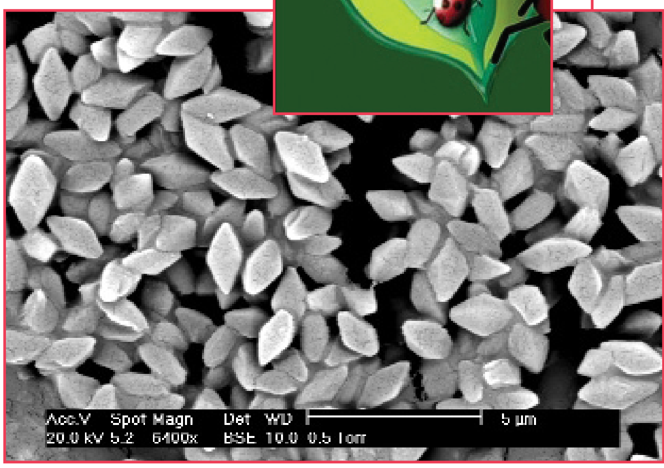
Microbials: The need for a pragmatic approach

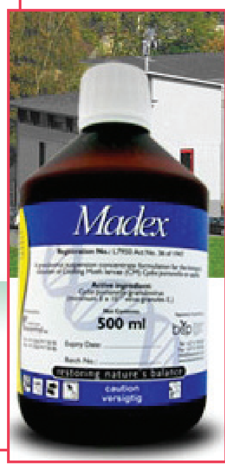
While there is an increasing support for more biological solutions as alternatives to chemical pesticides in both organic farming and IPM systems, the development and commercial success of biologicals is made more difficult because of the size of the companies involved and the fact it is a young, relatively undeveloped market. Among biologicals, microbials (microorganisms), which mainly include beneficial fungi, bacteria, viruses, as well as beneficial nematodes and yeasts, represent the market where probably the biggest number of companies are active. Although the results from small-scale assays done during the past ten years have shown promising results, relatively few of the tested microorganisms have shown consistent effects under field conditions and have made it to the market. Why has this happened? Is there a way to improve such disappointing situation? Is there a future for biocontrol products based on microorganisms? New Ag International went to investigate all ins and outs of this market that represents about one third of the biocontrol market worldwide.

One of the first commercial uses of microbials occurred in 1958. It was Bt (Bacillus Thurigensis) used in the USA. During the 1960s, several trial formulations were developed and in 1972 Abbott Laboratories introduced DiPel, the world's leading biological insecticide, based on Bt kurstaki strain. The introduction of synthetic pyrethroids slowed the development of Bt somewhat but insects began developing resistance and in the 1980s, many growers returned to Bt! Today, Bt continues to be the most widely used biopesticide in the world. In the meantime however, a number of other microbial products have appeared, with contrasted commercial successes. In 2005, only 26 microbial products for biological disease control with proven effects were marketed by commercial companies in the U.S. market. In Europe, 14 microbial products for disease control are registered and listed on Annex 1 of the Directive 91/414 EEC. This is already a tremendous progress compared to 10 years ago when only one microbial substance Paecilomyces fumosoroseus (fungal bioinsecticide) was listed in Annex I in 2001. The biocontrol industry dealing with microbials developed to a professional business especially during the last decade. Probably not enough and not quickly enough! Where is it going from there?

SIX DIFFERENT PRODUCT CATEGORIES

Microbial pesticides draw their name from naturally occurring microscopic organisms, or microbes, that are used to control pests. In





to the market and to its constraints

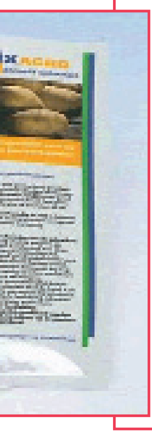
some cases the pesticidal activity may derive from metabolites produced by these organisms. In a reference book written by world leader in this market Valent biosciences corporation (and published by MeisterMedia in 2006: guide to understanding and evaluating Biorational Products), authors do a very good job in describing the six categories of microbials.

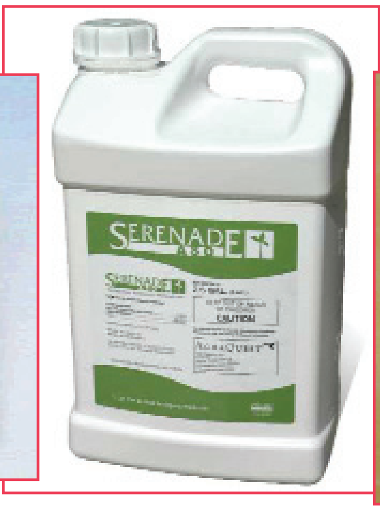
First the Bacteria: This includes a variety of unicellular organisms with insecticidal and fungicidal properties. The ability to manufacture these organisms through industrial fermentation, as well as an ability to store them for extended periods, makes them ideal for use as biopesticides. This category is largely dominated by the Bacillus Thurigensis, better known as Bt. Bts are bacteria that produce crystalline endotoxins, which disrupt digestive systems of many insect larvae. Bacteria account for at least 75% of all microbial product sales.

Then the Fungi: These fungi may display nematicidal, miticidal, insecticidal, fungicidal and/or herbicidal properties. They can also be manufactured through fermentation. In some countries, some fungi are also used as soil improvers and/or fertilizer substances: this is the case of Rhizobium Japonicum used for inoculating soyabean crop to create symbiotic nitrogen fixation. This is also the case for Glomus sp used as additive to soil and substrates to establish endomycorrhizal symbiosis that in turns facilitates the root absorption of water and nutrients. Beneficial fungi account for about 15% of the market.

Viruses are the third most important subcategory. They are described as intracellular parasites. They are highly specific non-living organisms that consist of DNA or RNA material protected by a protein coat. When a virus comes in contact with a compatible host cell, the DNA or RNA material is injected into the cell's nucleus. Bioinsecticides derived from viruses include polyhedrosis viruses and granulosis viruses, and can be used to infect plant-harming insects such as armyworms and bollworms. Viruses account for about 12% of the market for microbial products.

Three other categories of products belong to the microbials: nematodes, used primarily for the control of insect larvae; yeasts, which include a small group of products to control postharvest pathogens that promote fruit decay. These products may also act by stimulating natural defense mechanisms in crops; And finally Protozoa, which are single-celled organisms that can act as cellular parasites.





NEW FINDINGS ON BT INSECTICIDE

Researchers at the University of Oxford and Royal Holloway University of London have recently discovered that Bt works best if applied to young plants and is enhanced by the presence of the insect pests. The research was published in May this year in the open-access journal PLoS Pathogens.

Senior researcher Dr Mike Bonsall at the University of Oxford said: "Bt has been used commercially for about 40 years and is readily available to control pest moths and the like, but until now we've known very little about the natural abundance of the bacteria in the environment and what happens when we apply extra bacteria as a means of pest control. It's really important to understand what is happening so that we can, for example, know what factors might have an impact on the insects becoming resistant to Bt."

Bt is found naturally in soils and on plants and exists as many different varieties that each have a preference for infecting different organisms. Bt strains that are specific to certain insects rely on being able to infect those insects in order to reproduce. The researchers

studied a strain called ST8, which infects the Diamondback Moth - a pest that attacks cabbages, broccoli and related crops - and they found that the population of bacteria (either existing or applied) establishes itself more readily when the insects are present.
Lead researcher Dr Ben Raymond at Royal Holloway University of London said: "We found that our strain, ST8, is the most common in the environment already and it also seems to be best at getting onto the leaves where it can infect the moths. We think that the ST8 that exists naturally in the farm environment might well be colonising the plant as growing seedlings so it gets the earliest possible opportunity to infect the moths, which of course it needs to do to survive.
"This makes sense given that we also found that when there are extra insects in the environment the bacteria actually do much better and can be found in larger numbers. It also shows why spraying the plants, especially young ones, rather than the soil is the best way of using Bt to control insect pests."
The research team are also looking at factors that affect the chances of insects becoming resistant to Bt. In particular they are looking at the way the toxin that kills the insect and an antibiotic that Bt produces to get rid of competing strains of bacteria in the insect's gut both impact the evolution of resistance in the insect.

HIGH PRODUCTION COSTS AND A STILL QUESTIONABLE BUSINESS PROFITABILITY

A remarkable study was published earlier in May this year by a team of researchers working for the ENDURE programme in Europe. They identify four areas where the constraints to the development of biocontrol are apparent - size of the market, cost of production, costs of registration and business profitability - and use the real case of a microbial biocontrol agent (MBCA) to illustrate these points.
ENDURE's researchers say that contrary to the synthesis of chemicals, producing MBCAs requires a complicated and very expensive four-phase production process starting with fermentation and running through extraction, purification, and formulation and packaging. And throughout this process expensive measures to ensure there is no contamination have to be taken. As a consequence the MBCA in question is more than twice as expensive to produce compared to an equivalent chemical pesticide (see Table 1 below).
The good point is that the estimated cost for registering a microbial biocontrol agent is currently lower than that for a chemical pesticide, though the size of the investment is still very high in comparison with the market potential. ENDURE's researchers have carried out an evaluation which shows that bringing a MBCA to market is around four times less effective than its chemical equivalent (see Tables 2 and 3 below).

Table 1: Types of Microbials

Type	Target
Bacteria	Fly and beetle larvae, caterpillars, fungal and bacterial diseases, Soilborne pathogens
Fungi	Nematodes, whiteflies, aphids, thrips, beetles, locusts, grasshoppers, Fungal diseases, soilborne pathogens, weeds.
Nematodes	Beetle adults and larvae, grubs, caterpillars, flies, gnats, slugs.
Protozoa	Grasshoppers, locusts, crickets.
Viruses	Caterpillars.
Yeast	Leaf spot, fruit drop, greasy spot

Source: Valent BioSciences

AN INTERVIEW WITH

Bruce L. Kirkpatrick, Senior Director, Global Marketing and Business Management, Valent BioSciences USA


Courtesy of NAI

"At Valent BioSciences Corporation, we are very optimistic about the microbials market. The global market is strong – with 2010 expected to be one of our highest sales years ever. In addition, we are seeing future growth opportunities, particularly in Europe, the United States and Latin America.
Historically, microbials such at Bacillus thuringiensis-based insecticides have been used to improve cost and effectiveness of insect management programs. Strong demand for Bts used in a program approach with traditional chemicals is driving sales growth. High-quality microbials that are properly applied offer reliable control with an alternative mode of action for improved effectiveness and management of insecticide resistance. Microbials are also valued because they are soft on beneficials and won't flare secondary pests. New chemical insecticides have been introduced in recent years, and microbials will continue to be used with these new products in a program approach.
One area receiving increasing attention is residue management. As has been widely reported, several supermarket retailers are going beyond government residue requirements for chemical pesticides. Growers are responding with increasing use of microbials. Of course, product performance remains absolutely critical, and that means quality manufacturing and formulation are vital. We at Valent BioSciences are proud of our recent ISO 9001:2008 registration. We are also proud that growers continue to look to us and our leading brands as they address chemical residue concerns and other management issues. As one of our customers recently told us, "I use your microbial products because I know they are solving my problems without creating new ones."

A MORE THAN 600 MILLION EUROS MARKET STILL DOMINATED BY Bt

A very comprehensive survey recently published by CPL Scientific found that the biocontrol market in Europe was worth an estimated €204m in 2008 (vs abt 100 million in 2003), the majority used in protected crops, followed by grapevine and food production. Almost 40% of the market was made up of sales of beneficial insects, compared to 25% for micro-organisms and 21% for semiochemicals. In most cases MBCAs are being developed for small, if not niche, markets. Worldwide MBCA sales were €620 million in 2008 (€122m in Europe, i.e. 19,6% of total, which represents a substantial increase compared to 2003 when the share of Europe was only 13%) including products with insecticidal or fungicidal effects, compared to worldwide chemical insecticide and fungicide sales of €21 billion. MBCAs, with the exception of Bt products which can be used in larger crops such as grapes and cereals, are mainly used for speciality and covered crops, sectors which are growing, if at all, at only a slow rate. The organic market does look positive though, with some countries seeking to develop this sector (for example, France has set a target of turning 20% of its agricultural production area to organic methods by 2030).

The market for microbial- and nematode-based pesticides in Latin America, Africa and the Middle East is estimated to be approximately $82.7 million per annum at user-level in 2007/8. This is comprised of $74.6 million for Latin America and $8.1 million for Africa and the Middle East.

The proportion of the microbial pesticide market taken by Bt-based products in Latin America is approximately 40%. The only country that produces Bt products in the region is Cuba (and in Argentina where they produce under contract); other products are imported from the US, China, India and Spain. Bacillus thuringiensis products are generally viewed by users and extension workers to be too expensive for the market. Bt-based products are dominant in Africa and the Middle East; taking 77% 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 undeveloped in this region.

Table 2: Compared structure of the production costs for a microbial biocontrol agent (MBCA) and a chemical insecticide

	Typical Insecticide	MBCA	Comments
Sales value	100	100	
Type of production cost			
Raw materials	8*	29	40% lost material for MBCA by solid fermentation process
Packaging	1	2	
Energy and miscellaneous	1	2	
Manpower	5	9	
Consumables	2	3	
Amortisation	4	11	
TOTAL	**21**	**56**	

Source: IBMA

AN INTERVIEW WITH

Antonio Cutri, CEO of Intrachem Bio Italia

Courtesy of NAI

The company Intrachem Bio Italia S.p.A. was founded in 1981 by Giacomo Barabino in Milan (Italy) and with headquarters in Grassobbio (BG, Italy), it has been focusing on the development and marketing of novel tools for efficient plant nutrition and protection. Under the guidance of Antonio Cutri, CEO of the company since the early days, the company invested in novel techniques, acquired exclusive sales and distribution rights for a large range of products, and the intellectual property of several microbial control agents. As a result, Intrachem Bio Italia S.p.A. has become the company with the largest catalogue of biopesticides in Italy and maybe also in Europe, and with a portfolio of products for the international market.

"The interest for our microbials formulated products Lepinox® Plus and Rapax, AQ10® WG and Naturalis®, which used to be considered mere plant protection tools for a niche market, increased with the growing demand for organic agriculture. Nowadays they have become essential tools for IPM (Integrated Pest Management). In fact, the European Union compels Member States to promote low pesticide-input pest management and to implement IPM. Our policy consists in developing and placing on the market only products that have been officially authorized as plant protection products and that are of low/no risk for human health and the environment. The company refuses to take the easy shortcut of selling its products as fertilizers and/or plant strengtheners without any guarantee, as some other companies do.

With the registration of the trademark NO RESIDUE®, we aimed at promoting IPM strategies by creating a network for information exchange among all stakeholders in agricultural production (growers, farm advisers, retailers, large-scale organized distribution channels, extension services, etc.). Since the trademark NO RESIDUE identifies the company's biopesticides with no MRLs and no detectable residues, it is obvious that these plant protection products may become of sound importance for sustainable pest management.

Therefore, we are definitely expecting a future not only full of commitment, but also of satisfaction".

There is substantial room for growth in the market for microbial biopesticides in Latin America, Africa and the Middle East with currently available products. Africa, in particular, is almost totally undeveloped and with increasing trade in horticultural products into the EU and NAFTA regions, the market has the potential to substantially develop by 2015.

The North American microbial biopesticides market is estimated by the survey to be worth $127m at user-level in 2007; an increase of 16.3% since 2004. The US is the biggest user of microbials in the region with a market estimated to be worth $101m (79.7% of the total), followed by Mexico and then Canada.

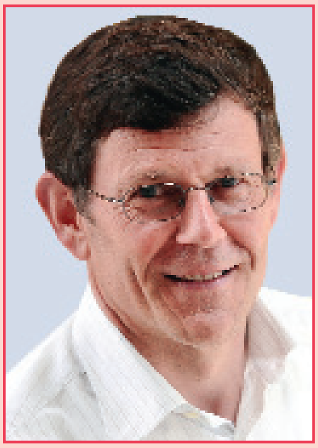
The proportion of the market taken by Bacillus thuringiensis (Bt)-based products has declined from an estimated 90% in the 1990s to 56.8% in 2007. This has been due partly to a steady down-turn in Bt use for caterpillar control and partly to increased sales of new products. The caterpillar Bt market in the US has declined in the face of competition from recently introduced chemicals. The Mexican Bt market has also declined, most notably in cotton and corn, in the face of competition from agrochemicals, GM crops and other biological controls. The largest Bt market in Canada is in forestry, particularly for the control of spruce budworm, Choristoneura fumiferana. This market fluctuates enormously with variation in insect numbers and, although historically low, has increased since 2004.The fastest growing sectors in the US have been the fungicidal product based on Bacillus pumilus and codling moth granulosis virus. According to the survey, prospects for growth in sales in the US overall remain good although there is no evidence for the meteoric rise predicted earlier in the decade. The market in Mexico for Bacillus subtilis and B pumilus has increased and there is a steadily growing sector in locally-produced, fungal-based products. Sales are large and product is cheap.

THE FUTURE: AN URGENT NEED FOR A MORE SYSTEMATIC APPROACH WHEN LAUNCHING NEW PRODUCTS

When evaluating the last two decades of biological control of plant diseases, a tremendous number of results have been obtained both in small-scale assays and in large-scale field experiments. Although the results from small-scale assays have shown promising results, relatively few of the tested microorganisms have shown consistent effects under field conditions and have made it to the market. Among the antagonistic bacteria, strains of Agrobacterium, Pseudomonas, Streptomyces and in particular Bacillus species constitute the active ingredients of several commercial products. Among the antagonistic fungi, a considerable portion of the available products harbour Trichoderma species as the active ingredient. From a statistical point of view, biological control represents only approximately 2% of the agricultural chemical sales, whereas fungicides represent about 15%. Based on these numbers one may argue that commercial application of beneficial microorganisms for biological control of plant diseases is, for most part, wishful thinking and has limited potential. However, given the use of biological control to manage diseases for which no other control strategies are available, one may argue that there are sufficient challenges to further develop biological control. The main question is how

AN INTERVIEW WITH

Martin Andermatt, President of Andermatt Biocontrol, Switzerland



Courtesy of NAI

The company Andermatt Biocontrol was founded by Dr. Martin Andermatt and Dr. Isabel Andermatt in 1988. Since then it has developed to become the leading company in Switzerland for biological based plant protection. The key expertise of Andermatt Biocontrol AG is the production of baculoviruses and entomopathogenic nematodes, as well as beneficial insects for greenhouses and stored products.

"The market of microbial biopesticides in Europe is still growing. This is especially remarkable, as this growth is based on old and well known microbials. There would be more products based on other active ingredients ready for the market but they are all blocked due to the embarrassing inefficient registration process in Europe.

We are focusing on Baculoviruses. We support our worldwide distributors in the marketing of our own TM products, but we are also selling raw material. Our codling moth granulovirus product MADEX is the leading CpGV product in Europe. It is available in almost all EU member states.

I think that there will be further growth for the microbial biopesticides in Europe. But this growth will be slow and will mostly depend on the registration hurdles. The optimistic stakeholders of Andermatt Biocontrol still hope, that the registration process will be handled more reasonably in the future. Therefore, since the first business year in 1988, we are reinvesting all profit in R&D to improve the existing production but also to develop new products. The production capacity for our virus products has consistently increased and will reach end of this year a capacity of 1 million ha-units per year. Currently six baculovirus-products are produced and sold by Andermatt Biocontrol against Cydia pomonella, Adoxophyes orana, Cryptophlebia leucotreta, Helicoverpa armigera, Spodoptera exigua and Spodoptera littoralis. Half a dozen more products are under development.

Table 3: Compared potential costs of registration for a microbial biocontrol agent (MBCA) and a chemical pesticide

Area	Study type	Cost for chemical (€)	Cost for MBCA (€)
Toxicity of the active substance	Acute studies (6 tests) Sub-acute (rat study) Mutagenicity Toxicity on cultured cells	140,000 140,000 40,000 10,000	140,000 120,000 May be waived Not required
Toxicity of the formulation	Acute studies Toxicity on cultured cells	140,000 10,000	140,000 Not required
Environmental fate	Soil, water, air	200,000	70,000
Biology	Mode of action etc	150,000	50,000*
Ecotoxicology of active substance	Birds, fish, bees, algae, daphnia, earthworms Beneficials	60,000 20,000	40,000 May be waived
Ecotoxicology of formulation	Birds, fish, bees, algae, daphnia, earthworms Beneficials	60,000 20,000	40,000 -
Residues	8 trials/crop Development of analytical methods	80,000 100,000	May be waived Variable**
Formulation	Physical properties, shelf life etc	200,000	220,000
Efficacy	8 field trials	40,000	40,000
TOTAL		**1,410,000**	**860,000**

Source: IBMA

to do it on a commercially viable basis! The potential market for MBCAs is highly fragmented, taking in a long list of crops such as carrot and onion which are generally bundled together as 'minor crops' of little interest to the large chemical companies. Because of the specificity of their products, MBCA manufacturers have to invest in these crops knowing that economies of scale can never be reached. Hence the interest of having a series of procedures in place that allow the screening potential candidates with the highest chances of success without spending outrageous money! And this is where the remarkable work of ENDURE people (a study funded by the European Commission and the Dutch Ministry of Agriculture, Nature and Food quality as part of the ENDURE project (EU FR6 project 031499), recently presented at an IOBC workshop in Graz, is of great use. "Stepwise screening of microorganisms for commercial use in biological control of plant pathogens" is a 35 page paper coordinated by Dr Jurgen Kohl of Plant Research International in Wageningen, Netherlands, which every company engaged or about to engage in the business of microorganisms should have on the desk of every employee!

Table 4: Compared estimated market potential for a microbial biocontrol agent (MBCA) and for a chemical pesticide

Year	Estimated sales value (€m)	
	Chemical pesticide	**MBCA**
1	0.1	0.05
2	1.2	0.15
3	6.0	0.90
4	15.0	1.50
5	35.0	3.50
Total early sales	57.3	6.10
Plateau sales	120.0	15.00
Registration costs	1.410	0.860
Ratio registration/early sales	2.4%	14.0%
Ratio registration/plateau sales	1.1%	5.7%

Source: IBMA

THE KEY TO POTENTIAL SUCCESS: PROPERLY SCREENING MICROORGANISMS FOR COMMERCIAL USE

Biological control products based on microbials are considered as plant protection products in most countries. Consequently, governmental regulations for the registration and use are applied as for synthetic chemical plant protection products. Detailed toxicological studies have to be undertaken to guarantee that there are no risks for producers, users, and consumers when products are used. Furthermore, studies are needed to ensure that no environmental risks will occur after use. Besides the toxicological profile of an antagonist, industries will also consider technologies for production and formulation and their costs, genetic stability of the antagonist, market size for the biocontrol product and the possibilities of patent protection for the application; "It is a significant step from the isolation of a microorganism showing antagonistic property to the commercial marketing of an economically viable biological control product", says Bernard Blum from IBMA. Numerous isolates of microorganisms can be found showing antagonism in model systems but amongst those only very

Table 5: Compared margin structure estimates for the production and sales of a microbial biocontrol agent (MBCA) and a chemical pesticide

%*	Chemical pesticide	MBCA
Sales value at plateau level	100	100
Cost of production	13	56
Gross margin	87	44
Cost of sales	21	15
Cost of research	8	12
Cost of administration	4	3
Earnings before investments, taxes and amortisation (EBITA)	54	14
Profit after taxes, provisions and amortisation	18	2

Source: IBMA

AN INTERVIEW WITH

Pierre Grammare, Sylvan Bio European Manager


Courtesy of NAI

SylvanBio is a world leader in the production of fungal cells using solid-substrate fermentation technology. The company draws on its expertise and extensive experience in culture isolation and maintenance, research and development, quality control, commercial propagation and customized formulation to produce a variety of products for use in agricultural as well as health care applications. SylvanBio's capabilities include the production of both mycelial based products and the concentration of fungal spores as well as the concentration of secondary metabolites derived from these.

"Biological Control Agents and plant stimulators are one of our new areas of development. In order for this industry to grow it must consolidate and with this in mind, we are looking at establishing partnerships with various complementary businesses with a view to optimizing our worldwide structure and existing production capacity. This will allow the manufacture of a range of high quality products at controlled costs.

Customers demand efficient, reliable and sustainable products and to enable us to meet their needs SylvanBio acquired, in 2007, a dedicated facility in France where we have developed an R&D department and quality control laboratory to further satisfy the needs of the marketplace. With production facilities and staff now in both North America and Europe, we are well-positioned to address a wide spectrum of developmental and regulatory issues across a diverse geographical base. We help our partners develop innovative delivery systems and participate in field trials to ensure product performance

Finally, a major hurdle to our industry development is the registration of new products and the associated costs. However, it is pleasing to note that 5 new micro-organisms out of the 14 listed at European level were added in 2009 and the new European regulation coming into force in June 2011 should further speed up the launching of new bioproducts".

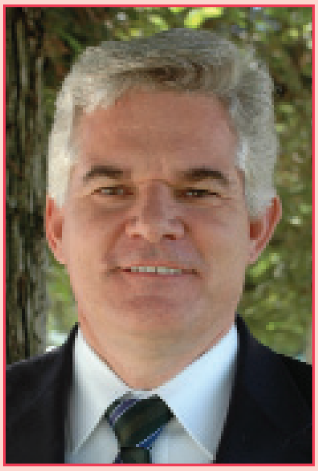
few may fulfill requirements for commercial use. Consequently, knowing and considering such requirements when a screening program is initiated will help to select candidates which fit better into commercial use. An exceptional and rare example for such a screening which included commercial aspects in an early stage is the selection of bacterial antagonists against Gibberella pulicaris causing dry rot of stored potatoes. This was in 1997! However, reviewing the literature on biological control leads to the conclusion that the majority of screening programs primarily focus on the efficacy, tested in vitro or in planta, as the main criterion. And this is of course not the way to go. For example, mass production may not be cost effective or a targeted market too small to allow an implementation of a new biological control product.

Kohl and his colleagues propose a systematic, stepwise antagonist screening comprising 9 steps (see

Table 6: The main suppliers of Microbials, members of IBMA

Abitep GmbH, Germany	IAB, Spain
AGR Sarl, France	Intrachem Production S.r.l., Italy
Agraquest SA, USA	Isagro spa, Italy
Agrauxine, France	Ithec SAS, France
Agrifutur, Italy	JSC International Limited, UK
Agro-Levures et Dérivés SAS, France	K+S France SAS, France
Agrometrix Blum GmbH, Switzerland	Koppert Biological Systems, Netherlands
Alfarin Quimica SA, Spain	Kwizda Agro GmbH, Austria
Amaro Tavares & Filho, Lda, Portugal	Landi REBA AG , Switzerland
Andermatt Biocontrol AG, Switzerland	Lantmannen BioAgri AB, Sweden
Avantagro SL, Spain	Marrone Bio Innovations, USA
Bayer CropScience AG, Germany	Mase Laboratories AB, Sweden
Becker Underwood Limited, USA	Massó Comercial Química SA, Spain
Biocare, Germany	Meristem Quimicas SL, Spain
Biocolor SL, Spain	MIP System Agro SL, Spain
Biocontrol Technologies SL, Spain	Motuma Bvba
BIOFA AG, Germany	Natural Plant Protection (NPP), Japan
Biomor Limited, Israel	NewBiotechnic SA (NBT), Spain
Biopacific Desarrollos Biotecnologicos Ltd, Chile	Nixe Laboratoires
Biopreparáty sro, Czech Republic	Novozymes Biologicals SA, Denmark
Bio-Protect GmbH, Germany	Nufarm SAS, France
Biosani Lda, Portugal	Pheromones International Trading Company, Spain
Biotech International Ltd, India	Probis GmbH, Germany
Biotop, France	Prophyta GmbH, Germany
Biotus Oy, FinlanD	Rationale Biopesticide Strategists, UK
Biovitis SA	Rivale SARL, France
Bordeaux Montesquieu Association, France	RJC Limited, UK
Boyut Dis Ticaret Ltd , Turkey	Seipasa SL, Spain
Certis USA LLC, USA	Stockbridge Technology Centre Ltd, UK
De Ceuster Meststoffen nv, Belgium	Sylvan-Bio Europe (Somycel) SA, France
De Sangosse SA, France	Tecnicas de Control Biologico SL, Spain
DKSH Switzerland Ltd, Switzerland	T. Stanes & Co. Ltd, India
E-Nema GmbH, Germany	T.S.G.E. Technology Sciences Europe Ltd, UK
Fargro Ltd, UK	Valent Biosciences Corporation, USA
Futureco BioScience SL., Spain	Verdera Oy, Finland
G.I.E. Lacroix, France	Xeda SRL, Italy
Green Universe Agriculture, Spain	
Gyah Bazr Alvant Corp (GBA Corp), Iran	

AN INTERVIEW WITH



Courtesy of NAI

Marcus Meadows-Smith, CEO of Agraquest, USA

"I believe that biopesticides are poised, as never before, for explosive growth. With the converging drivers of world population growth, retailers responding to consumer demand for pesticide-free food, and the increased regulation of pesticides and residues driven by concerns for human and environmental safety, the industry is seeking sustainable solutions for farming.

A new approach to food production that combines increased productivity with clean food and reduced environmental impact is rapidly developing. I describe this new approach as "low chem," combining consistent and highly effective new microbial biopesticides with the best synthetic pesticides to deliver season-long pest control and increased crop yields.

One good example of a highly effective microbial biopesticide is our SERENADE fungicide, whose high growth amongst conventional growers in the last 24 months is enabling these types of sustainable solutions. SERENADE is a proprietary biofungicide that has been developed globally in a wide range of crops and was granted its European Annex 1 listing in 2007. Originally developed as a foliar product, a new SERENADE formulation was launched in 2010 as a treatment for soil and seedling diseases as well as yield enhancement. In response to strong demand, we now have over 10 new microbial biospesticides in field trials from our rich pipeline of novel insecticides, nematicides and fungicides.

Our company, with one of the largest R&D teams committed exclusively to the commercialization of biopesticides, is committed to turning its low chem vision into market share. Most of the major agrochemical manufacturers are considering biopesticides either to fill gaps in their portfolio or for resistance management, while balancing grower needs for effective pest control with the regulatory pressures to reduce environmental impact."

Table 7: The 9-step procedure for screening new microbials for successful commercial launch

Step	Criteria	Costs per isolate (Low → High)
Step 1. Assessment of targeted crop, disease and markets	marketing, targeted disease	
Step 2. Origin and isolation of candidate antagonists	ecology, production, market	$$
Step 3. High throughput screening	production, safety, ecology	$
Step 4. Database mining	IP protection, safety, ecology, environmental risks, marketing	$
Step 5. Efficiency testsing in bio-assays	efficiency	$$$$$
Step 6. Preliminary assessment of mass production	production	$$$$$$$$$$
Step 7. Pilot formulation and registration costs	production, efficacy, ecology, safety, environmental risks	$$$$$$$$$$$$$$$$$$$$
Step 8. Up-scaling mass production and full field testing	production, efficacy	$$$
Step 9. Integration in cropping systems	efficiency, environmental risks	$$$

Percent selected isolates: 100 – 1

Note: Stepwise screening of microorganisms for commercial use in biological control of plant pathogens. For each screening step, specific categories of selection criteria are considered, screening costs per isolate are estimated ($) and the percentage of assessed isolates is given (■).
Source: Jurgen Kohl, project ENDURE/PRI/IBMA/INRA/CNR

table 7). Different categories of criteria all relevant for commercial development are discriminated such as marketing, microbial ecology, mass production, safety, protection of intellectual property rights (IPR), environmental risks, and biocontrol efficacy. Such criteria may be considered when new programs for biological control development are initiated by industries and scientific institutions in collaboration with funding organizations.

Within each step, criteria are evaluated which are tested in similar approaches at comparable costs per candidate, e.g. in high throughput screening experiments (Step 3) or data mining in various date bases (Step 4). In Step 1, the targeted crop, disease and market is studied so that specific screening criteria can be defined. Thereafter, origin and isolation techniques of candidates are considered (Step 2). Candidates are preliminary tested in high through put systems (Step 3) and, after determination of the candidates at species level, data available in data bases on the specific species are evaluated (Step 4). The antagonistic potential of suitable candidates selected during the earlier evaluations steps are tested in bioassays (Step 5) and the feasibility of mass production of such selected candidates is assessed (Step 6). For a limited number of candidates pilot formulations are developed and tested again in bioassays. Costs and opportunities for registration are preliminary estimated (Step 7). In Step 8 the production of a few candidates is scaled up and pilot formulations are subsequently tested under field conditions. The most promising formulation of the best candidate is selected and then tested in crops at different locations and seasons with full integration in existing crop protection strategies or those under development (Step 9).

A DIFFICULT COMPETITION WITH CHEMICAL PESTICIDES

Joining forces between a number of (too) small suppliers in the market (more than 100!) will probably be the only way to finance and properly put in place a pragmatic approach to innovation (consider commercial questions early!), a definite prerequisite to commercial success! The future will tell whether some products currently at the development stage in companies (e.g microdochium dimerum against botrytis on tomato at Agrauxine,) or in multi-partners projects (e.g. Trichoderma against cucumber rhizoctonia by FAPESP in Brazil, verticillium lecanii against aleurods on strawberries by Koppert and CIREF in France) or at Universities (use of Candida Oloephila as post harvest treatment of fruits in Gembloux-Belgium) will reach step 9 and harvest a commercial success! They will probably have a hard time: Comparing estimated production and other costs relative to the sales value at plateau level highlights large differences between chemical pesticides and microbial biocontrol agents. In fact, say ENDURE researchers (see Table 5), the gap between the two in terms of estimated profit is nearly 10-fold in favour of a chemical pesticide! Without governmental support and incentives to help develop this industry, it will be difficult to increase the share of microbials in the plant protection market! ■