%. All the major markets in the region are characterised by few if any biopesticide imports. The majority of the products available for use in these countries has been researched, developed and manufactured locally albeit, often, with advice and assistance from NGOs or government. This has been particularly the case for fungal-based biopesticides and for entomopathogenic viruses.

The proportion of the European microbial pesticide market accounted for by Bt-based products has declined from an estimated 90% in 2000 to around 50%. The largest increases since 2005 were seen in non-Bt bacteria, notably B subtilis, and in fungal-based products, including C minitans and Trichoderma-based products. There have also been significant increases in viral product sales and a steady rise in the nematode market. The largest individual European biopesticide market is Spain, followed by Italy and France.

Brazil and Cuba are the largest biopesticide markets in Latin America, followed by Colombia. All three are characterised by few if any biopesticide imports. In fact, the Latin American biopesticide market as a whole is characterised by government and NGO-encouraged local production. The proportion of the microbial pesticide market taken up by Bt-based products in Latin America is approximately 40%. Bt-based products are dominant in Africa and the Middle East, taking around two-thirds of the overall microbial biopesticide market. There has been little development of local production for local use projects in Africa. Fungal- and viral-based products are therefore comparatively underdeveloped in this region.

CPL places bacterial products as accounting for around two-thirds of total sales of microbial pesticides. Bt alone accounts for over 50% of total sales. They are followed by fungi, which account for just under 20%, while viruses make up over 10%. Other products, including nematodes, make up the remaining 5% of sales.

“What’s interesting is that even after 40 years in the market, Bt sales continue to grow even today. How many active ingredients still show growth after 40 years?” asks Valent Biosciences’...
Marrone Bio Innovations (MBI) is a leading global provider of natural pest management and plant health products for the agricultural crop protection and water treatment markets. Comprised of naturally occurring microorganisms and plant extracts, MBI’s effective and environmentally friendly products provide improved crop yield and quality while managing pesticide resistance and residues. MBI’s crop protection products are primarily applied in conventional production programs with chemical pesticides, and are suitable for organic operations as well. The company also addressing new markets where there are no available conventional chemical pesticides or whether the use of such pesticide is not desirable or permissible because of health and environmental concerns.

With the global population soaring, the world’s food production by the year 2050 will need to double according to current estimates. Protecting crops and improving yields will require new product solutions that not only control pests, but also address consumer and legislative concerns focused on health and the environment. Like many biopesticides, MBI’s natural pest management products are part of this solution. They are exempt from conventional chemical residue tolerances, limit the development of pest resistance, have low toxicity, and pose low risk to non-target organisms including mammals, birds, fish, and beneficial insects. In some countries biopesticides have a shorter regulatory approval process than conventional chemical pesticides due to their low-risk profile.

MBI's award-winning fungicide and bactericide, Regalia®, is currently sold in North America, Latin America and select European countries, treating foliar and soil diseases of food and ornamental crops. The company has recently launched its new insecticide Grandevo™ in the US. It is a novel, broad-spectrum microbial product for the control of both sucking and chewing pests. As part of its growth strategy, MBI is entering into strategic agreements to distribute its products to markets outside of its core sales territory of high-value specialty crops in the US.

In the water treatment market, MBI's new product Zequanox® selectively kills invasive freshwater mussels that cause significant infrastructure, ecological and property damage. Currently used to treat hydroelectric power facilities, the company is testing Zequanox's potential application for industrial facilities, irrigation systems, aquaculture, drinking water, and recreational waters.

MBI discovers new products through its efficient, proprietary discovery and development platform and by in-licensing select technologies. MBI has developed both a portfolio of EPA registered biopesticides and a pipeline of new products in early and late stages of development, including herbicides, insecticides and nematicides. All of MBI’s offerings address the growing global demand for effective, safe and environmentally responsible products.

Contact Info:
Julie Versman  VP International Business  jversman@marronebio.com  www.marronebioinnovations.com
At Marrone Bio Innovations, we deliver on our mission to discover, develop and market breakthrough products for managing weeds, pests and plant diseases.

Our work has resulted in effective, naturally derived products such as **Regalia**—named 2010 Best New Biopesticide by Agrow for its control of fungal and bacterial diseases in food and ornamental crops. Our newest product, **Grandevo™**, offers broad-spectrum control of both sucking and chewing insects with efficacy equivalent to chemical products. Both Regalia and Grandevo strengthen integrated pest management programs, reduce residues, and help to improve yields and quality.

Committed to meeting the needs of growers today and tomorrow, Marrone Bio is developing a growing pipeline of new herbicides, insecticides and nematicides.

strategic marketing manager, Rick Melnick. He says that the reason for the consistency in Bt sales is that products based on it are efficacious, cost effective and work well as a partner with almost every traditional chemical programme.

**trends . . .**

Going through *Agrow* articles over the last couple of decades, it becomes evident that start-ups within the industry in the 1990s and early 2000s were not viewed much differently from the internet start-ups that had proliferated before the great internet stock market bust of 2000. The companies that caused that mostly comprised entrepreneurs with fanciful notions of market figures and sales projections, waiting for cash injections from larger players to get them up and running; barring a few, most biopesticide products had yet to prove their worth. Large crop protection companies were wary of dabbling in a market where growth prospects were hazy and the giants could not be much bothered about niche products with the potential of a few million dollars and shelf-life issues on top of that.

Marrone Bio Innovations’ founder and chief operating officer Dr Pamela Marrone provides an interesting insight into these changes, having got first-hand experience of setting up a string of ventures in the area in the last couple of decades. She started Entotech, a subsidiary of Danish company Novo Nordisk in 1990. When the company was sold to Abbott Laboratories in 1995, she started AgraQuest. The going proved to be tough in those years as the perceived benefits were not appreciated by the majority. The market for biopesticides was small and growers and their consultants saw the products as “snake oils”. “We were ‘pigeonholed’ into organic-only rather than for mainstream farming,” she says.

It was a bit of an unfair test for biopesticides as they were being judged on their stand-alone efficacy in controlling pest problems, rather than their being part of integrated programmes. Since then, biopesticides have improved to where they are as effective as many chemical pesticides and when used as part of integrated programmes, can improve the efficacy of existing chemical pesticides. Additionally, demand for safer alternatives to chemicals has grown significantly and the benefits of biopesticides are now more widely-known and accepted. The efforts of industry organisations such as the Biopesticide Industry Alliance in the US have gone a long way in winning the support of regulators and growers.

The going was much easier when Dr Marrone left AgraQuest in 2006 to start another venture, Marrone Bio Innovations. “It is really fun doing another company when the market is more receptive and I can apply so many lessons learned to the new company.”

**companies . . .**

It becomes evident that the environment was quite turbulent for the biopesticide industry, which consisted of quite a few small companies with few products but optimistic outlooks, which did not quite materialise in some cases. Some of them ceased to exist while others were taken over wholly or in parts by larger players. A few survived and count among some of the well-known players today. We present some the backgrounds of a few companies and trace the inter-relationships between quite a few of them.

**AgraQuest** was formed in 1995 by Dr Marrone after leaving Novo Nordisk subsidiary Entotech when it was sold to Abbott Laboratories (the agricultural business interests of which were acquired by Sumitomo Chemical to form Valent BioSciences). She left the company in 2006 to start another new venture. Marcus Meadows-Smith took over as CEO in 2008. He initiated a strategy change and strengthened R&D capabilities.

“From designing products for the organic food sector that were ‘good enough’ for conventional agriculture, the company focused on designing products for conventional agriculture that were superior to the market-leading synthetic pesticides and could still be used for organic food production,” says Mr Meadows-Smith.

AgraQuest has invested over $140 million in its R&D engine to date. Mr Meadow-Smith says that AgraQuest is differentiated
from smaller companies, which have only spent a fraction of this on R&D and do not possess the competence to develop a product that can compete in the conventional pesticide sector.

The company’s growth has largely been organic and it claims to have grown by over 30% each year. Within the NAFTA region, it has its own sales and distribution network, while outside that it follows a partnership model and has formed deals with BASF, DuPont and Brazilian company Iharabras, among others. It continually seeks in-licence or acquisition opportunities. “To date we have tested over 150 products from smaller biopesticide companies, but so far only two in-licensing products met our rigorous efficacy hurdle for development and launch into conventional agriculture,” he says. The company has a portfolio of seven new products expected to enter the market over the next 3-5 years.

Marrone Bio Innovations (MBI) was formed in 2006 when Dr Marrone left AgraQuest. The going this time round was easier as the conditions for starting a biopesticide venture were much more congenial in 2006 than in 1995. Founded in a garage, the company has grown to have 80 employees and occupies 25,000 sq ft (2,323 m²) of laboratory, office and pilot plant.

The company considers organic as well as inorganic growth as potential revenue-producing strategies with the opportunity for robust growth. It has established partnerships with Syngenta, FMC, and Scotts and also has a direct sales force throughout North America. MBI has had three biopesticide ais registered by the EPA and has two additional ais awaiting approval.

Valent BioSciences was formed in 2000 when Sumitomo Chemical acquired Abbott Laboratories’ agricultural business interests. It claims to have the largest intellectual property platform of any biorational company in the world. Its products in the microbial insecticide market are based on Bt. DiPel (Bt subsp kurstaki) and XenTari (Bt subsp aizawai) remain the leading microbial insecticides in the world, it says. Valent employs approximately 130 people.

Manufacturing is currently managed through Abbott Laboratories, which has been its manufacturing strategic partner since the acquisition in 2000. Valent is building a new US manufacturing facility in Osage, Iowa where all manufacturing processes will be transferred to in 2014.

The company’s operating model is that of direct access to target markets. “While we use Sumitomo affiliate companies and multinationals as marketing and distribution partners, we feel it is essential to control the stewardship of our products and brands down to the grower level with direct product management,” says chief operating officer Mike Donaldson.

Certis USA was formed in a similar manner when Mitsui & Co acquired Thermo Trilogy in 2001 and renamed it Certis USA. It then acquired Bt bioinsecticide products from Ecogen in 2002, which it, in turn, had purchased from Mycogen in 2000. But there was also a preceding series of acquisitions in this case. Thermo Trilogy was formed in 1996 to acquire the biopesticide R&D portfolio from W R Grace. Thermo Trilogy also acquired product lines of Biosys in 1997 and Bt bioinsecticide products from Novartis in 1997. Certis USA mostly develops ais discovered by others.

Certis Europe was launched in 1991 offering conventional ais and biopesticides to horticulture and specialty crops. It has 13 ais in its commercial portfolio and five are in development. Product types include microbial insecticides, nematicides, pheromones and virus products.

Pasteuria Bioscience was spun out of Entomos in 2003. The company started with the idea of using natural remedies for controlling nematodes by figuring out how to produce an obligate parasite of nematode pests. The challenge was to grow bacteria in production-scale fermenters rather than reproducing them in nematodes – a costly and non-scalable process. Technology co-operation between CDG Labs and Entomos advanced the technology to create Pasteuria Bioscience. “Our current focus is to deliver spores as a seed coating,” says company chairman Dr Al Kern.

**current situation . . .**

Biopesticides have come to the fore in recent years as a result of a number of factors. The pesticide industry has been forced to re-examine the priority of biopesticides in its strategic planning as a result of: negative PR suffered by chemical pesticides as a result of vociferous, although often less than veracious, claims by environmentalists and NGOs; enhanced resultant consumer concerns over residues; often arbitrary secondary residue standards set by food retailers; and regulatory squeezing such as the EU Directive on the sustainable use of pesticides (2009/128) and France’s environmental initiative, Grenelle l’Environment.

The fairly recent interest of the bigger agrochemical players in licensing deals and strategic alliances attests to the fact that continued on page X . . .
Valent BioSciences Corporation is a worldwide leader in the research, development and commercialization of highly effective low-risk, environmentally compatible technologies and products for the agricultural, public health, forestry, and household markets.

Through the power of biotechnology, Valent BioSciences develops biorational products that create value and solve problems for its customers around the world. These products include environmentally compatible bioinsecticides and plant growth regulators that are naturally occurring or chemically derived, and are used in sustainable systems. Customers and industry peers alike consider our technology assessment, formulation expertise, development experience, product quality, and market positioning as “best-in-class.”

Intellectual Property:
- 125 Patent families, 500 Active Cases
- 100 trademarks in 125 countries
- 725 product labels
- 800 product registrations in 94 countries

Ag Microbial Products:
- Bacillus thuringiensis subsp. kurstaki Strain ABTS-351, principal brand, DiPel®: Biological control of lepidopteran pests in vegetables, fruits, nuts, vines, and row crops.
- Bacillus thuringiensis subsp. aizawai Strain ABTS-1857, principal brand: XenTari®: For control of armyworm and diamondback moth in vegetables and row crops.
- Bacillus thuringiensis subsp. tenebrionis Strain NV-175, Brand: Novodor®: Biological control of coleopteran species such as Colorado Potato Beetle and elm leaf beetle
- Myrothecium verrucaria, Brand: DiTera®: Biological control of nematode species in banana, grape, turf, and cole crops.

Plants Growth Regulator Products:
- GA3, principal brands, ProGibb®, Berelex® and RyzUp®: improves yield and quality on table grapes, citrus, cherries, and many other fruit and vegetable crops. Used for post harvest quality on a range of crops. Promotes vigorous growth and yield increases.
- GA4A7, principal brand, Regulex®: Reduces russet, improved fruit finish and packout on apples.
- 6-BA, principal brand, MaxCel®: Fruit thinning and sizing of apples. Yield increase on table grapes and vegetables.
- GA4A7/6-BA, principal brand, Promalin®: Improves fruit shape, increases size and reduces russet on apples. Improves fruit set on pears.
- AVG, brand, ReTain®: Manages fruit maturation and ripening for optimum harvest, quality, and storage on apples. Reduces PFA on walnuts, resulting in yield increases.
- S-ABA, principal brand: ProTone®: Promotes coloration in red table and wine grapes. Promotes stress tolerance in plants by controlling stomatal closure, water relations, and photosynthesis.

Public Health Products
- Bacillus thuringiensis subsp. israelensis Strain AM65-52, principal brand, VectoBac®: Biological control of mosquito, black fly, filter fly, and midge larvae.
- Bacillus sphaericus 2362 Strain ABTS-1743, principal brand, VectoLex®: Biological control of Culex mosquito species and many species of Aedes, Psorophora and Anopheles mosquitoes with extended action.
- Bacillus sphaericus 2362 Strain ABTS-1743 + Bacillus thuringiensis subsp. israelensis Strain AM65-52, brand VectoMax®: Biological control of mosquito larvae in multiple habitats.
- S-methoprene, brand, MetaLarv®: Control of floodwater mosquitoes under dry-down and re-flood conditions.

Forestry Products
- Bacillus thuringiensis subsp. kurstaki Strain ABTS-351, principal brands, DiPel® : and Foray®: Biological control of lepidopteran pests including gypsy moth, spruce budworm, and pine processionary moth.
Our Business is Biorationals

For more than 40 years, Valent BioSciences has been the most trusted source of highly effective and dependable biorational products for global agriculture, public health, and forestry applications.

Known by business partners around the world for its unsurpassed market knowledge and quality control standards, by end users for its unrivaled product support, and by peers for its unparalleled commitment to the science behind biorational product development, Valent BioSciences remains the world leader in the demand creation, development, and delivery of biorational products.
Biopesticides

...continued from page VII

biopesticides have started to figure in their strategic plans (See 2011/2012 corporate biopesticide deals table, p XIX).

**Syngenta** views biopesticides as an integral part of its strategy. More specifically, it sees them as part of an integrated solution that complements traditional, especially on a crop-specific basis. The company acknowledges the advancement of the technology leading to “new strains, formulations and applications, improved performance, and more reliable products”. Biopesticides have become attractive to growers by “increasing the number of options for effective pest control, mitigation of resistance issues, and residue management”. The public also has a favourable perception of biopesticides, which helps to create a positive regulatory environment, it says.

The company is involved in research and development in the area and is working on products, some of which have come through licensing-in and partnerships with other companies in the biocontrol arena. Last year, Syngenta entered an exclusive global technology partnership with Pasteuria Bioscience to develop biofungicide products based on the soil bacteria, *Pasteuria* spp. It also signed a distribution agreement with MBI for Europe, the Middle East and Africa. That was followed by Syngenta’s venture capital subsidiary, Syngenta Ventures, acting as one of the main investors in a $25.4 million financing for MBI. Syngenta says that it is always on the lookout for promising biopesticide start-ups that it could fund and any requests for the same are to be routed through the website: www.sygentathoughtseedsers.com.

**BASF** believes in an inclusive approach with a consideration of all solutions available - synthetic or natural in origin. The company thinks that biologicals alone show lower biological efficacy compared with synthetic chemistry but a combination with synthetic crop protection products enables farmers to reap the benefits of both categories.

The importance of biopesticides for the company can be gauged from its Smart Protection programme, which involves spray programmes combining chemical and biological crop protection. Farmers spray conventional products until shortly before harvest and then switch to a biological product during the critical pre-harvest period. That provides farmers the dual benefit of residue control and resistance management.

BASF sees that as the best way to guarantee that farmers and consumers get optimal results in terms of crop and food quality and to ensure its sustainable production. It believes that biological control agents help address key demands of farmers and the food value chain globally. It points to the introduction of “secondary standards” for residues by retailers in response to the pressure of consumer groups. These standards exceed those of official regulatory bodies and may vary from retailer to retailer. At the same time, consumers and retailers have high quality standards for fresh fruits and vegetables. Consequently, the company currently focuses on in-licensing biological control agents to complement its Smart Protection programme. It entered a licensing, supply and distribution agreement with AgraQuest for the biofungicide, Serenade (8 *subtilis* strain QST 713), in many countries in Europe, Africa, the Middle East, Asia and Latin America.

**Bayer CropScience** says that the status of biopesticides in agriculture is still very much an emerging market, but one that is growing. The company has identified opportunities for biopesticides in growing market segments such as fresh fruit and vegetables and seed treatments, product development manager Dr Jennifer Riggs declared at the CropLife America conference in Washington this month. Bayer expects the sectors to expand by more than 10% per annum between 2008 and 2016.

The company is looking to partner with organisations that have identified products. It acquired *B firmus* technology among assets of the Israeli biopesticide company, AgroGreen, and launched it as a biofungicide seed treatment, Votivo. The product is among the six ais for which Bayer has set a combined peak revenues target last year of €1,000 million ($1,334 million at the current rate). It was launched as a combination seed treatment, Poncho Votivo (clothianidin + *B firmus*), for use on maize last year.

**Monsanto** believes that recent developments in biopesticides make them a promising tool for growers around the world. The company says that it is always interested in exploring new options for pest control and is beginning work and research in this area, through collaborations and its own efforts. It entered into a three-year collaboration with AgraQuest in 2010 to evaluate the potential use of AgraQuest’s pipeline of biopesticide leads to develop seed treatments for Monsanto’s core crops and vegetables. The company also has an agreement with Bayer for its seed treatment, Poncho Votivo, for use in Monsanto’s Acceleron seed treatment range for maize and soybeans in the US.

UK pest control company **Exosect**’s CEO, Martin Brown, views these actions as promising signals for the biopesticide sector. He says that the bigger companies are not just moving into venture capital investments, but also towards an open innovation business model, firstly by using facilitator companies such as Yet2.com and NineSigma.com. But as these facilitators work across many industries, “we are seeing the larger corporations launch their own open innovation platforms to attract new technologies”. He cites the open innovation platforms of BASF, DuPont and Syngenta as examples.

“The open innovation business model has veered the industry away from the trend of acquisitions as larger corporates can
scan a range of small technology companies, pick and choose the technology, and license it for their own projects without the huge financial cost and risk of acquiring an entire company.” Mr Brown gives the example of his own company’s technology platform, which could be used across a range of industries, and how it may not make sense for one company to purchase his entire company.

Valent BioSciences’ Mr Donaldson throws in a note of caution, stressing that over the last 30 years, similar entries into the market from large multinationals have been seen, only for them to exit in due course. The opportunities provided to these companies by biorational products seem important, from a PR standpoint, but they quickly find that the way you have to develop and sell these products is very different from that of a traditional chemical product. In the past, they concluded that the return on investment for a chemical product in their system was much more than for a biorational. “Over the last 15 years, every major multinational company has been in the Bt business … every single one exited the market after a short time.” He explains that that they found these products did not fit their culture and competencies. “Today, there are signals that the current multinationals may look at these products differently. Only time will tell whether they have learned from the past and can effectively manage both traditional and biorational products under the same business processes.”

discussion and development process . . .

How does the discovery and development of a biorational pesticide compare with that of a conventional pesticide?

Dr Marrone says that developing a traditional chemical treatment is significantly more time consuming and expensive than developing a biorational. Referring to some much-quoted figures within the industry, she says that it takes approximately ten years and costs over $250 million to move a chemical pesticide from inception through to the approval stage. Comparing MBI’s screening technology to that, she says that it takes MBI about three years to achieve EPA approval and costs anywhere from $3 million to $5 million.

Another parameter of comparison is the number of ais passing through the screening process to end up with a commercially viable product. Dr Marrone says that it takes roughly 140,000 candidates for a conventional pesticide, whereas it only takes 1,500 candidates for MBI to discover one biorational product. The first in-house product developed at MBI, a bionsecticide, was discovered after screening 496 microbes. Approximately 100–200 organisms are tested each week. In total, MBI has screened more than 16,000 micro-organisms.

Dr Marrone says that the discovery of new chemical leads has decreased since 2005 and it has become increasingly difficult to convert a new lead into a new product launch, as indicated by the steep decline in new product debuts from 2002 to 2010. She expects fewer new chemical aids to be launched over the next 10–20 years.

AgraQuest provides a cost estimate of around $25 million to globalize a biorational in key agricultural markets around the world.

Pasteuria says that the differences between biopesticides and chemical pesticides occur at the discovery and screening levels. But once the product has been identified, the process is quite similar for either type of product. In terms of costs, it says that once an organism with specific activity has been identified, scaling up the known biological activity is likely to be less costly.

Certis Europe has a different business model and says that for biopesticides it is more reliant on independent research, generally in universities, which come up with suitable candidates but leave commercial application to companies like itself that acquire the rights and do the development work. The biggest challenge lies in formulation and stability as growers want these products to behave like a conventional chemical, which is often not the case with natural compounds.

Valent says that its R&D programmes focus more on later stage molecules that have shown a positive proof of concept for its needs, but need further development and scale up to become a commercial product. “We are also constantly looking for libraries of natural materials that we can screen ourselves, or through collaborators, and then build upon those natural materials that show promise;” it notes.

The company agrees that it costs less to bring a biorational product to market than it does a synthetic chemical, with most of those reductions lying in the regulatory area. “Since our products have natural origins, regulatory requirements – while still substantial – would be less than for a molecule invented in the lab,” it says. “We estimate that development of a biorational product that can be launched on a global scale, would cost somewhere around 20% of a normal chemical product, but the time for commercialisation would have a similar ratio.” The company cautions that the estimates can vary significantly depending on the technology and the stage of development.
Regulations and regulatory support

It is thought that biopesticides have an easier approval process than conventional pesticides, with lower data requirements and shorter approval timeframes. We talked to companies and regulators and present some of their views.

Companies

Prophyta agrees that there is the advantage of relatively cheap registration as many microbial products do not need chronic and sub-chronic toxicology studies. Also, the “very expensive residue (metabolite) studies” are not necessary.

Certis Europe says that the costs for preparing the regulatory package are lower as the task is less onerous for biopesticides because many higher-tier studies, such as ecotoxicology, are not triggered. But it feels that it is more difficult to get an EU registration for a biopesticide than for conventional chemistry. It says that typically one or two ais enter the EU Annex I every year.

Dunham Trimmer outlined regulatory obstacles in earlier years and how they are being overcome. Mr Dunham says that 8-10 years ago, it was difficult to register biopesticides in many countries outside the US as the standards were designed for traditional chemical products and biopesticides just could not match the standards. That was not because of difficulties with the products, but due to the differences between microbial and chemical formulations and the difficulty in adapting the regulatory guidelines to biopesticides. The registrant had to spend a great deal of time explaining many differences between biological and synthetic products.

Today, many countries, especially produce-exporting countries, have developed specific biopesticide regulatory guidelines that are different from those of chemicals, in some way less stringent and in other ways more difficult. There has been a reduction (but not elimination) in the number of toxicology studies required.

EU approvals

The EU has approved 25 microbial biopesticides. They include seven bacterial-based products, four of which are insecticides derived from Bt variants, and three fungicides derived from other microbes. Sixteen fungal-based products have been approved, most (11) of which are for use as fungicides, with four products authorised for use as insecticides and one as a nematicide. Two virus-based products, both for use against Lepidoptera, are approved. In all, more than half (14) of all approvals are for fungicides with virtually all the remainder being insecticides.

There is considerable overlap of biopesticide approvals between the EU and the US EPA. These encompass six bacteria (including all four Bt products approved by the EU), nine fungi and two viruses. Regulatory approval is shared by a further five organisms where complete matching of the strain involved has not been determined. Three fungal-based products (one insecticide and two fungicides) have been approved by the EU, but not the EPA.

– compiled by Hazel Blake
Regulators

The US EPA encourages the development of safer pesticides, including biopesticides. By reducing the data requirements, approval timeframes, and registration costs associated with biopesticide registration, it offers a streamlined process for developers and potential registrants. On being asked to specify the lesser data requirements, it said that biochemical and microbial pesticides are subject to tiered data requirements, wherein certain higher-tier data requirements, such as chronic toxicity and mutagenicity studies, are not typically triggered for biopesticide registration.

Additionally, as the majority of biopesticides are lower-risk products and offer less chance of residue exposure, they are typically exempt from the requirement of a tolerance or maximum residue limit (MRL). In general, establishing a tolerance or MRL takes longer than an exemption, the EPA says.

The Agency’s microbial pesticides branch has around 100 registered active ingredients. When added to the 400 registered with the biochemical pesticide branch, the total is around 300.

The EPA Office of Pesticide Programs (OPP) started encouraging biopesticides in 1994 with the establishment of the Biopesticides and Pollution Prevention Division (BPPD), which is responsible for all regulatory activities associated with biologically-based pesticides. Among other similar milestones, the Agency lists:

- The Pesticide Registration Improvement Act of 2003 (PRIA I) codified a lower cost and approval timeframe for affected pesticide decisions by creating a more predictable evaluation process. PRIA also promotes shorter decision review periods for reduced-risk applications.
- The Pesticide Environmental Stewardship Program (PESP) is a BPPD partnership programme that works with the pesticide-user community to promote IPM practices.

EPA approvals

The EPA lists 90 different microbial-based biopesticides. These include 40 live bacterial-based pesticides, 33 live fungal-based products and 11 live viral-based products. Six listed biopesticides are active ingredients expressed as a transgene in genetically modified bacteria or yeast that are then killed before use as a topical application. All six products are intended for the control of insect pests. Various Bt delta-endotoxins account for almost half (20) of the bacteria-based ais.

More than a third (41) of the products are insecticides, 29 are fungicides, ten bactericides, five herbicides, four nematicides and one a viricide. Of the 73 biopesticides that have a registrant or producer, five are produced by AgraQuest while six were originally registered by Ecogen. OmniLytics and Thermo Trilogy (now Certis USA) each were listed as registrants for three products. A further nine companies (Abbott Laboratories, Bio-Innovation, Eco Soil Systems, EcoScience Produce Systems, Kemira Agro (now Verdera), Mycoforestis, MycoLogic, Novozymes and Prophyta) each registered two products. Mitsui subsidiary Certis purchased certain biopesticide products from Ecogen in 2002, which had purchased products from Mycogen.

- compiled by Hazel Blake

The Food Quality Protection Act of 1996 (FQPA) changed the way that the EPA regulates pesticides by measures such as requiring the EPA to expedite approval of “reduced-risk” pesticides.

The USDA’s National Organic Program has increased interest in and demand for biopesticides.

higher performing products are available), offsetting some of the advantages.

Bayer’s Dr Riggs estimates that the development of a biocontrol agent takes around six years to complete and costs €5.5-6 million ($7.3–8 million).

Biopesticides and organic farming . . .

Contrary to general perception, the biopesticide industry does not seem keen on being aligned more with the organic sector than with the chemical crop protection industry. There is the clear realisation that organic farming remains a niche and minute market segment and the aim of biopesticide companies is to play a larger role in conventional agriculture. That role would be through greater emphasis on IPM and the adoption of sustainable agriculture by the crop protection industry and by growers.

Pasteuria’s Dr Al Kern says that the company’s approach is to find control alternatives that are based on natural products and are as “green and soft” as possible. “Organic is a ‘pure play’ market and is more limited in scope,” he says.

Certis Europe and Certis USA concur, saying that organic agriculture is not the key driver and plays only a small part in their overall sales. Certis USA declares that biopesticides have been, and will continue to be, used together with chemicals in IPM programmes. It says that the vast majority of its products are used by conventional growers who, to meet today’s farming challenges, need sustainable alternatives, resistant pest
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management, shorter re-entry or pre-harvest intervals, and low pesticide residues from products for market flexibility in the US and export markets.

MBI estimates that over 80% of its sales are in conventional farming, although it says that organic is a fast-growing niche and important to the biopesticide industry.

For AgraQuest, the organic segment represents 3-7% of revenues. “We continue to support organic as a life-style choice, but the focus of our R&D is to develop products that meet the efficacy and cost hurdles of the conventional grower and sustainably help feed the world.”

Valent’s proportion of sales from the organic market is similar to AgraQuest’s, amounting to about 5%. “It’s an important 5%, but we’d be asleep at the switch if we were banking on growth within that 5% to take our company into the future,” says Mr Melnick. Companies that want to be a significant player cannot afford to just focus on organic segments. They must become a core part of a “normal” grower’s pest management and productivity programme.

Exosect’s Mr Brown echoes a similar sentiment. “I think that all companies developing crop protection products, be they biopesticide or conventional [chemical], will be targeting the conventional market first, and if their products are suitable for organic agriculture then all the better, but the organic market alone is not sufficient to get a return on investment for biopesticides or any crop protection product.” He feels that the goal is to make the food production system a sustainable one and to do that, biopesticides need to be embraced by the conventional agricultural sector because it’s this sector that is providing the majority of food and having the greatest impact on the planet’s resources. He believes that this is already happening and there is an emerging “bio-conventional” sector.

Dunham Trimmer’s Mr Dunham says that biopesticides work best in an IPM programme designed to reduce the incidence of resistance, meet production needs such as re-entry intervals, meet the chemical residue demands of the retail consumer and supermarkets and provide economical control of pests over the production period. As a result, biopesticides are not limited to organic growers, but are being integrated more and more into pest control programmes in conventional agricultural systems.

opportunities . . .

AgraQuest sees lots of opportunities in the industry and not many major threats. Grower needs for residue and resistance management will continue to drive biopesticide demand and growth. The entry of big companies into the arena is also viewed as a positive step that will provide distribution channels, help service grower needs and bring additional credibility to the sector.

Among the key drivers for biopesticide demand, Mr Meadows-Smith lists: chemical residues, which will drive demand from consumers, growers and regulators; resistance management, which will be manufacturer driven; and regulatory pressures.

“We see food retailers and consumers driving some trends: European food retailers like Marks & Spencer or Aldi are focusing on produce with pesticide residues below the regulated MRL [maximum residue limits] standards; global companies like Unilever and WalMart are focusing on sustainable food production models through groups like the Sustainability Consortium,” he says.

A case of serendipity

German biopesticide company Prophyta provided an interesting example of serendipity leading to the discovery of a biopesticide. In the former Institute for Cultivating Oil and Forage Crops in Malchow on the Baltic Sea island of Poel, scientists were instructed in 1988 to produce the spores of the fungal plant pathogen, Sclerotinia trifoliorum. These were to be used for the breeding of resistant cultivars. Propagation of the fungal plant pathogen functioned well until the pathogen suddenly ceased to grow. Investigation showed that the pathogen itself had been attacked by a fungal parasite, Coniothyrium minitans. Dr Peter Lüth, managing partner of Prophyta, was one of the researchers and was convinced that this fungal parasite had the potential for a natural pesticide process. After the reunification of Germany, this fungus became the first project of Prophyta and led to the development of its first product, Contans WG.
Within the EU, the sustainable use Directive is expected to drive growth as it entails the preparation of national action plans by member states. Some of these, such as France’s Ecophyto 2018, which aims to halve pesticide usage by 2018, would act as further spurs.

Valent lists a number of factors working in the industry’s favour: sustainability issues; growing population and reduction of arable lands; better technology in formulation and delivery systems; and greater acceptance among end users. “Biorationals make sense - scientifically and from a business standpoint,” says Mr Donaldson.

Mr Dunham says that biopesticides are being commonly used on fruit and vegetables due to the need for an IPM programme or effective resistance management, which is especially demanding in the specialty crop segment. There is starting to be more of an interest in biopesticide use in row crops as well, for economic reasons and for resistance management.

Mr Brown (Exosect) says that the microbial sector will not remain niche as a consequence of the three Rs (tighter Regulation, insect Resistance and reduction in Residues). It is becoming much harder, taking much longer and becoming much more expensive to bring a new ai to market. Therefore, the larger crop protection industry is already looking outside its own R&D to smaller R&D companies (including those that are developing microbial technology), because they offer the sustainable modes of action that those larger companies require.

Prophyta’s Dr Peter Lüth feels that as the big chemical companies enter the biopesticide industry, the threat to its survival has disappeared. The trick is to develop products that are as effective and as applicable as chemical products, but not more expensive.

Pasteuria’s Dr Kern feels that pesticides are a needed part of production, but the conversion to softer pesticide products that are more selective, derived from nature, cost effective and “safer” is under way and needed.

Mr Dunham (Dunham Trimmer) says that some companies often overlook the interaction between theirs and other products.
anonymous biocontrol company. He also cautions that there are still too many “snake oils” in the market that are damaging the reputation of good biological products.

BioWorks’ president and CEO, Bill Foster, echoes the sentiment, cautioning against unregistered, untested products that bypass quality control/assurance testing and in some fashion “contaminate” the market.

Mr Melnick of Valent has similar advice, saying that the biopesticide category has to constantly guard against products with claims that cannot be backed up. “If there’s any threat, it’s whenever an over-exuberant researcher or entrepreneur exaggerates their claims.” But he says that there are more products that perform than there were just a few years ago.

Certis USA advises against hype and unrealistic expectations.

MBI feels that lengthening timelines and increased costs for registration are the biggest threat. This can damage or even kill small start-up companies that need timely and predictable regulatory actions to attract investors and to launch products and get revenues.

Pasteuria’s Dr Kern feels that the threat is from the unwillingness or slowness to invest in and try new technologies to solve pest problems, boost production and serve the environment and mankind.

Certis Europe’s corporate marketing manager Kevin Price’s list contains: the lack of intellectual property protection (patents on strains); consistent quality (when scaling up production); the challenge of grower knowledge and their awareness of how to use the products; and the length of time in the registration process – products with lower risk profiles should move faster. Fast-track national schemes, such as in the UK, are no longer being supported by the government, he says.

**outlook . . .**

Syngenta says that the market is growing, and sees the best areas for growth in the integration of biocontrols with chemical aids, and not necessarily only on a particular geographic basis.

Dr Lüth estimates that the biopesticide industry will grow much faster than the chemical pesticide industry to probably triple by 2020. But there will be a limit as it will not go beyond a 10% share of the entire pesticide market.

Dr Marrone believes the prospects for the biopesticide industry to be promising as products are costing less to develop and commercialise, and have a faster time to market.

Mr Meadows-Smith prefers thinking about biopesticides as being an integral part of the crop protection industry, and the agricultural inputs industry at large. “We believe biopesticides will become an essential tool in every progressive grower’s toolkit as they develop solutions to meet the challenges of highly productive and sustainable farming. We don’t believe this is due to any single technology or milestone, but rather a result of the next green revolution that is driving today’s agriculture.”

Mr Donaldson feels that biorationals are no different than conventional products in the sense that manufacturers have to be able to take these products to market and stand behind not only their claims, but also how they are used and regulated. “If you’re not able to do that – conventional or biological – then you don’t belong in this business.”

Mr Brown predicts a gradual metamorphosis within the crop protection industry. “The biopesticide sector will continue to grow, however, we believe that the structure of the industry will evolve from the individual sectors (biopesticide, conventional chemistry, seed treatment, biotechnology) to a much flatter and less distinguishable structure,” he says. “We are already seeing product development using technology from across these sectors, not just as an IPM programme but actual individual products that are made up of a synthesis of technologies and we refer to this as the emergence of a bio-conventional sector. Biopesticides will become a mainstream choice of active.”
A founder of the biopesticide industry, AgraQuest has been delivering on its promise of better food and a better world for more than 15 years, using microbial genetic information to discover, develop, manufacture and commercialize crop protection products to control insect and disease pests and increase crop yield. Today, AgraQuest is among the world’s leading biopesticide companies, with multiple products on the market and a promising development pipeline.

Built on the premise that the same natural products chemistry that influences modern pharmaceutical discovery should result in innovative tools for plant pest control, AgraQuest today specializes in delivering the many benefits of biopesticides within integrated production programs alongside the best crop production technologies.

AgraQuest’s biopesticide fungicides and insecticides offer growers unique benefits including improved crop quality, increased yields and reduced environmental impact. These products have multiple modes of action that help growers reduce the likelihood of the development of pesticide resistance. They also deliver harvest and labor benefits through their short restricted entry and pre-harvest intervals. AgraQuest’s biopesticides are exempt from residue tolerances, making them an easy choice for growers aiming to export their crops.

Traditionally, biopesticides delivered a low concentration of active components, meaning high cost-of-use compared to the low use rates and consistent control delivered by conventional crop protection products. AgraQuest’s focus on microbial genetics, chemistry, and advanced fermentation results in products with low use rates, consistent performance, and similar costs to synthetic pesticides.

AgraQuest’s unmatched biopesticide development capabilities are based on the company’s investment in strategic areas of R&D excellence: microbial and plant genomics, fermentation, natural product chemistry, nematology, formulation and microbiology. With the largest private team of scientists focused solely on biopesticides, AgraQuest has a deep pipeline of new products poised to enter global markets over the next five years.

These same areas of excellence give AgraQuest a scientific understanding of the modes of action that lead to superior product design. The company’s scientists deliver specialized products with active metabolites that directly control pests like insects and pathogens, activate plant defense systems, and promote plant growth processes. Additionally, AgraQuest’s manufacturing capabilities consistently rank among the best in world.

With impressive R&D capabilities and superior product offerings, AgraQuest continues to expand their product reach beyond traditional biopesticide markets to conventional foliar and soil pest control, seed treatment, animal health and nutrition and specialty markets like BASF, Bayer Environmental Science, Bayer Animal Health, DuPont, Monsanto, and Pfizer.

Never before has the integration of biopesticides into food production been so important. As the global population grows past nine billion people in the coming decades, the next green agriculture revolution will be powered by products that facilitate greater farmer productivity, sustainably grown clean food, and a reduced environmental impact. AgraQuest is committed to being a leader in the development of products that are part of this revolution, while providing a better food and a better world.
Biopesticide-related corporate deals

(January 2011 onwards)

US biopesticide company Marrone Bio Innovations appointed Canadian agrochemical company Engage Agro as exclusive distributor of its biofungicide, Regalia Maxx (Reynoutria sachalinensis extract), in Canada.

Sumitomo Chemical’s US biopesticide and biorational products business, Valent BioSciences, and the US post-harvest treatment specialist, Pace International, expanded a screening and evaluation collaboration to cover biorational fungicides.

Nufarm agreed to distribute a range of conventional pesticides and biopesticides in Canada for Sumitomo Chemical’s subsidiary, Valent Canada. The deal includes four bioinsecticides and five plant growth regulators.

US agrochemical company American Vanguard (Los Angeles, California) acquired a global licence to US pest control firm Summit Chemical’s Bt var israelensis (Bti)-based Bti Briquets for the control of mosquito larvae.

Mitsui & Co’s US biopesticide subsidiary, Certis USA, reached a global licensing deal covering bactrocera mycoides isolate Bmj.

US agrochemical company American Vanguard acquired exclusive rights to two biopesticides patented by US firm Summerdale Inc.

DuPont and the US biopesticide company, AgraQuest, agreed an exclusive French development and distribution deal for AgraQuest’s biofungicide, Bacillus pumilus strain QST 2808.

Marrone Bio Innovations reached an exclusive research and development agreement with US horticulture products firm Scotts Miracle-Gro.

Syngenta acquired exclusive rights to US biopesticide company Pasteuria Bioscience’s Pasteuria usgae-based turf biofungicide, Econem. The licensing and distribution agreement also covers future turf products developed by Pasteuria.

Swiss chemical company Lonza signed an agreement with US biopesticide company Pasteuria Bioscience for a process transfer and manufacturing plan to produce Pasteuria spp bacterial spores in Lonza’s biochemical plant in Koulim, Czech Republic.

US agrochemical company Gowen agreed to form a joint venture, EcoFlora Agro, with the Colombian bioproducts company, EcoFlora. Through the joint venture, Gowen and its global marketing companies will be the exclusive partner in developing, registering and marketing EcoFlora’s plant extract-based biopesticides.

Mitsui & Co’s agrochemical distribution company, Certis Europe, and the Spanish biopesticide company, Futureco Bioscience, formed a strategic alliance in Spain and Portugal.

FMC and Marrone Bio Innovations agreed a development and distribution deal for the latter’s Regalia Maxx biofungicide in Latin America.

FMC entered into two exclusive agreements with the Danish bioscience company, Chr Hansen, covering the global development and supply of biopesticides for agricultural and ornamental markets.

Mitsui & Co’s US biopesticide subsidiary, Certis USA, appointed Canadian agrochemical firm Engage Agro, as distributor for its bioinsecticide, Cyd-X (Cydia pomonella granulosis virus), in Canada.

Bayer CropScience agreed to supply its seed treatment, Poncho Votivo (Bacillus firmus + clothianidin), to Monsanto for use in its Acceleron seed treatment range for soybeans in the US.

Syngenta entered into an exclusive global technology partnership with Pasteuria Bioscience to develop biofungicides based on the soil bacteria, Pasteuria spp.

Marrone Bio Innovations raised $25.4 million from a private round of financing. Among the new investors is Syngenta’s venture capital subsidiary, Syngenta Ventures.

AgraQuest raised $17.7 million in its latest round of financing.

Syngenta signed an agreement with Marrone Bio Innovations for exclusive distribution rights in Europe, Africa and the Middle East for Marrone’s biofungicide, Regalia.

South African biological farming products company Madumbi Bio Farms (Gillitts) acquired a majority stake in Swiss biopesticide company Andermatt Biocontrol’s South African subsidiary, Andermatt South Africa.

AgraQuest agreed distribution deals with Guatemalan distributor DuWest and Ecuadorian company Interoc for its biofungicide, Sonata (Bacillus pumilus strain QST 2808), in various Latin American countries.

Certis USA and Andermatt Biocontrol agreed to develop viral insecticides for the NAFTA region.

Bayer CropScience and AgraQuest extended their US home and garden products deal for Serenade (Bacillus subtilis strain QST713) to Europe. Bayer agreed to market the biofungicide in the US consumer market in 2009.
Biopesticide patent watch

Agrow Intelligence identified biopesticide and related patent applications published in 2011 and in the first quarter of 2012.

Review of patents – 2011

Our patent watch has revealed 51 patent applications in total for 2011, of which nine related to mixed chemical and biological compositions and the remaining 42 concerned biological strains. Particular activity was noticed around a BASF chemical/biological fungicidal patent on a specific strain of *Bacillus subtilis* and a chemical compound pertaining to either the azole or strobilurin family. BASF was also the company with the most published patents in 2011. Bayer CropScience and the Ohio State University Research Foundation both followed with three patents each.

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<td>Method and agent for controlling plant disease using bacteria of genus <em>Bacillus</em></td>
<td>Itsuki</td>
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<td>US20110262416A1</td>
<td><em>Bacillus subtilis</em> strain having antagonistic activity for controlling plant diseases</td>
<td>Korea Research Institute of Chemical Technology</td>
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<tr>
<td>US20110236361A1</td>
<td>Effective control of viral plant disease with strains of <em>Pseudomonas oleovorans</em></td>
<td>Lee; Yong Jin</td>
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<td>US20110301030A1</td>
<td><em>Saccharomyces cerevisiae</em> strains with phytosanitary capabilities</td>
<td>Lesaffre</td>
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<td>US20110009260A1</td>
<td>Methods and Compositions comprising <em>Trichoderma atroviride</em> for the biological control of soil-borne plant pathogens and promoting plant growth</td>
<td>Lincoln University</td>
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<tr>
<td>US20110183846A1</td>
<td><em>Curvularia</em> strains and their use to confer stress tolerance and/or growth enhancement in plants</td>
<td>Montana State University</td>
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<td>US20110160057A1</td>
<td><em>Morinda citrifolia</em> based antimicrobial formulations</td>
<td>Morinda/Tahitian Noni International</td>
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<tr>
<td>US20110274673A1</td>
<td><em>Bacillus amyloliquefaciens</em> strain</td>
<td>Novozymes Biologicals</td>
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<tr>
<td>US20110028321A1</td>
<td>Method and bacterium for promoting the growth of <em>Racomitrium canescens</em> and seed plants</td>
<td>Okayama University</td>
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</table>
## Biopesticides

**Review of patents – Q1 2012**

Our patent search has revealed six biopesticide patent applications for the first quarter of 2012.

<table>
<thead>
<tr>
<th>Publication number</th>
<th>Title</th>
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<tr>
<td>US20110200572A1</td>
<td>Compositions for stabilising <em>Bacillus</em> spp spores and methods of use thereof</td>
<td>Osprey Biotechnics</td>
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<td>US20110059048A1</td>
<td>The fungus <em>Fusarium solani</em> strain ‘FS-K’ and its use in the biological control of plant pathogens and in the enhancements of plant growth and productivity</td>
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<tr>
<td>EP2389434A2</td>
<td>Novel <em>Pasteuria</em> spp strain</td>
<td>Pasteuria Bioscience</td>
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<td>US20110280839A1</td>
<td>Entomopathogenic fungi and uses thereof</td>
<td>PWC Tower</td>
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<td>US20110256102A1</td>
<td>Plant disease controlling composition, plant disease controlling method, and novel microorganism</td>
<td>Sumitomo Chemical</td>
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<td>US20110182862A1</td>
<td>Endophytic fungus and uses therefore</td>
<td>Synthetic Genomics</td>
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<tr>
<td>US20110027246A1</td>
<td>Novel <em>Bacillus thuringiensis</em> strain for inhibiting insect pests</td>
<td>Taiwan Council of Agriculture</td>
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<tr>
<td>US20110293570A1</td>
<td>Isolation of novel bacteria contributing to soil-borne disease suppression</td>
<td>The Ohio State University Research Foundation</td>
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<tr>
<td>US20110027233A1</td>
<td>Prothioconazole-tolerant <em>Cryptococcus flavescens</em> strains for biological control of <em>Fusarium</em> head blight</td>
<td>The Ohio State University Research Foundation</td>
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<td>US20110020289A1</td>
<td>Novel mycovirus, attenuated strain of phytopathogenic fungus, plant disease controlling agent, method of producing mycovirus, method of attenuating phytopathogenic fungus and method of controlling plant disease</td>
<td>Tokyo University of Agriculture and Technology</td>
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<tr>
<td>US20110020286A1</td>
<td><em>Trichoderma atroviride</em> SC1 for biocontrol of fungal diseases in plants</td>
<td>Trentino Siliuppo/ Fondazione Edmund Mach</td>
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<tr>
<td>US20110038839A1</td>
<td>Composition of entomopathogenic fungus and method of production and application for insect control</td>
<td>United States Agriculture</td>
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<tr>
<td>US20110182871A1</td>
<td>Novel micro-organism and plant disease control agent using the micro-organism</td>
<td>University of Yamanashi</td>
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<tr>
<td>US20110274659A1</td>
<td>Biological control agent for plants</td>
<td>Unknown</td>
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<td>US20110243906A1</td>
<td>Strain of highly mosquitocidal <em>Bacillus</em> spp</td>
<td>Unknown</td>
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<tr>
<td>US20110229543A1</td>
<td>Formulation and delivery of <em>Bacillus thuringiensis</em> subspecies <em>israelensis</em> and <em>Bacillus sphaericus</em> in combination for broad-spectrum activity and management of resistance to biological mosquito larvicides</td>
<td>Valent BioSciences</td>
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<tr>
<td>US20110064710A1</td>
<td>Novel <em>Bacillus thuringiensis</em> isolate</td>
<td>Valent BioSciences</td>
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www.agrow.com XXI
Social media chatter on biopesticides

When we initiated a discussion on biopesticides in Agrow’s LinkedIn group, comprising over 4,000 members, the result was an animated expression of views. We present some of the comments here.

To view the entire discussion, please log in at http://lnkd.in/i9y55K.

“Niche or mainstream?” To be successful, biopesticides - in particular microbial ones - need to be integrated in wider crop management systems. This makes it more complicated for the grower who needs more training and support that distributors are not inclined to provide. This argument goes rather for niche. On the other side, we see that major companies tend to complement their product range with such products. They have sensed the necessity to step over the ‘chemical only’ paradigm and see the advantages of marketing wholesome crop solutions, including seeds. This may be more successful for large, technically oriented growers (co-operatives or integrated companies) who are open to such innovation. This argument goes for mainstream.”

Michel de Rougemont, owner of Swiss consultancy, Enterprise Consulting

“Most biocontrol products were developed by an individual and brought to market by that person. We do not see $100 million spent to bring such products to market. Thus if you consider biological control only on the amount of manufactured value, it seems it is not growing. However, this is misleading. Almost all greenhouses in the modern world are now completely under biological control for insect pests as bumble bee pollinators are very sensitive to pesticides. Many growers use biological control products they produce themselves. In Brazil and Costa Rica, I saw growers treat crops with Trichoderma they grew on heated rice and applied as a foliar pest control”

George Lazarovits, George, director of research at A&L Biologicals, Canada

“Biopesticides can go mainstream only if they perform robustly and consistently OR if regulators regulate out most chemical pesticides from the market. I cannot see either situations happening in my lifetime. In the quest to produce enough food to feed the ever growing population, whether you like it or not, we need to continue using the more robust and consistent chemical solutions and products. Some MNCs have started to dabble in biopesticides, but I am certain that they know where exactly the technology and market is and also where the technological and marketing constraints are with biopesticides. Having said that, there have been significant improvements made in certain biocicals during the past 20 years. Other improvements will continue no doubt.”

C S Liew, board member and shareholder at Sotus International, Singapore
“Biopesticides should be sub-classified according to certain factors. If they want to compete with mainstream chemicals, they need to perform consistently according to regulatory specifications. Virus products in citrus and apple production against codling moth and false codling moth have proven to compete with and also out-compete mainstream chemicals. As a whole, the bio-insect control market has improved with leaps and bounds in the past five years and can compete with chemicals. I still have my doubts about fungicides but even in that market the technology is improving fast.”

Johannes van Dyk, area manager north at Becker Underwood, South Africa

“Biopesticides have a great potential for use against trans-boundary pests such as the desert locust. Field trials conducted under FAO auspices have shown efficacy of Metarhizium spp against several locust species and earned endorsement by FAO and key donors. Hurdles to be overcome include cost, patent constraints, and costs of registration. More needs to be done to adapt existing formulations for use against annual grasshopper pests, thus increasing familiarity and confidence of national plant protection authorities.”

Carl Castleton, SPS consultant at Securefoods, Brazil

“Microbiological pesticides can compete with the chemical products if they can be produced at a reasonable cost. The largest cost is in keeping the biologicals alive so they are able to deliver the viable effect on the pest we are seeking to control.”

Peter Hallberg, account and sales representative at Perham, US

“The regulatory question is critical. Traditionally, there has been a sharp divide in the regulatory treatment of fertilisers on one hand and pesticides on the other. As new products have emerged, regulators have tried to attach them to one of these frameworks rather than thinking through whether there would be a more appropriate approach. This has led to some particularly strange logic in the area of biocontrol, where products with totally different natures are expected to be submitted to a battery of expensive data tests that were initially designed for synthetic chemicals. Until there are proportionate data requirements, biopesticides are likely to remain a niche.”

Kristen Sukalac, doctoral student of business administration at Université de Paris Dauphine, France

“Biocontrol agents or products will need to be regulated no less stringently than conventional chemical agents. ‘Naturally occurring’ does not equate to ‘naturally safe,’ especially if and when produced and used on an unnaturally large scale. You can see how, even to this day, many people and governments still resist GMOs. We need to learn from that. We need to ‘sell’ to the public and develop the needed new regulatory framework at the same time.”

C S Liew

“I agree that natural does not mean good. But part of a risk assessment can be to evaluate the additional applications against background levels. If the application levels are similar or lower, then it is unlikely that the applications create a novel risk. Additionally, the ‘natural’ products might have risks that the chemical products don’t. I am definitely not saying that biocontrol products shouldn’t be regulated. But they need appropriate regulation, not copy/paste regulation from a different category of products.”

Kristen Sukalac

“Apart from the regulatory framework, there are multiple challenges of biologicals, one of them is results. As opposed to chemicals, biologicals take a much longer time to act and most farmers, apart from well educated farmers and organic farmers, want to see immediate results. Secondly, most biologicals have a short shelf-life of one year or so. So by the time it reaches the shelves, it is more than 2-3 months old if you need to ship them. Thirdly, it involves a lot of concept selling and distributors in many countries do not have that concept and they would rather sell fast-moving products than talk and sell the same.”

Saratendra Ng, deputy manager of international business at Excel Crop Care, India

- compiled by Leila Nabih
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