Innovative and Sustainable Solutions for the Entire Biological Development Process

"Battelle Crop Protection Solutions offers complete turn-key solutions for the entire development and regulatory process of biologicals, including bioformulation development, modelling, GLP product safety testing and regulatory consultancy for biologicals".

- Dominik Reinhard

During a recent interview with AgroPages, Dominik Reinhard, MBA, European Head of Commercial Sales, Crop Protection Division at Battelle, highlighted the company's extensive expertise in assisting with bioformulation development and supporting clients in the registration process for biopesticides and biostimulants. With a strong reputation in both the U.S. and Europe, Battelle is renowned for its role as a reliable partner in formulating successful regulatory compliance strategies.
"We provide innovative full-scale registration and re-registration support, as well as expert advice in dossier compilation for conventional crop protection products and biologicals", said Dominik Reinhard in a recent interview with AgroPages.[1]

The interview dives into various aspects, including Battelle's capabilities in biologicals and bioformulation, challenges and solutions encountered during bioformulation development, the company's regulatory consultancy service and service strategy. Moreover, Dominik Reinhard provides valuable insights into the opportunities and challenges in the biological market.

Q1. Could you introduce Battelle's capabilities in biologicals and bioformulation? What is the business model?

Battelle is a global applied science and technology organization that provides innovative and sustainable scientific solutions to the agrochemical industry. Our scientific research, STEM, and philanthropic initiatives provide purpose, support climate resilience, and strive to end world hunger,

enabling our clients to develop innovative solutions to agriculture's most complex challenges. Our contract formulation development lab in Havant, UK offers unique solutions to the biological plant protection industry based on fee-for-service or innovative, alternative outsourcing models including licensing, co-development, or co-investment.

The agrochemical industry is a sector in transformation with a significant need in finding alternative solutions to conventional plant protection products including the rapidly evolving market of biologicals. Battelle knows that being on top of the latest trends and having the knowledge

[1] https://news.agropages.com/News/NewsDetail---43842.htm

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of how to apply new technologies and methods is critical to solving tough challenges. Battelle's breadth of services runs deep with decades of biological, bioscience, and agrochemical formulation, which allow us to provide solutions to the unique challenges of agricultural bioformulation. We base our innovative and sustainable scientific solutions on an integrated approach to research, development, and regulatory compliance.

Our dedicated team of multidisciplinary experts is comprised of analytical chemists, microbiologists, and formulation chemists, some having 25-40 years of experience with multinationals in formulation and bioformulation R&D. The formulation work is largely focused on amendment selection and screening, optimization, encapsulation techniques, content determination (e.g., analytical and microbiological), seed treatment and on-seed testing, storage stability testing, proprietary technology development, process development and scale-up, manufacturing support, and in-pack storage stability testing. Battelle's team has experience with various biological active ingredients (AIs) such as botanicals, semiochemicals, and microorganisms. We can develop multi-purpose formulations and types such as SC, WP, WDG, OD, EW, and CS for different applications such as foliar, soil, or seed. Work-related to molecular characterization and identification, genomics, proteomics, and metabolomics, as well as high-throughput microbial screening and phenotypic characterization, is developed in Battelle's lab in Columbus, Ohio in the U.S. In both labs, Battelle develops its internal R&D to gain knowledge to better support our clients as well as to generate proprietary technology that can be offered commercially.

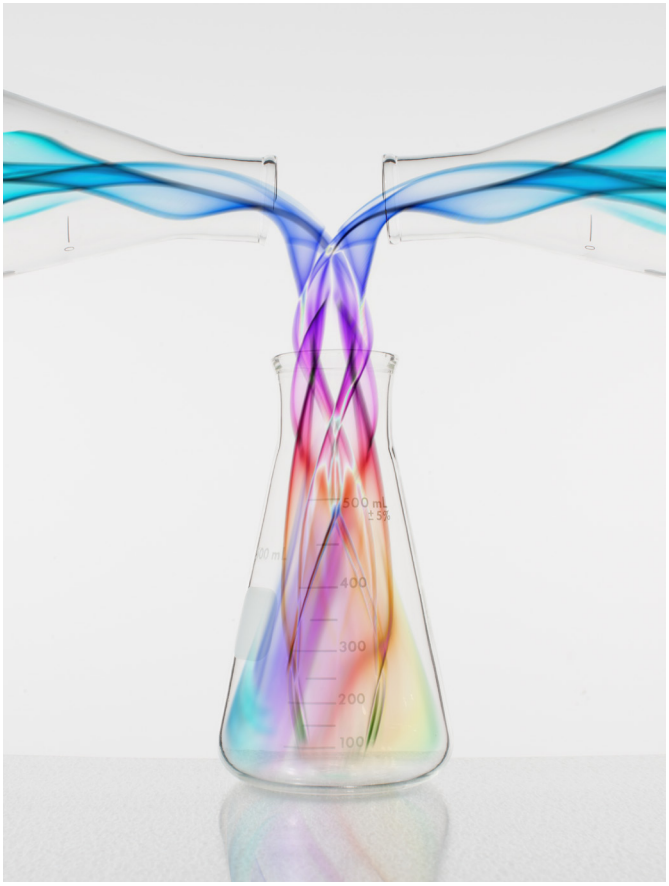
Furthermore, Battelle provides regulatory support for biological dossier preparation and risk assessments for the world's most important markets including Europe and the U.S. To round out the service offerings, we also provide GLP-compliant product safety testing, which is planned to soon include microbial formulations.

Q2. What are the challenges and countermeasures of bioformulation development? Could you share some specific cases? Such as how Battelle is improving stability for microbial formulations?

Microbial products are based on living microbes, either single species, a mixture of selected species, or complex consortia. The robustness of microbes varies highly between species and strains. Consequently, maintaining the microbial population and efficacy in distribution and storage can be challenging. One of the objectives of bioformulation development is finding the right balance between keeping the microbes alive and avoiding rapid growth or death.

Discovering the most suitable formulation type for a product is also demanding, but crucial to

enhancing the stability, shelf life, and performance of microorganisms in field conditions. As in the case of conventional agrochemicals, microbial products can be formulated as solids or liquids. The choice depends on the intended application mode, the microorganism's mode of action, compatibility with other components (e.g., different AI, water), and, foremost, stability of the microbe AI (e.g., robustness, stable form). Microorganisms can face different challenges when applied as seed treatment, foliar, or directly into the soil. In this case, the selection of additives (e.g., co-formulants, adjuvants) to add to the formulation, is essential for the microorganism's survivability and efficacy. Additives are needed to protect against adverse environmental conditions such as desiccation, UV light, and wash-off, as well as to guarantee good performance and quality of the formulation (e.g., dispersibility, suspensibility, flowability). Nevertheless, co-formulants and adjuvants commonly used in conventional agrochemical formulations are not always compatible with microbes, compliant with desired markets (e.g., organic), or safe. Despite, the evident shift in the range of additives being offered to the biological market, we are still in need of more alternatives, especially options that comply with the requirements of certain markets (e.g., organic market for biostimulants) and that avoid high costs for the final product.



Additionally, other challenges to be taken into consideration are equipment compatibility and packaging. Farmers often need to use the same application equipment as conventional products. Consequently, chemical compatibility and specific physical properties might be required for the microbial product. The choice of formulation type and technology is key to solving any potential incompatibility. Gas production by the microorganism or need for water exchange may affect pack selection and/or requirements.

Formulation development of a microbial product can be a complex process, however, it is essential to obtain a commercially viable, cost-effective product and to not jeopardize the sector's reputation.

As previously mentioned, Battelle invests in its internal R&D to provide solutions to common problems faced by our clients. Our ongoing R&D aims to enhance microbial formulation stability through various approaches. These include:

1. Testing microbial compatibility with novel and conventional co-formulants and adjuvants.
2. Designing liquid formulations (e.g., SC, OD, and EW) for gram-negative bacteria or gram-positive non-spore-forming.
3. Exploring alternative seed stickers that can help to replace some of the common polymer-based ones.
4. Developing encapsulation technologies to improve microbial compatibility with other AIs.
5. Ensuring stability in liquid and on-seed forms.

Q3. Could you introduce Battelle's regulatory consultancy service? And share some changes of regulation and policy on biologicals of your company's target markets? What is the service strategy in response to these evolving changes?

Besides assisting with bioformulation development, Battelle supports our clients with their registration process for both biopesticides and biostimulants. Battelle has a long-standing reputation in the U.S. and Europe for being a trusted partner for formulating successful regulatory compliance strategies. We provide innovative full-scale registration and re-registration support, as well as expert advice in dossier compilation for conventional crop protection products and biologicals. Our work is supported by a team of multidisciplinary scientific experts with complementary skill sets and various backgrounds from the crop protection, contract research, and regulatory consulting industries and national authorities. Our teams in the UK and U.S. help with study design and global registration, data gap analysis, dossier preparation, risk assessment, and submission including advice for product defense. The latest modifications in the European framework applied for biostimulants (regulation EU No. 2019/1009) and those to be implemented for biopesticides (e.g., new data requirements for approving active substances and new data requirements for authorizing products) seem to be a constructive change to the biologicals market. For biostimulants, the new regulation in force since July 16, 2022, appears to represent an opportunity for companies to invest in a new range of products and access the whole EU market more easily. For biopesticides, the new rules should accelerate the approval and authorization of biological plant protection products containing microorganisms and provide a better direction on test methods and guidance documents to be used. Nevertheless, the consequences and challenges that come with the new regulations are yet to be fully understood, and although the intention is to ease the overall registration process, that might not be the initial result. For this reason, Battelle is developing a new team of regulatory experts that will exclusively focus on the challenges of biological plant protection products. Our key to success is to deliver tailor-made solutions to our clients that are deeply anchored around a purely biological mindset.

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Q4. What impact from the EU Fertilizing Products Regulation do you see on the biostimulant industry?

Plant biostimulants are known for their ability to enhance nutrient uptake and efficiency, improve soil quality, and, consequently, enhance crop growth, as well as increase crops' tolerance to abiotic stress. The Fertilizing Products Regulation (FPR) (EU) 2019/1009 is the recognition of plant biostimulants' role in the industry and its trends towards sustainability.

The positive impact of FPR becomes evident, especially when considering the increasing inquiries from clients seeking guidance on how to approach the harmonized marketing process or how to start developing biostimulants. These clients are well aware of the potential opportunity to access the EU market.

It is important to note that the FPR entered into force on July 16, 2022, which means that we are still in a period of adaptation. Some matters still need to be addressed and fully clarified. For instance, the respective guidelines and guidance are still being developed. Additionally, only a limited number of microorganisms are recognized as being safe to use as components of microbial plant biostimulants. Only four genera of microorganisms (Azotobacter spp., mycorrhizal fungi, Rhizobium spp., and Azospirillum spp.) are allowed, which excludes many others that are currently being used or developed. Despite the European Commission's powers to amend the positive list included in CMC 7 of the FPR to include more microorganisms, there is still no formal procedure that has been defined by the Commission. Equally important, the FPR does not provide data protection for applicants. Altogether, these are limitations that might lessen the immediate interest of companies and consequently block innovation and deprive Europe of alternatives to more sustainable agriculture.

Battelle has been keeping in contact with competent authorities and DG GROW to provide the best possible support to our clients in strategy development, data gap analysis, data generation support, dossier preparation, submission, and defense.

Q5. Can you describe the current state of the biological market? What and where are the biggest opportunities and challenges for biologicals? What are the factors affecting changes in the biological market?

The current state of the biological market shows a positive demand for both biopesticides and biofertilizers. Importance and status may differ among countries and regions across the globe, but overall, environmental concerns, consumer demand, organic farming, and regulatory pressures on conventional crop protection products are driving the demand.

Benefits of biologicals such as protection against abiotic and biotic stresses, increase of plant nutritional value, and improvement of soil quality are well known. So too are the hurdles and challenges that prevent them from achieving their full potential in the global market. Regulatory, product quality/shelf life and efficacy, formulation development, and cost are among the main obstacles that hamper a stronger positioning of biological products.

Nevertheless, where one sees challenges, others see opportunities. These hurdles that need to be addressed are the spur for the change we want to see in the biological sector. The fact is, even if the trend is positive, biological products will only be able to compete or be used in synergy with conventional products if some of these limitations and complexities are solved and better managed.

For instance, regulatory frameworks through the years have been seen by many to be a hindrance for biologicals, not only because of the major difference in the regulatory frameworks, procedures, and data requirements among countries/regions (e.g., US, EU), but also because of the lack of clear distinction between biologicals and chemicals. This, however, has been changing and there is a clear shift from the regulators to better understand biologicals and their importance in the sector (e.g., modifications to Regulation (EC) No. 1107/2009 and Regulation (EU) 2019/1009). Time and costs for registrations can also pose a major limitation to many companies. Regulators need to respond faster to this issue to avoid hindering innovation from SMEs, but also to comply with their demand for alternatives to conventional products (e.g., EU Farm to Fork initiative).

Biologicals, especially microbial formulations, have been facing skepticism from farmers. Lack of

efficacy and versatility, poor product quality, and shelf life are still damaging the image of microbials. However, new technology developments, not only from the private sector but also from collaborations between national institutes and academia, are changing this view. Currently, biologicals are more effective than they have ever been and are better formulated to be integrated into conventional agricultural practices. Products are becoming more versatile in terms of application range, resistant to environmental conditions, able to be formulated in combination with conventional AIs or other biologicals, and have shown better shelf life and storage under different conditions. Even the offer of co-formulants and adjuvants is becoming more diverse, with companies investing in new resources that are more sustainable, innovative, and biocompatible.

Biologicals are not new to the agriculture industry. However, for many years it was hard for them to compete with conventional chemicals. With the new research tools and a better understanding of their functions, formulation advances, and technologies, as well as the increasing trend for sustainable agriculture, consumer awareness, and supportive regulations, they finally have a chance to thrive as a valuable tool for farmers.

Q6. Could you give some advice for companies that would like to extend or enter into the biological field?

The general advice we can give to our clients is to be knowledgeable and realistic about their active ingredient (i.e., the strengths, incompatibilities, limitations, biology, and chemistry). You need to work to guarantee a stable active ingredient before formulating and understand that R&D is a key element to creating a robust and quality product. Also, you need to have a clear idea of the intention of product use, application, and market (e.g., EU and U.S. market, organic farming to avoid future regulatory hurdles, or the need to re-formulate). These are all notions that can help to ease both the formulation and regulatory journeys, and consequently save costs and time. Finally, being agile enough to pursue different approaches from conventional agrochemicals when formulating a biological product is key.

Q7. How can Battelle Crop Protection Solutions help companies in the biological market?

Battelle Crop Protection Solutions offers complete turn-key solutions for the entire development and regulatory process of biologicals, including bioformulation development, modelling, GLP product safety testing, and regulatory consultancy for biologicals.
Battelle has a long-standing reputation in the U.S. and Europe for being a trusted partner for formulating successful regulatory compliance strategies. Besides assisting with bioformulation development, Battelle supports our clients with their registration process for both biopesticides and biostimulants.
We provide innovative full-scale registration and re-registration support, as well as expert advice in dossier compilation for conventional crop protection products and biologicals.
Our end-to-end solutions approach allows us to provide support to our clients throughout the entire process, from the lab to the market. Battelle operates with an agile method, which speeds up the bioformulation development and winding registration processes.

Contact us today to talk to a Battelle Crop Protection Expert.

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