Developing Agrochemical Formulations - New Challenges, Solutions and Trends

Editor’s Note: The formulation plays an essential role in achieving the successful delivery and biological activity of any plant protection product, while its development is facing a series of new challenges. Accordingly, AgroPages recently invited three key players: Syngenta, BASF Crop Protection and Arysta LifeScience to share their insights on the new challenges, key influencing factors and potential solutions of the agrochemical formulation development, as well as their innovation formulation technologies/products etc.

Q1. What are the new challenges facing agrochemical formulation development, potential solutions and future trends?

Syngenta: Resistance of pathogens or pests to chemical agents is not a new issue facing the agrochemical industry but it is one that remains a key challenge for agrochemical formulation development. With resistance comes the continued need for identification of new active ingredients and subsequently the need to formulate them into usable products. All the simple molecules have been discovered, so the pipeline of new compounds is trending to be increasingly complex — higher molecular weight, more diverse chemical functionality and multiple chiral centers are not uncommon. This subsequently imparts additional complexity on both manufacture of the active ingredient and in producing formulations that exhibit the desirable biology, application and shelf-life characteristics.

In my opinion, the fundamental solutions haven’t and won’t change. It's about application of sound scientific know-how to work around the challenge. Through industry leading formulation science, Syngenta is able to offer some of the best and yet most complex products in the marketplace. Formulations containing five, six and even seven active components in a single premix are common in Syngenta’s product portfolio. These products provide the convenience and dose accuracy of a single premix with multiple modes of action, providing broad-spectrum control of pests. The technical hurdles of physically and chemically compatibilizing multiple active ingredients are done during formulation development, to mitigate these issues occurring in the mix tank at application.

The responsibility to produce new products that meet and exceed stewardship performance standards is an additional formulation challenge, whether it be reducing spray drift for aerial or ground spray application, dust reduction for seed treatments or improved operator safety. As formulation chemists, we’re looking to utilize innovative surfactant and coating technology to build in or tank mix additives that benefit or sustain biological activity, whilst addressing environment challenges and the safe use of pesticides.

BASF Crop Protection: Challenges in formulation development should be discussed in the context of product development and how customers experience our products.
What makes a good product? From a farmer’s perspective, a product should be robust, flexible to use, efficient and performing, cost competitive, convenient, safe and without residue concerns.

Developing robustness and flexibility in various weather conditions, such as rain, sun and wind, remain challenging for formulation development. To address these challenges, we focus on improvements in wash off, uptake, UV decomposition and off-target movements of active ingredients. Chemists develop polymeric stickers, surfactants, UV absorbers or drift reducing agents through proper formulation technology.

These improvements not only help a farmer run his operations profitably, but are also a crucial part of BASF’s sustainability strategy.

Other formulation trends are spurred by application constraints, such as low water volume or water quality, and from new application technologies, such as drones. Consequently, products must often be refined and adjusted so that inherent properties of the active ingredient, e.g. solubility and mixing compatibility, are managed effectively.

Arysta LifeScience: Modern agrochemical formulation development has faced significant challenges not only from a technical perspective, but also regulatory and market demands. The main challenges are:

The increasing demand for formulation quality, including the compatibility of multiple active ingredients in a single formulation and the controlled crystal growth of active ingredients.

The increasing regulatory pressures. Most regulatory authorities demand formulations that have minimal impact on the environment, which requires favorable ecotoxicity profiles with biodegradable additives, reduced use rate, and minimal pesticide residues on crops after spraying.

The cost-effectiveness of new formulations.

While it is costly to develop new pesticides, formulation innovation has become a means to address the above challenges. For future trends, formulation innovation should not be separated from the improvement in application technologies. Instead, application technologies, such as precision agriculture, will also play a key role in reducing chemical drift and using pesticides effectively.

Q2. What are the key factors in agrochemical formulation technology innovation? What initiatives did your company take to drive its innovation?

Syngenta: Customer experience is a primary focus for development of any Syngenta product. To a large extent, this and responsible environmental stewardship is what drives our formulation technology innovation. Biological efficacy, application behavior and shelf-life stability are
obviously core product performance attributes. Stewardship features associated with toxological endpoints, such as residues, runoff and acute toxicity, are equally important to advance our understanding, and, subsequently, to continue to develop technology solutions to support the safe use of pesticides.

Within Formulation Development at Syngenta we look to leverage knowledge and external interactions across the organization. By partnering with our commercial teams, we’re able to coordinate visits of our development scientists with channel partners, retailers and growers to see and hear firsthand how products perform. With this, we gain further insight in understanding the challenges and performance improvement needs to enhance their experience and agronomic practices. Additionally, our development scientists work closely with product stewardship and regulatory teams to ensure foresight on regulatory and environmental concerns. This subsequently defines our technology innovation to provide step-change improvements for items like reducing dust-off for seed treatment or reducing spray drift through formulation or application technology enhancement.

BASF Crop Protection: Innovations in formulation technology are derived from novel physicochemical presentations of active ingredients. Combining agrochemical formulation know-how with technologies from other disciplines drives this innovation approach. At BASF, central research units such as Advanced Materials & Systems Research, Bioscience Research and Process Research & Chemical Engineering offer a variety of technologies, which we systematically link to crop protection formulation research and innovation projects. Using these resources, we derive new encapsulation concepts or polymeric solubility promoters for active ingredients. Our colleagues from Bioscience Research closely collaborate with formulation labs on biological crop protection projects to develop novel product solutions.

We also foster partnerships with universities and research companies to combine their expertise with our formulation capabilities.

Digital technologies are becoming an integral part of R&D, resulting in quick access to clean data and new imaging methods. These tools will speed up processes and enable new pathways for formulation innovation.

Arysta LifeScience: Formulation technology innovation should address the current and future technical challenges generated by technology, regulatory authorities and the market. An advanced delivery system and the adjuvant technology will be the key areas in formulation innovation through integration with precision agriculture technology.

Arysta LifeScience R&D has global footprints, including in North America, Latin America, Europe, Africa and Asia Pacific. Our in-depth expertise covers agrochemical and biosolution formulations, seed treatment, and analytical capability to deliver customized solutions. The R&D teams are highly motivated and actively work on formulation innovations that meet increasingly stringent regulations and provide green and integrated solutions for growers.
Arysta LifeScience R&D actively works on formulation technology innovation that includes but is not limited to:

- Improved formulation quality with broad-spectrum control
- Enhanced biological efficacy by combining with application technology to improve grower yields
- Combatting herbicide-resistant biotypes with multiple modes of action (MoA) contained in a stable, fully optimized and user-friendly formulation
- Environment-friendly inerts with favorable ecotoxicity profiles to deliver high-performing and cost-effective formulations

**Q3. What do you think of the important role of adjuvants for formulation technology innovation? How can adjuvants drive its innovation?**

**Syngenta:** Formulating active ingredients involves balancing several competing factors such as physicochemical stability, regulatory profile and biological efficacy. Adjuvants can play an important role in this by boosting bio-performance and improving the environmental profile of a product. In turn, adjuvants help to realize the maximum potential of our active ingredients.

Traditionally, adjuvants have been used as uptake enhancers, but by carefully studying aspects of product delivery we now know that uptake is only one of a number of loss mechanisms that contribute to product performance. As such, we now utilize adjuvants to fulfil a range of roles including use as retention aids, spreading enhancers, rain-fastness aids and drift-reducing agents.

Innovation in adjuvant technology will continue to play an important role in addressing targeted delivery of pesticides to maximize crop capture and potentially further improve the environmental profile of products.

**BASF Crop Protection:** Adjuvants are the “salt in the soup” of any good formulation and are needed to manage inherent physical active ingredient properties and associated aspects.

Moreover, they play an important role in designing and tuning of product properties, for example, retention, spreading and uptake.

In addition to physicochemical formulation aspects and biological efficacy-improving features, adjuvants provide a means to influence mobility of crop protection products. Mobility control, in terms of reduced wash off, leaching and drift, is important to optimize the use rate and influence the e-fate of products.

Progress in adjuvant technology will probably not be a game changer in formulation innovation, but it is vital to new improvements in crop protection products.

**Arysta LifeScience:** Adjuvants are a key component in formulation technology innovation. Ideally, adjuvant technology should enhance the effectiveness of agrochemical formulations by
improving their biological efficacy. Key research activities for formulation chemists are:

- Improving foliar performance of pesticidal formulations
- Reducing the formulation waste that is caused by either bouncing off from leaves during spraying or drifting from targeted crops

To this end, Drift Reduction Technology (DRT) has become increasingly interesting with a focus on developing effective drift retarders and enhancing spray quality control.

Arysta LifeScience has implemented short-term and long-term plans to develop internal application technologies and initiate the investigation of adjuvants in formulation development. The application technology will assist formulators in screening adjuvants to improve pesticide uptake through leaf cuticles. This new capability will enable chemists to reduce the number of testing prototypes required in field efficacy trials.

Arysta LifeScience will also explore new collaboration opportunities and work with external solution providers to further enhance adjuvant technology.

**Q4. Which agrochemical formulations will see the best growth prospects? Which will face significant competition from other formulations or technology?**

Syngenta: Biocontrol products are based on naturally occurring compounds: minerals, microorganisms or plant extracts. They are used for biotic stress management in controlling fungal and bacterial diseases, arthropod pests, nematodes and weeds. Biocontrols can offer new modes of actions and high specificity for target organisms. In light of resistance and regulatory challenges, there is great potential for this segment of agrochemistry, and, subsequently, it’s an area of intensive research and product development activity. The synergistic use of biocontrols alongside chemical products may help manage the onset of resistance.

The challenge for the formulation chemist is that the active components tend to be produced commercially via fermentation processes. Consequently, the technical-grade active material typically contains large amounts of fermentation excipients, e.g., proteins and carbohydrates. These excipients can impact the product storage or application performance characteristics, necessitating additional formulation science insights in order to meet the performance standards of chemical products.

It’s unlikely in the short term that biocontrols will comprehensively exclude the need to supplement agronomic practice with conventional chemical products. At this moment in time, there just aren’t enough biocontrols developed that provide comparable efficacy or spectrum control to chemical products. But the investment in research and development is rapidly advancing this technology space.

BASF Crop Protection: The leading formulation technology by volume is SL (Soluble concentrate) technology used in non-selective herbicides, followed by EC (Emulsifiable concentrate)
technology and SC (Suspension concentrate) technology used in a broader range of indications. These liquid technologies account for roughly three quarters of total market volume. Growth of these formulation types depends mainly on regional market development and crop and corresponding technology preferences, and less on the specific technology.

Other technologies such as OD (Oil Dispersion) and CS (Capsule Suspension) formulations are garnering more interest. Both technologies are used if more prominent techniques fail or if special tactics are needed to manage active ingredient properties.

Arysta LifeScience: An agrochemical formulation consists of single or multiple active ingredients with other inert additives to form a chemically and physically stable mixture. When a formulation is developed, the type of formulation is determined by the physchem properties of the active ingredients. To determine a type of formulation, a formulator should also consider market facts, such as regulatory recognition and end-users’ preferences for specific regions.

The current trend is focused on the development of sustainable premix formulations, which include multiple active ingredients for a broad spectrum of control and ease of use. This leads to the increasing complexity of new formulations and technical challenges in improving compatibility. Generally speaking, agriculture technology should not be isolated from advanced technology in other industries. Advanced delivery systems are a key technology innovation and will contribute to resolving the challenges. Advanced delivery systems should be leveraged and integrated with the technologies that have been developed in other industries, such as pharmaceutical, cosmetics and materials science, with cost-effectiveness.

Environment-friendly formulations have also received increasing attention. The current focus for the agriculture industry is to utilize co-formulants with favorable ecotoxicity profiles; remove inerts from formulations that are banned and restricted by regulatory authorities; use environment-friendly solvents to develop Emulsion Concentrates (EC), Oil Dispersions (OD) and Suspo-emulsions (SE) formulations; as well as integrate biodegradable additives.

Q5. What innovation formulation technologies/products have been launched by your company? What are the agriculture concerns solved by them?

Syngenta: Syngenta is continuing to expand its biocontrols portfolio. In 2013, we launched Clariva® Pn nematicide, a biocontrol based on pasteuria nishizawai for control of soybean cyst nematode (SCN). This has been successfully launched in the U.S. and will launch in Brazil in 2018. We took this product one step further in 2017 with the launch of Clariva® Elite Beans, a 5-way chemical and biocontrol premix formulation, combining Clariva® Pn with our market leading soybean premix CruiserMaxx® Vibrance® Beans. Clariva® Elite Beans provides broad spectrum control against SCN, in addition to early-season insects and diseases.

Polymer microencapsulation technology has been used in the agrochemical industry for decades but remains a core formulation technology, one which Syngenta has adapted across our product
lines for multiple benefits. In weed control, this technology has been exploited to enhance product-application performance and achieve premix compatibilization of complex mixtures of active ingredients (*Acuron*, *Lumax EZ* and *Halex GT*). For insect and vector control, microencapsulated products have been developed that improve operator safety and exploit controlled release technology for enhanced bioefficacy (*Karate Zeon*, *Icon* and *Actellic*).

Syngenta has a healthy portfolio of new SDHI chemistries that have been successfully commercialized in recent years. *SOLATENOL™* is a potent SDHI active ingredient in a number of products, including the family of *ELATUS™* products. These products provide an effective solution for treating the most important and damaging diseases of cereals, including Septoria and Rust. They provide particularly long-lasting control, compared to competitor products. *SEDAXANETM* is an active ingredient that was developed specifically for seed treatment. Marketed under the umbrella brand *VibranceTM*, *SEDAXANETM* is formulated to boost a crop’s *RootingPower™*, by delivering enhanced disease protection that leads to stronger and more robust root systems, which increase moisture and nutrient uptake. *ADEPIDYN™* is our new broad-spectrum fungicide, marketed under the umbrella brand name *MIRAVIS™*. It delivers a step change in leaf spot control (such as *Cercospora, Alternaria* and *Venturia*) and excellent control of powdery mildew in many crops. *ADEPIDYN™* is also highly effective against difficult-to-control diseases, such as *Fusarium Head Blight, Botrytis, Sclerotinia* and *Corynespora*, which cause severe damage on key crops.

**BASF Crop Protection:** We have a broad range of products in our pipeline with innovative formulations, such as:

- **Seltima®**
  Seltima® is a highly innovative encapsulated formulation (Capsule Suspension), specifically developed for *F500®* in rice. The product has a completely different behavior when reaching the leaf surface or the paddy water. On the leaf surface, where the applied spray broth is drying, the encapsulated *F500®* is quickly released for an optimal biological performance. The adjuvant already included in the capsule formulation ensures optimal uptake and retention. In the paddy water, the capsules will stay intact and sink to the sediment. *F500®* released over time will bind to the sediment and will degrade. This behavior ensures necessary safety for aquatic organisms in the paddy water.

- **Engenia™**
  Engenia™ herbicide is a next-generation formulation, representing another significant step in dicamba innovation. With a heavier molecular weight and a stronger chemical bond, Engenia™ herbicide is formulated to provide maximum flexibility with the lowest use rate of all dicamba products currently available in the market, reducing the number of trips to fields and sprayer loading time. With a lower use rate, growers can stock less product and save more space.

- **Revysol®**
  Beginning at the earliest discovery stages, this new fungicide was designed to meet both the highest level of regulatory standards and outstanding biological performance. Extensive research
has shown its outstanding biological performance against a range of difficult-to-control pathogens, such as Septoria tritici and rust in cereals, in a multitude of crops. Beyond benefits for row and specialty crop growers, Revysol fungicide will also provide a new option for turf management and seed treatment markets. Pending regulatory approval, first market introductions of customized formulations are expected for the 2019/2020-use season.

Arysta LifeScience: Arysta LifeScience has launched a new integrated solutions program, ProNutiva®. ProNutiva® is an exclusive program that integrates biosolutions with conventional active ingredients to deliver crop solutions that meet the real-world needs of growers. This integrated technology has resulted in enhanced interaction and improved compatibility between biosolutions and agrochemical — for either premixes or tank-mixes — that go beyond current benefits expected by most growers.

To deliver innovative solutions, Arysta LifeScience R&D actively looks for technology innovation to improve formulation compatibility and bio-efficacy. The challenge of compatibility can be caused by high ionic strength media or extreme pH conditions or other factors.

Arysta LifeScience also works on advanced delivery systems through innovation, to develop value-added and differentiated products.