Regulating Pharmaceutical Plants: Meeting the Challenge

Cindy Smith
Biotechnology Regulatory Services
USDA-APHIS
Washington, DC

The United States Department of Agriculture's Animal and Plant Health Inspection Service (APHIS) has regulated genetically engineered (GE) organisms since 1987 and, in 2002, established Biotechnology Regulatory Services (BRS) to place a renewed emphasis and priority on biotechnology. APHIS has authorized more than 10,000 permits and notifications for the introduction of GE organisms and deregulated over sixty products for use, establishing itself as an international leader in the safe regulation of GE products.

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As the science of biotechnology and the landscape in which it operates continue to evolve, APHIS's role in regulating it becomes increasingly challenging. As a regulatory authority of this rapidly growing technology, we must ensure that we protect US agriculture, allow for the safe development of GE organisms, and not unduly inhibit the advancement of the technology. One important challenge is to keep up with the science's technological advances. An increasingly broad array of traits is being engineered into plants as scientists discover more genes from a wider assortment of organisms that might be useful to improve agriculture, protect the environment or benefit consumers. But perhaps one of the most challenging technological trends of the past few years, from a regulatory perspective, has been the use of agricultural crops to produce pharmaceutical compounds and other items not intended for food or feed. One regulatory challenge is to allow the cultivation of these and have effective systems in place that will prevent them from being mixed with other crops, some of which are to be used as food or feed. In addition, pharmaceutical technology has prompted interest from a new range of stakeholders. Since 1987, BRS has issued 110 pharmaceutical and industrial permits in eleven crops; however, less than 350 acres have been grown since 2002.

Another important challenge is the changing social and political landscape. US citizens are becoming increasingly interested in biotechnology and want to play a larger role in government decision-making. In addition, citizens can be skeptical of the government and are willing to take action against government decisions. We have also seen an increase in the activity of public-interest groups who want to represent constituent views of the science and how government should regulate it. One outcome of this is that government agencies have become the target of lawsuits. In addition, biotechnology does not enjoy the same level of acceptance internationally as in the United States, posing an even greater challenge beyond our borders.

Biotechnology Regulatory Services

Since its inception just 3 years ago, BRS has undergone significant reorganization and is better prepared to anticipate and respond to the challenges being brought forth by the evolving nature of biotechnology and the landscape. The newly reorganized BRS goes well beyond a staff of scientists to evaluate permit applications and petitions for deregulation. It includes a Compliance and Inspection Branch, a Communications and Capacity Building Branch, a Regulatory Analysis Branch, an Office of Science, and a forecasting function that help BRS address these challenges and keep pace with the advancing science. In addition, we have developed five priority areas of emphasis that set program direction and provide the foundation for decision-making. These priority areas are the key to BRS's ability to meet the challenges of regulating biotechnology in general, and specifically, plants engineered to produce pharmaceuticals.

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Environmental Impact Statement

To ensure that our regulations remain effective as the technology advances, APHIS is currently preparing an Environmental Impact Statement (EIS) that will be used in revising its regulations. The updated regulations will leverage the additional authorities of the Plant Protection Act of 2000, significantly broadening APHIS's authority and positioning the USDA to address a broader range of issues, including human health. In the Notice of Intent that was published in January 2004, we stated that we are considering numerous revisions. One change we are considering is the implementation of a multi-tiered, risk- and familiarity-based permitting system to replace the current permitting and notification system. With respect to pharmaceuticals, another change we are considering is a new mechanism for maintaining regulatory oversight after a crop is commercialized. This mechanism would feature increased transparency and efficiency, and a greater role for the states. We are also considering the establishment of safety criteria that might allow for the deregulation of certain pharmaceutical crops.

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Reducing the Regulatory Burden

BRS is also committed to reducing the regulatory burden as appropriate to the risk. We appreciate that this is especially important for publicly funded researchers and small businesses. In pursuing this goal, we requested feedback on ways we could reduce regulatory burden in our January 2004 Federal Register notice that announced our intent to prepare an environmental impact statement on our proposed regulation changes. In addition, we have held workshops with the Pew Initiative on Food and Biotechnology and with USDA's Agricultural Research Service and Cooperative State Research, Education, and Extension Service to identify possible regulatory barriers and potential solutions. The IR-4 program for pesticide registration for use on minor crops has been proposed as a model that the government might follow to reduce the burden imposed on researchers and small businesses who are developing GE crops. It has also been suggested that alliances might be established between small businesses and university researchers such that the burden on generating required data might be shared, and thereby not be prohibitive to any individual researcher or small company who might seek to develop a GE crop.

Fostering the Technology

In addition to maintaining rigorous regulation, it is critical that we administer a compliance program that is strong enough to ensure the safety of the science while also allowing for the advancement of the technology. This is especially true for higher risk crops, such as those used to produce pharmaceuticals. BRS's Compliance and Inspection Branch is dedicated exclusively to ensuring that researchers maintain compliance through defined procedures that include violation-prevention efforts, risk-based criteria for quality inspec-

tion, standardized inspection and auditing processes, uniform enforcement, and thorough documentation of any compliance infractions. We also make investigation results available for public and stakeholder viewing. Compliance specialists and APHIS inspectors perform targeted inspections and audits of field tests and use established criteria to thoroughly evaluate all potential compliance infractions.

The second priority is ensuring that our regulatory process and decision-making are transparent to stakeholders and the public.

The second priority is ensuring that our regulatory process and decision-making are transparent to stakeholders and the public. Being transparent about our processes, decisions, and activities is critical for building public confidence in the regulatory system. We also understand that it is particularly important to be transparent in regard to pharmaceuticals. We must meet the challenge of fulfilling this objective while also protecting developers' confidential business information. Part of our transparency efforts include following the National Environmental Policy Act (NEPA), which establishes the criteria on when to conduct an environmental assessment (EA). We make available on our Web-site all EAs conducted for pharmaceutical and industrial field tests, or in cases that we do not conduct an EA, we post APHIS's categorical exclusion criteria and all NEPA decision documents. We also announce the EAs in the Federal Register and allow for a comment period. Our Web-site also provides a listing of all pharmaceutical permits along with their current status, accompanying decision documents, total acreage, and any supplemental permit conditions. Though confidential business information (CBI) limits our ability to post all permit applications, we post as much information as we can. In one recent case, we posted permit applications where little or no CBI was claimed and in another recent case, we summarize the non-CBI information from permit applications in our EAs. In addition, even when specific location and size information of field tests is claimed as CBI, we provide the general location and size information. We have also completely redesigned our Web-site and have included a stakeholder registry that allows registered stakeholders to receive updates and other information relevant to selected topics of interest, such as regulation activities, communication and outreach, capacity building, and compliance issues.

In another effort to ensure transparency, in 2004, we held multiple public meetings to discuss issues associated with the BRS proposal to revise regulations. BRS met with twenty-two stakeholder groups and heard a wide range of viewpoints on the proposed revisions and provided clarification on some of our agency's objectives. In the near future, we will be holding similar stakeholder meetings on a monthly basis as we complete the process of developing a Programmatic EIS on our proposed regulatory changes.

Assuring Safety

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to achieve this priority, we face the challenge of obtaining all of the available scientific information needed in order to make sound science-based decisions. To help achieve this goal, we have expanded our staff to include a diversified collection of scientific expertise in science fields, such as plant pathology, botany, entomology, ecology, animal science, virology, environmental science, biochemistry and molecular biology. To keep pace with this ever-evolving technology, BRS staff and scientists attend and host meetings and workshops, read literature, and interact with outside scientists, stakeholders, and the public. Additionally, in 2002, BRS established the Office of Science, which works with the research community to identify biosafety research priorities and to communicate biosafety research results for the use of regulators globally. As part of its agenda, the Office of Science addresses scientific issues associated with pharmaceuticals and in August 2004, conducted a workshop on confinement that focused largely on pharmaceutical crops; more than 100 scientists and experts from six countries participated. The Office of Science also helps maintain science as the centerpiece of regulatory decision-making amidst the challenges of diverse political, economic, and personal viewpoints associated with the technology. We also encourage biotechnology research and are looking into the possibility of becoming a funding agency in the future, such that we might target areas of research that we identify as having a pressing need.

The fourth priority is maintaining communication, coordination, and collaboration with the full range of stakeholders.

Communicating with Stakeholders

The fourth priority is maintaining communication, coordination, and collaboration with the full range of stakeholders. BRS works to meet the challenge of recognizing and reaching out to a broad range of stakeholders and interests. In regard to pharmaceuticals, it is particularly important to reach out to a broad diversity of stakeholders that includes not only the biotechnology industry and researchers, but also stakeholders such as in the food industry, commodity groups, public interest groups and the states. For example, we recently met with a food-industry group to discuss additional science-based measures that BRS should consider for two pharmaceutical field tests.

In another example, we work closely with the states on issuing permits, particularly for pharmaceuticals. We provide information to support their decision-making, which may involve adding additional permit conditions to address the state's concerns or, in some cases, providing support such that the state has a full understanding of the science.

The fifth priority is establishing international leadership.

International Leadership

Finally, the fifth priority set forth by BRS is establishing international leadership to ensure that international biotechnology standards are science-based, international regulatory capacity-building is supported, and international implications of domestic policy and regulatory decisions are considered. BRS faces the challenge of providing international leadership to ensure the development of science- and risk-based regulatory systems while maintaining effective working relationships in which we recognize and respect the differences in their systems and they are in turn receptive to our approach and the benefits that it can offer. In addition, we must consider the international implications of any domestic policy decisions that we make and ensure that the policies that we put in place domestically can be applied equally internationally. These important international partnerships are now serving as a starting point for international discussions of the regulation and confinement of pharmaceutical crops.

Through our evolving regulatory structure, dedicated compliance function, focus on science and risk, increased transparency and communication with a broad range of stakeholders, we are focused on these priorities and managing the challenges posed by new trends such as pharmaceutical crops. As the science progresses, we will continue to evaluate the implications of new technologies, enhance our processes and procedures, and develop appropriate regulations to meet the challenges posed by this new science while continuing to safeguard American agriculture, the nation's food supply and the environment.

Cindy Smith currently serves as deputy administrator for the Animal and Plant Health Inspection Services (APHIS) Biotechnology Regulatory Services (BRS). She has been charged with providing leadership to BRS, the newly formed APHIS program that was created as a result of a restructuring of APHIS's biotechnology regulatory functions in June of 2003. BRS is responsible for the regulation of the import, interstate movement and field-testing of transgenic plants, and is currently evaluating the role it will play in the regulation of transgenic animals and arthropods.

Ms. Smith has worked at APHIS since 1979, playing various roles across four APHIS programs: Plant Protection and Quarantine (PPQ); Biotechnology, Biologics and Environmental Protection (BBEP); Wildlife Services(WS); and BRS. Prior to assuming her leadership role with BRS, she most recently served as associate deputy administrator of Wildlife Services, the federal program protecting agriculture, natural resources, property and humans from wildlife damage.

Smith obtained a masters degree in management from the University of Maryland in 2000, and holds a BS in microbiology, also from the University of Maryland (1983).