WHITE PAPER

The Next Wave of Agricultural Materials Innovation is on the Horizon

Introduction

The term agriculture refers to the active production of useful plants or animals. The earliest indications of agricultural activity come from roughly 14,000 years ago in what is now known as the Middle East. It wasn't long until other plant cultivation and animal husbandry efforts popped up in other locations around the world. The plants and animals raised by those diverse peoples centered on the flora and fauna native to each location.

Today, agricultural production occurs nearly worldwide and is an international industry. A look at some of the recent annual production volumes gives perspective to the importance of agriculture to every person on the planet:[1,2,3]

- Vegetables: 1.1 billion metric tons
- Grains: 2.6 million tons
- Oilseeds: 600 million tons
- Beef: 61 million tons
- Pork: 103 million tons
- Poultry: 11 million tons

Since the earliest beginnings of agriculture, humans have been challenged with maximizing agricultural output and preventing losses due to over-farming, weather, disease, pests, and other adversities.

The earliest records of fertilizer use are from nearly 8,000 years ago. From that time to the mid-20th century, manure was the primary fertilizer used. In the 18th century, ground bones became another well-used fertilizer and a few minerals such as gypsum were in limited use. In the 19th century, research identified nitrogen, phosphorus, and potassium as essential elements for plant growth, and nitrogen-based fertilizers were developed.

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According to The Fertilizer Institute, a fertilizer is any combination of specific nutrients designed to provide the nourishment essential for growth and maintenance of crops.

Commercial fertilizer use was limited until after World War II when modern soil chemistry and plant nutrition research began identifying an ever-increasing number of fertilizer sources and formulations. By the late 1940s, about 2 million tons of chemical fertilizers were used annually. That volume has grown to more than 20 million tons per year today.

A brief history of the recorded use of crop protection chemicals begins in the Middle East roughly 4,500 years ago when sulfur compounds were used to control insects and mites. Since that time diverse cultures around the world have used oil, ash, sulfur, salt, lime, mercury, arsenic, lead, nicotine, pyrethrums, and other naturally occurring chemicals to control insects, fungi, weeds, and other pests.

The first synthetic pesticides were developed in the 1930s and 1940s including the herbicide 2,4-D and the insecticide DDT. The synthetic pesticide industry grew strongly after World War II. Pyrethroid insecticides were developed in the 1960s, and the well-known herbicide glyphosate was developed in the 1970s. Since then, the research and development of many pesticides has continued, along with other crop protection approaches.

According to the U.S. Environmental Protection Agency, a pesticide is any substance used to prevent, destroy, repel, or lessen the damage of any pest. It includes herbicides, insecticides, fungicides, and numerous others.

In modern times, the agricultural materials industry is comprised of the fertilizers segment and the agrochemicals segment. These materials are used to protect crops and improve their growth and fertility and have played a significant role in achieving current agricultural production rates.

Fertilizers are grouped into macronutrient, secondary nutrient, and micronutrient categories based on the amount needed by plants:

- Macronutrients: nitrogen (N), phosphorus (P), and potassium (K).
- Secondary nutrients: calcium (Ca), magnesium (Mg), and sulfur (S).
- Micronutrients: boron (B), chlorine (Cl), copper (Cu), iron (Fe), manganese (Mn), molybdenum (Mo), nickel (Ni), and zinc (Zn).

The agrochemicals segment includes a wide range of products including crop protection chemicals (pesticides), plant growth regulators, seed treatments, soil conditioners, and others.

As the global human population continues to increase and the available arable land continues to decrease, it becomes ever more crucial to improve the yield and quality of agricultural products.

The Markets by Revenue

The global fertilizers market in 2019 was $196.9 billion USD. The market is expected to grow to nearly $208 billion USD by the year 2026.[4] The macronutrients account for more than half of the fertilizers market:[5,6,7]

- Nitrogen, $54.6 billion USD in 2019
- Phosphate, $51.6 billion USD in 2016
- Potassium, $24.7 billion USD in 2019

The remaining portion of the fertilizer market is comprised of secondary nutrient and micronutrient fertilizers.

The global agrochemicals market was $243.1 billion USD in 2019. The market is expected to grow to nearly $300 billion USD by 2024.[8] A few of the top subsectors generating these revenues include:

- Crop protection chemicals, $58.38 billion USD, with herbicides comprising nearly 75% of this subsector[9]
- Biologicals, $7.2 billion USD[10]
- Plant growth regulators, $5.72 billion[11]
- Soil conditioners, $5.4 billion[12]

The Markets by Region

In 2018, global agricultural NPK fertilizer use was roughly 188 million tons with the following breakdown:[13]

- Nitrogen, 109
- Phosphorus (phosphate), 41
- Potassium (potash), 39

The top regional fertilizer consumers were (in million tons):[13]

- Asia, 103.8
- Americas, 50.9
- Europe, 23.1
- Africa, 6.7
- Oceana, 3.6

In every region, nitrogen fertilizer was used in greatest volume.

Also in 2018, global agricultural pesticide use was roughly four million tons with the following top categories:[13]

- Herbicides, 1.2
- Fungicides and Bactericides, 0.5
- Insecticides, 0.4

The top regional pesticide consumers were (in million tons):[13]

- Asia, 2.2
- Americas, 1.3
- Europe, 0.5
- Africa, 0.08
- Oceana, 0.07

Regional markets for crop protection chemicals have evolved and shifted over the last two decades.

As population growth and farming technologies have progressed in the emerging markets in Asia, Middle East/Africa, and Central/South America their usage of crop protection chemicals has increased rapidly. As a global percent of total demand these regions have outpaced the demands in Europe and North America.[14]

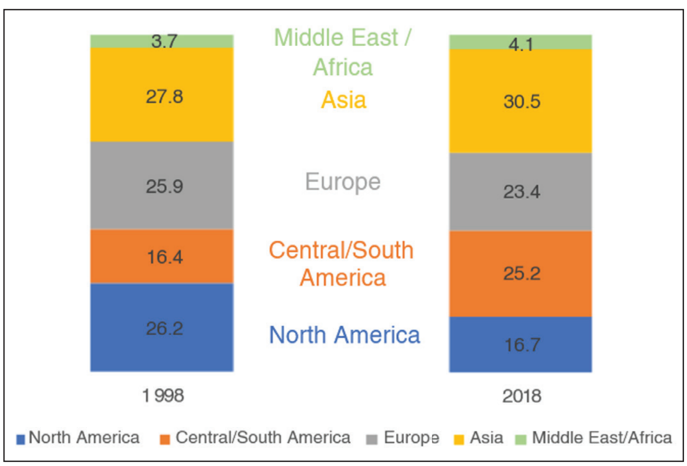

Figure 1. Crop protection regional market development from 1998 to 2018 (% of global total consumption)[14]

Fertilizer and Agrochemical Challenges

The fertilizer and agrochemicals industries face a number of challenges to its continued innovation and growth.

Societal and Climate Pressure

Our expanding global population is increasing the need for food and, therefore, agricultural output. Income growth in developing countries is also driving demand for more meat, fish, fruits, vegetables, sugar, and vegetable oils, amid decreasing consumption of cereal crops per capita. These changes are challenging in enough when the amount of agricultural land is stable; it becomes even more of a challenge as agricultural land is being lost to industrial and community growth. Some nations actually "rent" land in under-developed countries in Africa and Southeast Asia to provide security of land and food supply for their country.

Add to this the impact of drought and other climate-related issues, and the pressure to increase yields and reduce loss to pests grows ever greater. Fertilizer and agrochemical companies are feeling the pressure to improve their product offerings and develop innovative approaches to help feed the world.

Product Development Investment

Agricultural research and development (R&D) costs and timeframes continue to increase, particularly for agrochemical developers. In the period from 1995 to 2014, the time and costs typically required to develop a new agrochemical increased from 8.3 to 11.3 years and from $152 to $286 million USD. The costs have continued to increase, especially for environmental studies, toxicity studies, field studies, and product registration.[15,16]

The number of new agrochemicals making it to market peaked in the 1990s, then started to decline in the early 2000s. **It is estimated that out of every 160,000 candidate molecules evaluated, only one new agrochemical makes it to market today.** Contributors to this conundrum include the difficulty in finding novel active ingredients and increasingly stringent regulations for agrochemical registration and use.[15,16] And yet, R&D is still critical to a company's growth. Strategies some agrochemical companies have used to address this growing challenge include collaborative partnerships and a drive for truly innovative approaches.

Regulations and Registrations

The regulatory authorities in many regions and countries continue to tighten restrictions on fertilizer and agrochemical registration and/or use. One of the most aggressive regulatory programs is found in the EU where the number of registered agrochemicals continues to decline as risk/hazard criteria have become more stringent. The time required for review of registration applications is often prolonged, especially when the review process is multi-layered as it is in the EU and Brazil. Re-evaluation of previously registered products also puts existing agrochemical authorizations at risk, as is the case in Japan following amendments to that country's agrochemical regulation law in 2018. These and other regulatory considerations are important for agrochemical R&D and commercialization planning.[16]

Generic Off-patent Products

As new active ingredient discoveries decline and older patents expire, the number of generic agrochemicals on the market increases. Generic manufacturers have advantages over new product developers including substantially lower R&D costs and time to registration. This allows generic agrochemicals to be sold at lower prices than the original product and encourages greater sales volumes of generics. As a result, some generic manufacturers are among the top agrochemical producers.[15,16,17]

Adjacent Markets Pressure

Fertilizer and agrochemical companies must also consider how advances in adjacent markets can impact their business. A few adjacent markets that are making headway in the agriculture industry include the development of biologics, gene editing, expansion of precision agriculture, use of advanced robotics and drones, use of machine and deep learning, and others. These emerging technologies have the potential to decrease the need for fertilizers and/or agrochemicals, but also to provide them with new opportunities for innovation, partnerships, and expanded service offerings.

Fertilizer and Agrochemical Trends

The saying that "necessity is the mother of invention" is certainly true in today's fertilizer and agrochemicals industries. The challenges just discussed, and others, are driving innovation and trends in these agricultural materials segments. Here we review some of the trends emerging in response to these challenges.

Integration of New Technologies

Fertilizer and agrochemical companies have begun looking for ways to integrate new technologies into their processes to help them meet changing customer expectations, accelerate their R&D efforts, and open new business opportunities. **This synthesis of long-standing business approaches with new technologies has the power to transform fertilizer and agrochemical producers into providers of diverse and integrated products and services.**

One example of this type of integration is the adoption and support of precision agriculture. The goal of precision agriculture is to increase sustainability by optimizing yields with precise fertilizer and agrochemical usage according to need. Precision agriculture pursues this by using information technology and machine learning along with a range of automated tools such as field sensors, drones and robotics, GPS-guided soil sampling, autonomous vehicles, variable rate technology for product applications, and numerous others.16 Companies who integrate precision agriculture into their business offerings greatly expand their range of support and expertise for the benefit of their customers.

Fertilizer Innovations

As noted earlier, the global fertilizers market is expected to grow to nearly $208 billion USD by the year 2026. Because of this, innovations in the fertilizer industry can have significant impacts on agriculture and food supplies.

Development and use of enhanced efficiency fertilizers (EEF) is a continuing trend in the fertilizer industry. EEFs reduce nutrient losses to the environment and increase nutrient availability to crops. They accomplish this by slowing the release of nutrients for uptake and/or altering the conversion of nutrients to forms that are less susceptible to losses. Successful use of EEFs can improve yields, reduce fertilizer impacts on the environment, and improve long term soil health.[18]

Another trending research area is in improving nutrient delivery to the soil and, ultimately, the plants growing in that soil. Nutrient replenishment of soil can be improved by placing fertilizers deeper within the subsoil at depths of greater than eight inches below the ground surface. Research indicates that this type of subsoil fertilization has the potential to increase yields by 50% or more. Efforts are underway to develop efficient new delivery systems to get fertilizer nutrients into the subsoil. Nanoparticles are one delivery method under investigation for this purpose.19

Increasing the sustainability of the fertilizer industry is another trending area of innovation. Methods are being investigated for the production of nitrogenous fertilizers using carbon-neutral input materials rather than natural gas feedstocks. The search for nutrient sources from recycled materials is also being pursued to reduce the impact of nutrient mining on the environment.[19]

Genetically Modified Seeds

Genetically modified (GM) seeds is another technology that has been embraced by many fertilizer and agrochemical producers. **The development and use of GM seeds is one means of reducing crop loss and increasing yield by addressing crop stressors.** Such stressors include biotic factors such as insects and weeds, and abiotic factors such as suboptimal temperatures, drought, and other physical environment characteristics. GM seeds are engineered via gene editing to produce desirable traits in crops. The primary traits of most current GM seeds are herbicide tolerance and insect resistance, both of which help address biotic stressors. GM seeds that address abiotic stressors are also under development.[16]

The adoption of GM seeds has increased rapidly in some countries since their market introduction in the 1990s. As GM seed use expanded over the past two decades, the introduction of new agrochemical active ingredients has decreased, as depicted in Figure 2.[14]

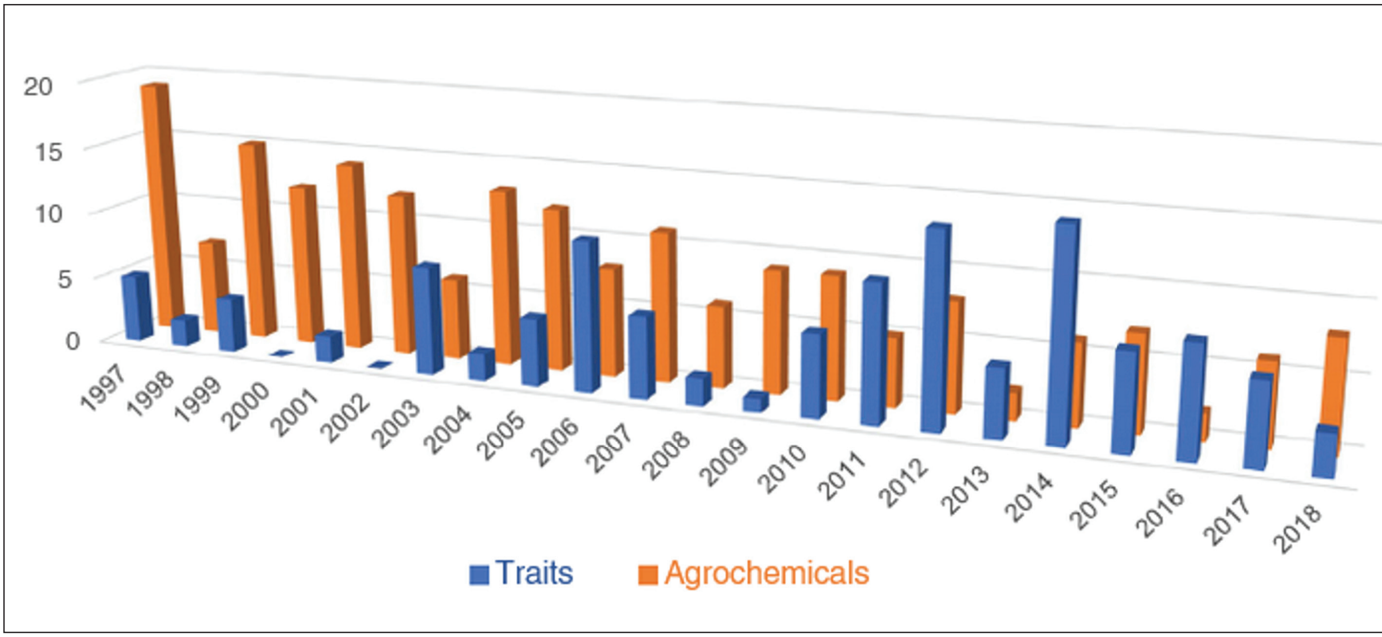

Figure 2. Number of new active ingredients and GM trait introductions[14]

The use, trade, and tracking of GM seeds are regulated worldwide. GM seeds are used the most in the U.S., Brazil, Argentina, Canada, and India. Only two E.U. nations, Portugal and Spain, have used GM seed. **Today, more than 90% of U.S. corn, upland cotton, and soybeans is grown from GM seeds.**[20]

The GM seed market has grown at three times the rate of the crop protection chemicals market since 2001. In 2016, GM seed sales reached $20.4 billion USD. That figure rivals herbicide sales which comprise the largest portion of pesticide revenues. Amidst this boom in growth, some large agrochemical companies acquired GM seed companies, a move that has boosted their revenues.16 It is hoped that increased development and use of safe, sustainable GM seeds will be a helpful part of efforts to reduce crop loss and increase yields.

IPM and Biologicals

Integrated Pest Management (IPM) and bio-based chemicals are considered more sustainable than conventional practices and products. IPM proactively monitors pest populations and intervenes in a variety of ways to prevent pest damage to crops without harming the environment. IPM uses digital technologies to monitor crops and addresses potential problems using mechanical tools and bio-based fertilizers and/or pesticides rather than conventional materials. IPM can be a double-edged sword for fertilizer and agrochemical companies: it can reduce demand for conventional materials but also increase demand for new biofertilizers and biopesticides.[16]

Beginning in the 1990s, an average of 10 new biopesticides have entered the market each year. This rate of new product introduction outpaces that of other pesticides, although their overall market share is less than 10% of the total crop protection market. Additionally, most countries have fewer regulations for biopesticide product approvals, thus lowering R&D and registration costs. It is not uncommon for a biopesticide or other biological to be developed and commercialized in 3-5 years at a cost of $3-5 million USD. The development of biopesticides is a growing opportunity for agrochemical companies to respond to increasing consumer demand for more sustainable pest management approaches.[15,16,21]

External Partnerships

Fertilizer and agrochemical companies are embracing collaborative partnerships with other companies to diversify their business offerings. Each partner brings their expertise to the table and, together, they can help each other improve or innovate their products and services. One example of the success of this approach is Adama's launch of numerous new products after partnering with several agricultural technology companies.[15]

Another external partnership is the "asset-light" business model. A fertilizer or agrochemical company decreases their capital investments and R&D efforts by acquiring active ingredients from other companies that do the R&D "heaving lifting." This allows them to get their products to market faster and focus more on marketing and other commercialization activities.[15]

Fertilizer and Agrochemical Analytical Needs

The fertilizer and agrochemical industries use comprehensive analytical analysis programs that span from product development and registration through the production process to final product.

Fertilizer Analytics

The **R&D** of new fertilizer formulations requires analytical scrutiny during both the formulation development phase and the field-testing phase. During formulation R&D, raw materials are tested for composition, concentration, and purity. Each proposed formulation undergoes a battery of tests to confirm its physical and chemical properties:

- Determination of physical properties such as wear rate, particle size and shape, particle size distribution, crush resistance, fineness, moisture, pH
- Identification of all components in the formulation (active ingredients, additives, etc.)
- Quantitation of active ingredients (macronutrients, secondary nutrients, and micronutrients)
- Detection and quantitation of heavy metals such as arsenic, cadmium, chromium, lead, mercury
- Detection of impurities and degradation products

Field studies of interim fertilizers test the response of crops to a formulation. Data from comprehensive field trials are crucial for fine-tuning an interim formulation and preparing best application recommendations for a range of field conditions.

Important considerations in field trials include diverse field conditions and treatments such as:

- Different soil types and cultivation histories
- Different climates and hydrology
- Soils with varying nutrient levels
- Soils with different microbial populations
- A range of formulation application parameters (application rate, application timing, placement, irrigation protocols, and so forth).

Fertilizer **production** requires ongoing quality assurance and quality control (QA/QC) monitoring to ensure the efficiency and accuracy of the production process and the quality of the final product. Similar to R&D testing needs, raw materials used in production are scrutinized for composition, concentration, and purity. As the workflow proceeds, monitoring is conducted at strategic checkpoints to ensure the process maintains high purity levels, efficiency, yield, and throughput.

Final product testing includes confirming the composition, quality, and safety of the fertilizer it is shipped to customers. The analyses conducted are similar to those for interim R&D formulations.

Table 1. Fertilizer Processes & Considerations

Fertilizer Production QA/QC Considerations		
Raw Materials	**In-Process Monitoring**	**Final Product**
• Composition • Concentration • Purity	• Presence of contaminants • Efficiency • Yield • Throughput	• Physical properties • Composition • Active ingredient concentration • Purity

Agrochemical Analytics

The testing conducted during agrochemical R&D provides much of the information required for product registration. The analyses and studies conducted typically include the following, along with other country-specific requirements:

- Active ingredient and product chemistry and equivalency
- Product formulations
- Product performance
- 5-Batch analysis
- Residue chemistry
- ADME studies (Absorption, Distribution, Metabolism and Excretion)
- Toxicity (human, domestic animal, and ecological)
- Environmental fate and transport
- Field dissipation
- Bioaccumulation
- Post-application exposure

Highly sensitive protocols and instruments are needed to achieve the very low detection limits needed for the chemical analyses.

Reliable **production** of agrochemicals is only possible when the industry's technical needs and challenges are successfully met. Some needs and challenges are common to all types of agrochemicals, others are segment specific. From raw materials to end product, agrochemical production uses a series of integrated steps that include QA/QC checks throughout the process. The first step in every agrochemical manufacturing workflow is analysis of raw materials for composition and purity before they enter the production process. As the workflow proceeds, monitoring is conducted at strategic checkpoints to ensure the process maintains high purity levels, efficiency, yield, and throughput.

Final products are evaluated for adherence to registration and use specifications such as composition, active ingredient concentration, purity, and stability. Final product testing also evaluates a battery of physiochemical properties:

- Partition coefficient
- Physical state
- Moisture
- Melting & freezing points
- Boiling point, relative density
- Surface tension
- Water solubility
- Organic solvent solubility
- Octanol/water partition coefficient
- Dissociation constant
- Flammability
- pH
- Viscosity
- Oxidizing or reducing properties
- Rate of hydrolysis (cold)
- Spectra (UV, UV/Vis, IR, NMR, MS)

Formulation-specific analyses may include the particle size distribution and shape of powders, the Zeta potential of colloidal suspensions, and the droplet size of sprays.

Table 2. Agrochemicals blends Processes & Considerations

Agrochemical Production QA/QC Considerations		
Raw Materials	**In-Process Monitoring**	**Final Product**
• Composition • Concentration • Purity	• Presence of contaminants • Presence of intermediates • Efficiency • Yield • Throughput	• Composition • Active ingredient concentration • Purity • Stability and shelf life • Physiochemical properties • Formulation-specific properties

Waste Management Testing

Process wastewater and other process wastes are generated by manufacturing facilities of all types. The contents of these and other waste streams produced by a fertilizer or agrochemical production facility depends on the materials and processes used at the facility.

Process wastewater discharge to an off-site treatment facility requires a permit from the facility and periodic sampling and analysis. The treatment facility will set the parameters for testing, waste volume and content limitations, and reporting. Some facilities use on-site wastewater treatment operations. The treated water may then be discharged to a local system or as a point-source discharge to a nearby water body. Permits are required for both options and will require sampling and analysis, volume and content limitations, reporting, and other locale-specific requirements.

Other process wastes may include off-specification or contaminated materials. Characterization, storage, and transport of the wastes must comply with national, state, and local requirements. A special permit may be required if any wastes are classified as hazardous or otherwise specially regulated. The waste disposal or treatment facility will require analytical data on the content of each unique waste stream to ensure their acceptance of the waste complies with the terms of their operating permit.

Employee Health and Safety Monitoring

The materials used and produced at fertilizer and agrochemical manufacturing facilities must be tightly controlled to prevent employee exposure. Potential routes of exposure include inhalation of volatile and semivolatile organic compounds and airborne particulates, dermal absorption of chemicals, and incidental ingestion of chemicals and particulates.

A comprehensive exposure prevention and monitoring program is essential to protect employee health and comply with regulatory standards. Some of the components of an effective health and safety program include:

- Personal protective equipment (PPE) requirements
- Target parameters to be monitored
- Sampling and analysis schedule and SOPs
- Analytical sensitivity requirements
- Remedial action alternatives
- Regulatory reporting requirements, schedule, and means
- Record-keeping practices
- Other regulatory-specific requirements

A well-designed, consistently implemented employee health and safety program not only protects employees, but it also helps the company avoid costly regulatory penalties and liability lawsuits.

Environmental Monitoring

Fertilizer and agrochemical manufacturing facilities typically require an air permit from national, regional, and/or local regulatory agencies. The permit specifies the parameters that must be monitored via air sampling and analysis, analytical methods approved for the analyses, the monitoring schedule, and reporting procedures to maintain the permit. The parameters to be monitored depend upon the materials, processes, and products at the facility.

A stormwater pollution prevention plan may also be required, depending on the extent of outside storage or operations at the facility. The plan includes sampling and analysis procedures for stormwater discharges, remedial action plans, and record-keeping and reporting procedures.

Summary

The fertilizer and agrochemicals industries have a long history of innovation that has helped improve food availability and quality for the world. Today, they face new challenges around the increasing need for food, decreasing agricultural land, climate-related impacts, and agrochemical resistant organisms. Exciting new discoveries and advanced technologies are poised to usher in the next wave of fertilizer and agrochemical innovation.

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