NATURAL RESOURCES & ENVIRONMENT

ABA SECTION OF ENVIRONMENT, ENERGY, AND RESOURCES

Enlisting Modern Technologies to Ensure a Safe Food Supply

By Lynn L. Bergeson

Nanotechnology, biotechnology, and synthetic biology are the ploughs and tractors of the twenty-first century. These precision farming tools are ensuring a sustainable food supply otherwise threatened by climate change and population growth, among other global challenges. Genetically modified *E. coli* is being used to produce synthetically derived pheromones, substances beneficially used in agricultural applications to attract, capture, and eliminate harmful pests. Nanopesticides and nanofertilizers are being effectively used in drought-stricken regions, eliminating or minimizing the need for conventional agricultural chemicals. These and similar technologies are essential to enable today's agricultural professionals to compete with an increasingly unforgiving Mother Nature and an ever-increasing demand for food.

These emerging technologies do not come without potential risks, however. How to regulate them is a subject upon which stakeholders disagree.

Against this backdrop, this article considers emerging agricultural technologies, and discusses domestic agricultural oversight systems and their ability to keep pace with innovation. As discussed below, the domestic governance system is capable of addressing comprehensively the potential risks posed by these evolving technologies. The system, however, could be improved by better integration of measures to educate policy makers and regulators on these technologies, and greater involvement by the private sector in facilitating a predictable flow of information on these technologies to all stakeholders.

Naturally occurring nanomaterials have been a part of the food processing industry for years. Nano-enabled tools and engineered nano-sized agricultural chemicals used in more dispersive applications—meaning the direct and intentional release of nanomaterials into the environment—are of more recent origin and understandably are viewed with caution, if not skepticism.

Government and private sector nanotechnology research and development have resulted in a growing number of commercialized products entering the market. Specifically, nanoagrochemicals, nanopesticides, and nanofertilizers are products of growing interest, given their demonstrated ability to deliver favorable results. As Melanie Kah notes in her paper, *Nanopesticides and Nanofertilizers: Emerging Contaminants or Opportunities for Risk Mitigation?*, Front. Chem. 2015:3, 64 (Nov. 16, 2015), a growing body of scientific literature has prompted some to speculate that a "revolution" in current agricultural practices is under way. Relevant nano applications include the use of nano and micro-emulsions, nano and micro-encapsulations, nanoparticle-based fertilizers, and the use of nanomaterials to improve photocatalytic efficiency. Nanotechnology-based biosensors reflect the utility of these technologies. They assist farmers in targeting areas for crop optimization and work in atypical environments such as in saline water, an especially useful feature to aquafarmers. Higher crop yields are expected to be achieved using nanoscale sensors that detect the presence of a virus or disease well before crop damage occurs. In addition, ongoing research is devoted to realizing the potential of nanotechnology to improve nutrition. Nanocapsules are being engineered to release nutrients targeted at certain areas of the body at optimal times of the day.

Sometimes referred to as "extreme genetic engineering," synthetic biology applies the same fundamental principles of traditional recombinant DNA, but at a much greater scope and speed using biological tools and methods. In October 2015, the Woodrow Wilson International Center for Scholars issued a *Synthetic Biology Project Report*, highlighting evolving synthetic biology technologies, including those pertinent to the agricultural sector, and focusing on the challenges to market entry for new product innovators. As alluded to above, one synthetic biology technology utilizes genetically modified *E. coli* to produce pheromones to aid in pest mitigation by attracting, capturing, and eliminating pests without the use of harmful chemicals or other pollution-causing agents. Other technologies being developed include a suite of tools using engineered yeast and fermentation techniques that produce foods, including animal-free milk products, and certain flavorings. Other technologies use engineered microalgae to produce algal butter and vegan proteins.

In a less obvious "agricultural" arena, synthetic biology applications are increasingly used to modify ornamental plants. These plants are valued for their flowers, leaves, scents, texture, fruit, stem, and bark—or simply for their unique aesthetic forms. They have been bred to accentuate desirable traits and minimize undesirable ones through traditional cross-breeding, grafting, and other techniques.

With synthetic biology, new opportunities are emerging to modify ornamental plants in ways that were not available through conventional techniques. Below are two examples of a burgeoning market in which companies are seeking to use modern synthetic biology and genetic technologies to develop ornamental plants and grasses with desirable characteristics, some of which offer significant environmental benefits.

Bioluminescent plants. Scientists at BioGlow LLC (BioGlow) inserted genes from luminous marine bacteria into *Nicotiana alata* (jasmine tobacco), a common flowering ornamental plant, producing a plant that is autoluminescent, meaning it glows in the dark with only standard plant nutrients. Glowing Plant, Inc. (Glowing Plant) also developed a luminescent plant. Building on technology similar to BioGlow's, Glowing Plant inserted genetic material into *Arabidopsis thaliana* (thale cress) using a "gene gun." Genes from *Photinus pyralis* (common eastern firefly) and two synthetic variants of genes from *Aequorea victoria* (crystal jelly) are inserted into the plant's genome. While these are not food applications, the technologies are expected to have broader agricultural application.

"Greener" grass. A January 1, 2015, *New York Times* article describes commercial efforts to develop genetically modified grass that requires less mowing, is deeper green in color, and is resistant to damage by the herbicide glyphosate. Andrew Pollack, *By 'Editing' Plant Genes, Companies Avoid Regulation*, N.Y. Times, Jan. 1, 2015 According to the article, using a gene gun, the manufacturer introduces genetic material from other plants that are not considered plant pests.

Agricultural Biotechnology

While the use of genetically modified organisms (GMOs) is not a technology new to the agricultural sector, the modern use of genetic engineering to recombine DNA in different organisms to the precise degree and speed that transpires today is what differentiates traditional biotechnology from more contemporary agricultural biotechnology. The availability of insect resistant crops capable of expressing *Bacillus thuringiensis* (Bt) protein has greatly increased corn, potato, and cotton crop yields. Genetic engineering and enzyme optimization are tools used to produce biofuels, resulting in energy-dense and high-yield crops. Pesticide-resistant crops save farmers time and money. The use of biochemical pesticides and advanced biotechnology tools that integrate nano-enabled devices are also on the horizon. The list of biotech innovations is long, and the implications are significant.

Oversight of Agriculture in the United States

Agriculture in the United States at the federal level is primarily governed by domestic farm bills renewed every five years. The most recent farm bill was enacted in 2014 and covers a range of topics, including conservation, commodities, farm credit, and rural development. Governance is both a federal and a state and local responsibility. The U.S. Department of Agriculture (USDA) is the federal agency responsible for the farm bill's implementation.

Other federal laws and state programs regulate specific aspects of agriculture. The Plant Protection Act (PPA) regulates the movement of plants, and treatment of plant pests, noxious weeds, and related organisms. Genetically modified crops are subject to the jurisdiction of multiple federal agencies under the Coordinated Framework for Regulation of Biotechnology. Issued in 1986, the Coordinated Framework sets forth an organizational blueprint for federal agencies and establishes lead responsibilities for the federal oversight of products of biotechnology. The core premise of the Coordinated Framework is that the legal authorities that existed in 1986—authorities that remain largely unchanged today—provide federal regulators with sufficient oversight authority to address any potential health or environmental risk that a biotechnology product might pose.

Under the Coordinated Framework, three federal agencies are principally responsible for regulating products of biotechnology: USDA—in particular the Animal and Plant Health Inspection Service (APHIS), the U.S. Environmental Protection Agency (EPA), and the U.S. Food and Drug Administration (FDA). APHIS is responsible for regulating field trials of genetically modified crops and plants under the PPA. EPA regulates genetically engineered microbes under the Toxic Substances Control Act (TSCA), and genetically engineered pesticides and pesticides incorporated into plants under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). FDA regulates a broad spectrum of products, including human and animal drugs, cosmetics, dietary supplements, food, food additives, and medical devices, among others under the Federal Food, Drug, and Cosmetic Act (FFDCA). How each agency regulates products of biotechnology, pursuant to what legal authority and when in the commercialization process regulatory oversight attaches, vary considerably.

In July 2015, the White House Office of Science and Technology Policy (OSTP), the Office of Management and Budget, the U.S. Trade Representative, and the Council on Environmental Quality directed EPA, FDA, and USDA to update the Coordinated Framework to ensure public confidence in the regulatory system and to prevent unnecessary barriers to future innovation and competitiveness. OSTP's July 2, 2015, blog entry notes that the complexity of the regulations and guidance documents developed by EPA, FDA, and USDA can make it difficult for the public to understand how the safety of products of biotechnology is evaluated and for small companies to navigate the process. Given the complexity of the regulations and the involvement of three agencies, the updating process will be challenging. On September 22, 2016, the White House published a proposed update of the Coordinated Framework and addressed specifically the roles and responsibilities of EPA, FDA, and USDA with respect to the regulation of biotechnology products.

Pesticides are a critically important part of agriculture and are regulated in the United States by EPA under FIFRA and FFDCA, as amended in 1996 by the Food Quality Protection Act (FQPA). FIFRA broadly defines a pesticide as "any substance or mixture of substances intended for preventing, destroying, repelling, or mitigating any pest." To approve a pesticide registration, EPA must conclude that the pesticide performs its intended function without causing unreasonable adverse effects on the environment. Optimally, EPA's risk assessment of a pesticide is predicated on robust and complete data. Because there may be, and usually are, gaps in the database for a pesticide, EPA risk assessors often estimate values and use professional judgment when performing risk calculations. The risk assessment process is iterative. New data and other information and revised assessment techniques may support a refined risk assessment. FIFRA authorizes EPA to obtain any additional data deemed necessary to maintain "in effect an existing registration."

Pursuant to FFDCA Section 408(b)(2)(A), the standard for establishing a tolerance (the amount of pesticide residue that may lawfully remain on food) is whether there is a "reasonable certainty that no harm" will result from exposure to the pesticide, including all dietary and other exposures. FIFRA registrants must obtain pre-market approval before commercializing their products, a process that can take years and requires significant data to support the safety finding that EPA must make under FIFRA.

U.S. Governance Approach to Evolving Technologies

How the United States regulates food and feed products derivative of evolving technologies is a function of the specific use at issue, the application of the legal authorities summarized above, and other constantly evolving policy considerations. The domestic approach is based on principles of risk assessment, risk management, and risk communication. It recognizes the economic value of the agricultural sector, the absolute need for food safety, and the value of broad stakeholder engagement at the national and local levels. The approach requires voluminous scientific data generated by manufacturers to form the basis of the risk management decisions made by the respective regulatory officials.

At a policy level, the federal government is squarely supportive of evolving technologies. A 2011 White House Executive Office policy document reinforces this fact and expresses the administration's view that a primary goal of the regulatory review process is to achieve "consistent approaches across different emerging technologies and to ensure the protection of public health and the environment while avoiding unjustifiably inhibiting innovation, stigmatizing new technologies, or creating trade barriers." Office of Science and Technology Policy, *U.S. Decision-making Concerning Regulation and Oversight of Nanotechnology and Nanomaterials*, June 11, 2011. Thus, at a policy level, the federal government has been and remains staunchly supportive of emerging technologies, and the executive branch, regardless of party, has supported the view that existing legal and governance authorities are sufficient to control potential risks derivative of these technologies.

A clear indication of this support was reflected in President Bill Clinton's creation of the National Nanotechnology Initiative (NNI) in 2000 under the 21st Century Nanotechnology Research and Development Act. Broad bipartisan support for the NNI has continued for years. The federal government's overarching view regarding the regulation of nanomaterials, consistently echoed by the 20 departments and independent federal agencies participating in the NNI, is that existing laws are sufficient to ensure safety.

With regard to nanomaterials used in food and feed applications, the U.S. approach is based on traditional principles of risk assessment that consider the physical-chemical properties of specific nanoscale substances and materials. Product applications are reviewed on a case-by-case basis, and no inferences adverse to the review are premised on size considerations alone. EPA's specific FIFRA policies on nanomaterials, as well as its adoption of risk assessment policies and approaches, have been evolving over the years. Under FIFRA, EPA has conditionally approved two nanosilver pesticide registrations, each considered a new "active ingredient" and subjected to the most stringent review under FIFRA. On December 1, 2011, EPA announced the conditional registration of HeiQ AGS-20, a nanosilver-based antimicrobial pesticide product approved for use as a preservative for textiles. On May 19, 2015, EPA announced a second conditional registration for a nanosilver-containing antimicrobial pesticide product named "Nanosilva." According to EPA, the product will be used as a non-food-contact preservative to protect plastics and textiles from odor- and stain-causing bacteria, fungi, mold, and mildew. EPA based its decision on its evaluation of the hazard of nanosilver after reviewing exposure data and other information on nanosilver from the applicant, and data from the scientific literature.

While EPA appears ready to embrace nanopesticides, other stakeholders have expressed a different view. The Natural Resources Defense Council (NRDC) sued EPA over both conditional nanosilver registrations. In 2013, the U.S. Court of Appeals for the Ninth Circuit granted in part and denied in part NRDC's challenge to HeiQ's registration, *NRDC v. EPA,* 735 F.3d 873 (9th Cir. 2013), providing NRDC with a largely esoteric victory on a narrow risk question that caused momentary recalculations in the risk assessment, but no commercial disruption. On July 27, 2015, two petitions for review of the Nanosilva conditional registration were filed in the Ninth Circuit. NRDC filed a petition, as did the Center for Food Safety and International Center for Technology Assessment. Both petitions ask the court to set aside EPA's final order granting the conditional registration, arguing EPA lacked the data necessary to issue the registration. Oral argument was heard in March 2016, and a decision is expected before the end of 2016.

A case study outlined in the referenced Woodrow Wilson Synthetic Biology Report illustrates the complexity of evolving technologies and the struggle to keep pace with the speed of innovation. In connection with the BioGlow product mentioned earlier, BioGlow submitted to APHIS information pertinent to support the regulatory review of the product. Following its review, APHIS concluded in 2013 that it did not have regulatory jurisdiction over the plants because the plants were not "plant pests," because no organisms used as sources of the genetic material to create the plants were plant pests, and the method used to genetically engineer the plants did not involve plant pests. APHIS reached a similar conclusion regarding Glowing Plant's product in 2014. APHIS concluded that because no plant pests, unclassified organisms, or organisms whose classification is unknown were being used to genetically engineer the plant, APHIS had no reason to believe that the plant was a plant pest, and did not consider the genetically engineered plant to be regulated under the PPA.

Cognizant of the need to modernize the oversight of genetically modified plants and other organisms, as noted above, the Obama administration initiated in 2015 a comprehensive updating of the Coordinated Framework, which is now under way. Whether the initiative will be sustained by the next administration is, of course, unclear. The hope is that the excellent work that is now underway will continue, as the Coordinated Framework needs modernizing to keep pace with the relentless press of innovation.

Areas for Oversight Improvement

As described above, federal oversight of agricultural technologies in the United States is comprehensive, complicated, and constantly evolving. The system is based on rigorous scientific analyses, and the considerations for product approval are comprehensive and robust. The U.S. government is openly supportive of, and keen to promote, technologies and their applications in the agricultural sector as a matter of policy, and views U.S. competitiveness with other countries enhanced by fostering a "can do" attitude. The United States' approach to managing potential risks is rooted in laws regulating "products," and not the technologies that produce them. The federal agencies charged with implementing these laws, EPA and FDA, respectively, have for years been actively engaged in reviewing, adapting, and modernizing the authorities available to them; their regulatory actions are properly calibrated to identify and manage, as appropriate, any potential risk that the products of these technologies may pose. Thus far, no known human and environmental health problems have been identified with regard to the products of any emerging technology.

There is need for improvement, however. Considering governance approaches that are more solicitous of public engagement and more cognizant of the values that risk-benefit decisions necessarily involve would improve our governance approach. Managing risk is about achieving a prudent outcome that is preferred over others. To make informed decisions that result in such outcomes, governance approaches must ensure that the public is sufficiently informed to make good choices early enough in the administrative process to make a difference.

As a corollary to better education, managing optics has become an important part of the process for any stakeholder. The media—particularly social media—play a significant role in framing issues and driving public opinion.

A second point that may contribute to greater coherence in the United States oversight system is a clearer conceptual framework for quantifying "benefits." The public and decision makers hear a great deal about risks from evolving technologies. Decision makers, however, hear too little about benefit, and what they do hear is not always managed in a way that enables a clear understanding of how risks and benefits should be considered in a regulatory context. Discussion of benefits is usually represented by a narrow and often stilted esoteric cost/benefit approach, with analysis of economically viable alternatives to the selected risk, typically allowing for less consideration of broader and more socially relevant issues such as the role technology plays as a socially disruptive agent. The long-range impacts of technology are seldom part of the debate.

The spread of the Zika virus offers an example of the need to better quantify benefits from a biotechnology application. In the United States, FDA recently asked for comment on Oxitec's draft environmental assessment of the Oxitec mosquito, a genetically engineered male mosquito strain that, when released into the wild, could result in an overall 90 percent reduction in the *Aedes aegypti* strain that is known to carry the Zika virus and other viruses. Other alternatives largely involve broadcast applications of pesticides, which are less targeted at non-native *A. aegypti* mosquitos.

The threshold question that FDA's review answered in the affirmative is whether the risk of a test releasing a limited number of genetically engineered male *Aedes aegypti* mosquitos over a limited geographical area is sufficiently low to justify the test. FDA concluded that the probability that the release "would have adverse impacts on the ecosystem is largely negligible."

The harm the Zika virus is known to cause is considerable. Based on the data, the Oxitec mosquito may well be the best weapon we have for combating its spread. Nonetheless, given the concerns that this technology invites, it is unclear how the public will respond, and whether, despite the FDA's conclusion, the fear of genetically modified mosquitos will trump the fear of becoming infected with the Zika virus.

A third point relates to the continuing acute challenge of ensuring technological literacy within the ranks of decision makers and the public at large. As technological innovations, especially those that impact the food supply, become more and more sophisticated, the demands placed on decision makers and their scientific staffs, if they have them, are increasingly steep. The urgent need for literacy must be filled by a reliable, credible, and systematic source of balanced information.

The same holds true for federal agencies. With budgets being reduced and declining staff, the resources currently are insufficient to ensure that persons deciding chemical risk-benefit tradeoffs have the tools and resources they need to make informed decisions. The Office of Technology Assessment (OTA) existed form 1972 until 1995, when it was disbanded, a victim of the Gingrich "Contract with America" period as it was deemed wasteful. This trend must be reversed if regulatory agencies are to maintain the high level of technological competence and literacy needed to ensure informed decision making. Otherwise, in terms of public communication or avoiding political controversy, it is an easier path for a regulatory agency to say "no" or "not yet" with respect to a new technology or product, instead of explaining why the science supports the new product.

This is where the private sector could improve and enhance its efforts to educate the public, the regulatory community, and lawmakers about new innovations, and help cultivate and maintain a high level of technological literacy—taking advantage of all forms of media. As noted earlier, how issues are framed and communicated is a critical part of the decisional process, and it is essential to ensure that the media is technologically literate and conversant with the issues. This could be done through public-private partnerships, enhanced funding to independent think tanks, or other means targeted at explaining new chemical innovations and ensuring that the regulatory bodies that assess them, and the public, are well informed about these innovations' risks and benefits.

With respect to innovations of any kind, and not just those pertinent to the agricultural sector, a large societal challenge is misinformation and the fear it cultivates, rapidly spread by social media. The private sector needs to step in and step up to become a more significant part of the public process if it has any chance of blunting the bad optics and politics that flow from agricultural innovations that are victims of misinformation. There are no risk-free options. There are only tradeoffs that must be based on informed decision making and an honest assessment of the values underlying these on which the options are based.

Conclusion

Ensuring a reliable and safe global food supply will only get harder as the effects of climate change and population growth intensify. Today's agricultural professionals are increasingly dependent upon evolving technologies to maximize crop yields, enhance vector control, and optimize the utility of dwindling land capacity. These new agricultural technologies are engineered to be sustainable. Domestic oversight of these emerging technologies comprehensively assesses and assures their safety, but more needs to be done to provide lawmakers, regulators, and the public with credible and current information about their risks and benefits. Given the financial constraints facing federal and state governments, the burden falls on the private sector to step up efforts to educate and promote the safety and value of these emerging technologies and the essential role they play in feeding the world.

