National Strategy for Modernizing the Regulatory System for Biotechnology Products

Product of the Emerging Technologies Interagency Policy Coordination Committee's Biotechnology Working Group

September 2016

About the Emerging Technologies Interagency Policy Coordination Committee

Assembled under the auspices of the National Science and Technology Council (NSTC), the purpose of the Emerging Technologies Interagency Policy Coordination Committee is to serve as a point of coordination for identifying and, where appropriate, addressing cross-cutting policy issues, such as regulatory approaches, associated with areas that affect multiple agencies and would benefit from a clear, consistently applied U.S. Government position. The group was established to help agencies develop, coordinate, and apply the broad range of policies associated with emerging technologies to further government interests and oversight, and to foster leadership and consistency internationally.

About the Office of Science and Technology Policy

The White House Office of Science and Technology Policy (OSTP) was established by the National Science and Technology Policy, Organization, and Priorities Act of 1976. OSTP's responsibilities include advising the President in policy formulation and budget development on questions in which science and technology are important elements; articulating the President's science and technology policy and programs; and fostering strong partnerships among Federal, State, and local governments, and the scientific communities in industry and academia. The Director of OSTP also serves as Assistant to the President for Science and Technology and manages the NSTC. More information is available at www.whitehouse.gov/ostp.

About the Emerging Technologies Interagency Policy Coordination Committee Biotechnology Working Group

The Emerging Technologies Interagency Policy Coordination Committee Biotechnology Working Group (Biotechnology WG), an interagency group organized under the NSTC, was established in response to a 2015 Executive Office of the President Memorandum for Heads of Food and Drug Administration, Environmental Protection Agency, and Department of Agriculture entitled *Modernizing the Regulatory System for Biotechnology Products*. That memorandum established the Biotechnology WG to take steps to increase the transparency, coordination, predictability, and efficiency of the regulatory system for the products of biotechnology.

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Executive Summary

The policy of the United States Government is to seek regulatory approaches that protect health and the environment while reducing regulatory burdens and avoiding unjustifiably inhibiting innovation, stigmatizing new technologies, or creating trade barriers.[1,2,3] These principles also apply to the update of the regulatory framework and systems that regulate the products of biotechnology put forward in this National Strategy for Modernizing the Regulatory Framework for such products. Federal agencies that regulate biotechnology products should strive continually to improve predictability, increase efficiency, and reduce uncertainty in their regulatory processes and requirements. It is critical that these improvements:

- maintain high standards that are based on the best available science and that deliver appropriate health and environmental protection;
- establish transparent, coordinated, predictable, and efficient regulatory practices across agencies with overlapping jurisdiction; and
- promote public confidence in the oversight of the products of biotechnology through clear and transparent public engagement.

While the current regulatory system for the products of biotechnology effectively protects health and the environment, in some cases, uncertainty about agency jurisdiction, lack of predictability of timeframes for review, and other processes have imposed unnecessary costs and burdens on small and mid-sized companies and academics. In response, in July 2015, the Executive Office of the President (EOP) issued a memorandum[4] (July 2015 EOP memorandum) directing the primary agencies that regulate the products of biotechnology—the U.S. Environmental Protection Agency (EPA), the U.S. Food and Drug Administration (FDA), and the U.S. Department of Agriculture (USDA)—to accomplish three tasks:

- update the Coordinated Framework for the Regulation of Biotechnology (Coordinated Framework) by clarifying current roles and responsibilities;
- develop a long-term strategy to ensure that the Federal regulatory system is equipped to efficiently assess the risks, if any, of the future products of biotechnology; and
- commission an expert analysis of the future landscape of biotechnology products to support this effort.

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[1] "Improving Regulation and Regulatory Review", Executive Order 13563, January 18, 2011.
[2] "Identifying and Reducing Regulatory Barriers", Executive Order 13610, May 10, 2012.
[3] "Principles for Regulation and Oversight of Emerging Technologies", Memorandum for the Heads of Departments and Agencies, March 11, 2011.
[4] Memorandum for Heads of Food and Drug Administration, Environmental Protection Agency, and Department of Agriculture, "Modernizing the Regulatory System for Biotechnology Products", Executive Office of the President, July 2, 2015. The memorandum can be found at https://www.whitehouse.gov/sites/default/files/microsites/ostp/modernizing_the_reg_system_for_biotech_products_memo_final.pdf

In directing the agencies to accomplish these three tasks, the Administration's goal is to ensure public confidence in the regulatory system and improve the transparency, predictability, coordination, and, ultimately, efficiency of the biotechnology regulatory system. This *National Strategy for Modernizing the Regulatory System for Biotechnology Products* was developed in order to satisfy the second of the three tasks identified in the July 2015 EOP memorandum and the accompanying proposed Update to the Coordinated Framework was developed to satisfy the first of the three tasks. EPA, FDA, and USDA have commissioned an independent study by the National Academy of Sciences (NAS) to satisfy the third of the three tasks.

Background

The discovery of the three-dimensional structure of DNA in 1953 by Rosalind Franklin, James Watson, and Francis Crick laid the groundwork for an era of innovation in the life sciences. Twenty years later, Stanley Cohen and colleagues described recombinant-DNA techniques that could be used to cut gene sequences from the DNA of one organism and splice them into the DNA of another organism.[5]

In response to concerns as to whether the "regulatory framework that pertained to products developed by traditional genetic manipulation techniques was adequate for products obtained with the new techniques,"[6] such as recombinant DNA, the Coordinated Framework for the Regulation of Biotechnology was published in 1986. It outlined a comprehensive Federal regulatory policy for ensuring the safety of biotechnology products and described oversight responsibilities under existing statutes and among the relevant Federal agencies. While the Coordinated Framework addressed which agency(ies) have oversight authority for biotechnology products, it "did not address how that authority should be exercised in the frequent situations in which a statute leaves the implementing agency latitude for discretion."[7] Thus, in 1992, the Coordinated Framework was updated to describe the "proper basis for agencies' exercise of oversight authority within the scope of discretion afforded by statute."[7]

In part, the oversight system established by the Coordinated Framework led to decades of development and commercialization of biotechnology products with applications in medicine, agriculture, energy, biomanufacturing, and environmental protection, and to the growth of a large and competitive biotechnology sector in the United States and worldwide.

Advances in science and technology have, however, dramatically altered the biotechnology landscape since the issuance of the 1986 Coordinated Framework and associated 1992 update, enabling the development of products that were not envisioned when the 1986 and 1992 documents were published. Consequently, a further update of the Coordinated Framework was needed to facilitate the appropriate Federal oversight by the regulatory system and increase transparency, while continuing to provide a framework for advancing innovation.

In July 2015, the Administration released a memorandum[4] (July 2015 EOP memorandum) noting that while "the current regulatory system for the products of biotechnology effectively protects health and the environment, in some cases, unnecessary costs and burdens associated with uncertainty about agency jurisdiction, lack of predictability of timeframes for review, and other processes have arisen. These costs and burdens have limited the ability of small and mid-sized

[5] Cohen, S.N., A.C.Y. Chang, H, Boyer, and R.B Helling. 1973. Construction of biologically functional bacterial plasmids in vitro. Proceedings of the National Academy of Sciences of the United States of America 70:3240–3244.
[6] https://www.aphis.usda.gov/brs/fedregister/coordinated_framework.pdf
[7] https://www.whitehouse.gov/sites/default/files/microsites/ostp/57_fed_reg_6753__1992.pdf

companies to navigate the regulatory process and of the public to understand easily how the safety of these products is assured."

That memorandum reiterated that the Federal regulatory system must protect health and the environment while reducing regulatory burdens and avoiding unjustifiably inhibiting innovation, stigmatizing new technologies, or creating trade barriers. It also initiated a process to modernize the Federal regulatory system for biotechnology products[8] and to establish mechanisms for periodic updates of that system.[4]

The objectives of the tasks described in the July 2015 EOP memorandum are to ensure public confidence in the regulatory system and to prevent unnecessary barriers to future innovation and competitiveness by improving the transparency, predictability, and efficiency of the regulation of biotechnology products and the coordination among regulatory agencies, while continuing to protect health and the environment.

This *National Strategy for Modernizing the Regulatory System for Biotechnology Products* (*Strategy*) sets forth a vision for ensuring that the Federal regulatory system is prepared to efficiently assess the risks, if any, of the future products of biotechnology. The *Strategy* and the accompanying proposed Update to the Coordinated Framework, which *inter alia* clarifies agency jurisdiction for biotechnology products, were developed by the Biotechnology WG. The Biotechnology WG was established by the July 2015 EOP memorandum under the Emerging Technologies Interagency Policy Coordination (ETIPC) Committee.

To inform the development of these documents and other activities described in the July 2015 EOP memorandum, the National Science and Technology Council (NSTC) published a notice of request for information (RFI) in the *Federal Register* to seek relevant data and information from stakeholders. In addition, the White House Office of Science and Technology Policy (OSTP), EPA, FDA, and USDA jointly held three public meetings, under the auspices of the NSTC, in different regions of the country to inform the public about their activities and seek public comments.[9,10,11] Transcripts of the public meetings, including oral comments received at the meetings, were placed in the public docket.[12] The third public meeting also included breakout listening sessions, and a summary of individual input received during those sessions is available in the public docket.[12] The Biotechnology WG reviewed all written comments submitted in response to the RFI, oral comments made at the three public meetings, and input from the breakout listening sessions, in preparing this *Strategy*. A general summary of the issues raised in

[8] "Biotechnology products" refers to products developed through genetic engineering or the targeted or in vitro manipulation of genetic information of organisms, including plants, animals, and microbes. It also covers some of the products produced by such plants, animals, and microbes or their derived products as determined by existing statutes and regulations. Products such as human drugs and medical devices are not the focus of the activities described in the memorandum (July 2015 EOP memorandum).

[9] http://www.fda.gov/NewsEvents/MeetingsConferencesWorkshops/ucm463783.htm

[10] https://www.epa.gov/regulation-biotechnology-under-tsca-and-fifra/modernizing-regulatory-system-biotechnology-products

[11] https://www.aphis.usda.gov/aphis/ourfocus/biotechnology/stakeholder-meetings/cf_meeting/

[12] http://www.regulations.gov/docket?D=FDA-2015-N-3403

public responses and a review of these responses is provided in Appendix 1 of the proposed Update to the Coordinated Framework. EPA, FDA, and USDA will continue to consider relevant public responses as part of future work related to the implementation of this *Strategy*.

In addition, as these agencies continue their work in pursuit of the objectives in the July 2015 EOP memorandum, consideration will be given to additional actions to clarify further their regulatory processes and procedures, as appropriate. In this regard, agencies will consider the results of the forthcoming National Academy of Sciences report on the *Future Biotechnology Products and Opportunities to Enhance Capabilities of the Biotechnology Regulatory System*.

Goals and Objectives

The goal of this *Strategy* is to ensure that the Federal regulatory system is equipped to efficiently assess the risks, if any, associated with future products of biotechnology while supporting innovation, protecting health and the environment, promoting public confidence in the regulatory process, increasing transparency and predictability, and reducing unnecessary costs and burdens. EPA, FDA, and USDA intend to fulfill this goal, including by addressing the following priorities identified in the July 2015 EOP memorandum.

Increasing Transparency

- Establish a timetable and mechanisms to work with stakeholders to identify impediments to innovation, focusing on building new, and augmenting existing, stakeholder collaborations to inform efforts, increase transparency, streamline processes, reduce costs and response times, and ensure the protection of health and the environment
- Coordinate the development of tools and mechanisms for assisting small businesses developing biotechnology products to navigate the regulatory system
- Develop a modernized, user-friendly set of tools for presenting to the public the regulatory agencies' authorities, practices, and bases for decision making for the regulation of biotechnology products, including digital services, to improve the interactions among FDA, EPA, USDA, the general public, and product developers, as well as updating these tools and practices regularly to ensure optimal transparency
- Engage with the public to discuss how the Federal Government uses a risk-based, scientifically sound approach to regulating the products of biotechnology, and clearly communicating to the public which types of products are regulated, which types of products are not regulated, and why

Increasing Predictability and Efficiency

- Develop a plan for periodic, formal horizon-scanning assessments of new biotechnology products to ensure that regulatory agencies are prepared for future products well before they reach the regulatory system

- Ensure product evaluations are risk-based and grounded in the best science available, including regularly adjusting regulatory activities based on experience with specific products and the environments into which those products have been introduced
- Identify changes to authorities, regulations, and policies that could improve agencies' abilities to assess expeditiously the potential impacts and risks arising from future products of biotechnology and to ensure the transparency, predictability, and efficiency of regulatory oversight for such products

Supporting the Science that Underpins the Regulatory System

- Develop a coordinated and goal-oriented plan for supporting the science that informs regulatory activities with regard to the assessment of biotechnology products, and to reflect these priorities in agency budget submissions

Increasing Transparency

EPA, FDA, and USDA have developed processes to communicate with the public and stakeholders, including consumers and small businesses. For example, all three of these agencies have mechanisms for soliciting and utilizing public input related to regulatory decisions. Examples include advisory committees of experts in key disciplines relevant to specific products or product areas;[13] opportunities for public input on regulations and guidance documents, through petitions on certain environmental assessments and impact statements, and through public meetings; webinars and workshops on the regulatory framework for interested stakeholders, including industry and consumers; and information on regulatory activities and updates for consumers posted on agency websites. The agencies' websites provide information to the public on agencies' activities, including guidance for developers of products subject to regulatory oversight, and consumer and public-oriented brochures and factsheets, many of which are available several different languages.

The proposed Update to the Coordinated Framework that accompanies this *Strategy* contains a table that summarizes the current responsibilities and the relevant coordination across EPA, FDA, and USDA for the regulatory oversight of biotechnology products, based on the scope of each agency's current authorities. Product developers who are uncertain regarding the relevant regulatory requirements, particularly small businesses, are encouraged to contact the agencies early in the product development process to obtain information from the agencies on potential safety and regulatory requirements that may be associated with their intended products.

[13] For example, EPA regularly holds meetings of its Federal Insecticide, Fungicide, and Rodenticide Act Scientific Advisory Panel (SAP) to solicit technical advice from recognized experts in their respective scientific disciplines on specific topics relevant to EPA's regulation of pesticides. These meetings generally are open to the public, and pertinent materials are made available to the public through EPA's website for the SAP (https://www.epa.gov/sap). The public also is given an opportunity to comment on the questions being posed to the SAP at each meeting.

Discussions with regulatory officials can provide information on the regulatory process most relevant to their product and how best to navigate the regulatory system.

Examples of existing mechanisms and activities are listed below

- **EPA, FDA, USDA, and OSTP hosted three public meetings to clarify current roles and responsibilities in different regions of the country at which, in total, over 800 people participated in person or by webcast.** The first meeting was held on October 30, 2015, at the FDA's White Oak Campus in Silver Spring, Maryland to inform the public about the activities described in the July 2015 EOP memorandum, invite oral comments from interested parties, and provide information about where and how to submit written comments, data, or other information. The second public meeting was held on March 9, 2016 at EPA's Region 6 Office in Dallas, Texas. The primary purpose of this meeting was to illustrate current Federal roles and responsibilities regarding biotechnology products by reviewing case studies of hypothetical products. The third public meeting was held on March 30, 2016, at the University of California's Davis Conference Center in Davis, California. At this public meeting, representatives from the EPA, FDA, and USDA illustrated the current roles and responsibilities of the EPA, FDA, and USDA regarding biotechnology products by discussing case studies of hypothetical products. In addition, breakout listening sessions were conducted that focused on three general thematic areas relevant to the tasks assigned to the EPA, FDA, and USDA in the July 2015 EOP memorandum – Governance; Education, Communication, and Outreach; and Improving Regulatory Certainty. Additional materials for all of these meetings, including agendas and presentations, are available on the meeting websites and in the corresponding docket on regulations.gov.
- **EPA, FDA, and USDA periodically host workshops to help small businesses developing biotechnology products navigate the regulatory system.** For example, in 2011 EPA, FDA, and USDA hosted a workshop during which case studies were presented by product developers and each of the three regulatory agencies described how they would engage with the developer as the product went through each of the three regulatory systems. USDA provides enhanced education, coordination, and outreach through its Specialty Regulatory Crop Assistance program and provides a detailed User's Guide to assist companies in preparing petitions for nonregulated status. FDA holds workshops on topics of emerging relevance to FDA to engage all stakeholders and obtain expert input into future directions and policy development. EPA, FDA, and USDA will continue to organize such workshops and to announce these through their respective stakeholder announcements, web portals, and *Federal Register* notices as appropriate.
- **EPA, FDA, and USDA provide information to developers and to the general public via their websites and through email systems**. These websites and email systems allow developers to pose specific questions related to those agencies' programs, including USDA's BiotechQuery, EPA's BPPDQuestions, and FDA's links for industry and consumer inquiries.

FDA also issues Constituent Updates to inform stakeholders of regulatory activities, such as public meetings or the availability of regulatory documents for public comment; as well as Consumer Updates and other information for consumers on a variety of topics. EPA provides guidance on its website regarding reduced Pesticide Registration Improvement Act (PRIA) fees for small businesses, and fee waivers for IR-4 submissions and Federal and state governments. EPA also keeps the public informed about biotechnology issues via its webpages and updates distributed to interested parties via email and the Federal Register. For example, EPA involves the public in regulatory decisions for significant new biotechnology pesticide products and for biotechnology microorganism products.

- **EPA, FDA, and USDA will continue to provide leadership in international fora to promote scientific competency, understanding of the U.S. regulatory approach, and regulatory compatibility worldwide for biotechnology products.** The U.S. agencies actively work to strengthen engagement between countries through coordinated and collaborative international initiatives. Through these efforts the United States shares technical and scientific expertise and supports the adoption of transparent, risk-based regulatory approaches grounded in the best science available, including with respect to the application of the most recent technical and scientific advances to the biotechnology products. These initiatives support attainment of shared global health and environmental protection goals while supporting greater regulatory predictability and reducing impediments to U.S. innovation and products worldwide. For example, experts from two U.S. regulatory agencies currently chair, and all three agencies actively contribute to, working groups in the Organization for Economic Cooperation and Development (OECD) on scientific and technical issues underpinning regulatory approaches for the products of agricultural and industrial biotechnology.

- **EPA Office of Pollution Prevention and Toxics (OPPT) is currently updating the *Points to Consider in the Preparation of Toxic Substances Control Act (TSCA) Biotechnology Submissions for Microorganisms (Points to Consider)* document.** This document identifies a broad range of risk assessment topics relevant to TSCA biotechnology submissions and provides technical support to assist those who must prepare microorganism pre-manufacturing notifications to EPA under TSCA. The *Points to Consider* do not currently provide specific support for product developers using the emerging technologies of algae production and advanced biotechnology. To keep its risk assessment process for biotechnology algae open and transparent, EPA intends to develop a separate document on the scientific and technological issues it currently understands to be key and unique for evaluating risks, if any, from the production and use of biotechnology algae. EPA will develop its *Algae Guidance for the Preparation of TSCA Biotechnology Submissions* document in parallel with updating the *Points to Consider* document. EPA held a public meeting on this effort on September 30, 2015. There will be a follow up meeting on October 27, 2016. See here for more information.

- **FDA has instituted a number of activities aimed at providing assistance to regulated small businesses.** These include small business assistance programs, which provide technical assistance to small companies; meetings to hear the views and perspectives of small businesses; educational workshops; informational materials; and an accessible, efficient channel through which small businesses can acquire information from the FDA. FDA publishes the Small Business Guide to FDA to help make small businesses' contacts with FDA as efficient and productive as possible. This guide is presented as a blueprint that small firms can follow to achieve their business aims consistent with FDA's mission on public health. FDA created openFDA in June 2014, to make FDA's public information more accessible and useful to developers. FDA has made a continuous effort to better understand the needs of the developer community and build on existing resources.
- **USDA organizes workshops with specialty crops groups to discuss the regulatory system and how best to navigate it.** FDA and EPA participate with USDA in these workshops, such as those hosted periodically by Specialty Regulatory Crop Assistance program and at periodic USDA annual Stakeholder Meetings, so that attendees understand how to navigate the regulatory system at all three agencies. In September, 2016, the agencies are hosting a workshop to provide regulatory assistance for public sector scientists and public and private sector crop developers on putting together a regulatory dossier for genetically engineered specialty crops.

Future activities

- **EPA, FDA, and USDA are exploring new opportunities to conduct sessions with industry, consumers, and other stakeholders, including at scientific conferences and at agency-hosted workshops, much like the annual USDA Biotechnology Regulatory Service stakeholder meeting.**
- **EPA, FDA, and USDA will review existing communication tools and, as appropriate, may revise existing or develop new user-friendly sources of regulatory information for product developers and the general public.** For example, FDA has information for consumers on its website about food from genetically engineered plants and about FDA's consultation process for developers of such foods. See "Consumer Info About Food from Genetically Engineered Plants," "How FDA Regulates Food from Genetically Engineered Plants," and "Questions & Answers on Food From Genetically Engineered Plants". FDA also regularly updates its Genetically Engineered Animals web page, including a current listing of all animals with related FDA-approved applications. In addition, FDA has developed a Strategic Plan for Risk Communication, which describes FDA's strategy for improving how the agency communicates with patients and consumers about regulated products. USDA maintains a variety of information on its website about how it protects plant health including a video overview of its biotechnology regulatory program. EPA and USDA

also regularly update their web page listings for registered and deregulated biotech products, respectively.

In addition, the agencies are reviewing the feedback received during the three public meetings and the fall 2015 Request for Information to better understand the specific areas of interest to the public regarding the regulation of biotechnology products and preferred mechanisms for conveying regulatory information. For example, the agencies are examining the feasibility of providing a single source for regulatory information so that developers can easily determine the appropriate regulatory pathway for their product. In addition, the agencies are examining the feasibility of expanding various types of training programs where product developers, particularly small companies, and the public would have opportunity to learn about the roles of the three regulatory agencies.

- **EPA Office of Pesticide Programs (OPP) will hold a "Plant-Incorporated Protectant (PIP) Data Requirements Symposium" on September 29, 2016 to describe for stakeholders and the public its thoughts on the types of data appropriate for evaluating a PIP product in the registration process.** This symposium is intended to be an opportunity for EPA scientists to describe the various types of information and data they would normally review when evaluating various types of PIPs, and to clarify expectations by describing procedures, new efficiency initiatives, and the regulatory approach that underpins EPA OPP's approach to PIPs. This meeting is also intended to help small businesses better understand EPA's requirements and thus to better navigate the regulatory system. USDA and FDA will also be participating in the Symposium to provide information on their respective regulatory systems. Learn more here.

Increasing Predictability and Efficiency

Consistent with the 1986 Coordinated Framework, the 1992 Update to the Coordinated Framework, Executive Order 13563, Executive Order 13610, the 2011 "Principles for Regulation and Oversight of Emerging Technologies" memorandum (2011 memorandum), and the July 2015 EOP memorandum, EPA, FDA, and USDA strive to develop and implement regulatory approaches to protect health and the environment while reducing regulatory burdens and avoiding unjustifiably inhibiting innovation, stigmatizing new technologies, or creating trade barriers. The 1992 Update to the Coordinated Framework describes a risk-based, science-based regulatory approach "to ensure that limited federal oversight resources are applied where they will accomplish the greatest net beneficial protection of public health and the environment."[7] The United States Government reiterated that this risk- and science-based approach to regulation applied to oversight of products of emerging technologies, such as synthetic biology and genetic engineering, in the 2011 memorandum.[3] This National Strategy reaffirms the centrality of this approach in the United States Government.

EPA, FDA, and USDA rely on horizon scanning techniques to detect early signs of important developments in biotechnology. The three regulatory agencies maintain staffs of experts, trained

in a variety of scientific disciplines, who keep up with knowledge in the various sciences important to understanding and evaluating biotechnology products. These agencies learn about new technologies and new products in development through a combination of activities, including participation in scientific and trade forums and discussions with national and international counterparts; monitoring scientific and trade literature; participating on technical advisory panels; maintaining membership in interagency, national, and international scientific organizations dedicated to state-of-the-art science and technology; and convening scientific advisory committees and public meetings. On occasion, EPA, FDA, and USDA have also sought advice on cutting-edge issues from groups of independent technical experts including, for example, the National Academies of Science, Engineering and Medicine.

Examples of existing mechanisms and activities are listed below

- **EPA, FDA, and USDA have commissioned an independent study by the National Academy of Sciences (NAS)** "Future Biotechnology Products and Opportunities to Enhance Capabilities of the Biotechnology Regulatory System." The study will identify (1) major advances and potential new types of biotechnology products over the next five to ten years, (2) potential future products that might pose a different type of risk relative to existing products and organisms, (3) areas in which the risks or lack of risk relating to biotechnology are well understood, and (4) the scientific capabilities, tools, and expertise that may be useful to the regulatory agencies as they oversee potential future products of biotechnology. NAS initiated the study in early 2016. Consistent with the July 2015 EOP memorandum, products such as human drugs and medical devices are not a focus of the study. The NAS committee held three public meetings in the spring and summer of 2016 to gather information for the study. The findings by NAS will be considered by the agencies in order to inform ongoing and future agency activities, including the implementation of the *Strategy*. EPA, FDA, and USDA will use the report to (1) gain a better understanding of future products and how they fit within the U.S. regulatory system; (2) consider any necessary updates to scientific assessments; (3) consider any necessary updates to regulatory processes or procedures; and (4) help enhance communication with stakeholders. The July 2015 EOP memorandum also notes that, due to the rapid pace of change in this arena, such independent external analysis should be completed at least every five years.
- **EPA, FDA, and USDA's frequent interactions with product developers.** All three agencies encourage product developers to begin discussions with the regulatory agencies early in the development process, as advance notice and information about products being contemplated enable the agencies to provide input to developers about the safety and regulatory issues relevant to their product. Staff from each of the three agencies routinely have discussions with their counterparts at the other agencies to share information (as appropriate) about products on the horizon or in the regulatory pipeline.
- **EPA, FDA, and USDA strive to use the best available science to address the protection**

goals established by their respective statutes. For example, USDA's authority under the Plant Protection Act identifies the aspects of plant health that need to be protected from harm (what to protect, where, over what period).[14] These aspects of plant health drive the collection of relevant information for a plant health risk assessment. USDA's environmental risk assessment is an iterative process that uses a scientific approach in which specific hypotheses are formulated and then either proven or refuted through the use of appropriate testing methods.

- **EPA OPP is modifying its approach to PIPs in breeding line intermediates (BLIs).** A BLI is used in plant breeding to bring together or "stack" several individual PIPs into seed. EPA's current approach requires a unique registration for each combination of two or more PIPs combined in BLIs. As companies combine multiple PIPs together, the number of BLI registrations needed to develop one combination PIP product increases. In light of this, EPA is proposing to modify its approach so that a unique registration for each combination of PIPs in BLIs would no longer be required. Rather, EPA will regulate PIPs in BLIs through conditions placed on the registrations of the individual PIPs to be combined in BLIs. This will result in a reduction in the number of registrations needed to produce a combination PIP product. Learn more here.

- **FDA's continuous efforts to expand regulatory science and the use of "smart regulation."** FDA's Strategic Priorities, 2014-2018, identified several cross-cutting strategic priorities and FDA's core mission goals and objectives, which are relevant to ensuring science- and risk-based product evaluations. For example, regulatory science and "smart regulation" are among the focus of FDA's programs. In addition, FDA's core mission goals and objectives include: (1) increasing the use of regulatory science to inform standards development, analysis, and decision-making; (2) increasing regulatory science capacity to effectively evaluate products; and (3) reducing risks in the manufacturing, production, and distribution of FDA-regulated products. For example, with respect to the safety of foods derived from genetically engineered plants, FDA's voluntary consultation process focuses on the characteristics of the plant species and the introduced trait. This process is consistent with international standards established by *Codex Alimentarius*.

- **USDA's encouragement of product development through its *Am I Regulated* process and its permit and notification system.** USDA developed the *Am I Regulated* process by which developers, including small private- and public-sector entities, will ask whether a proposed product would be subject to USDA regulations prior to requesting an authorization for a regulated activity. This allows USDA to have some early notification of products that may be about to enter the regulatory system and provides an additional window into emerging technologies. Also, through the USDA authorization system, which provides permits and notifications for regulated import, interstate movement, and field testing of

[14] Plant Protection Act of 2000; (PPA, 7 U.S.C. 7701 et seq.).

biotech products, the agency is able to learn about potential commercial products three or more years before they are commercialized.

- **USDA's efforts underway to revise its regulations at 7 CFR part 340.** On February 5, 2016, USDA published a notice in the *Federal Register* announcing that it is developing a draft programmatic environmental impact statement (EIS), required under the National Environmental Policy Act, that will evaluate a range of risk-based approaches to regulation that the Agency can take as it works to update its biotechnology regulations. The notice also invites the public to comment on the range of alternatives that USDA will study in the draft EIS, along with definitions that USDA plans to use in the draft EIS. Learn more here.
- **USDA developed an international product horizon scanning assessment.** Recognizing that future biotechnology products are currently being developed in other countries, USDA has developed, and shares with EPA and FDA, annual Vulnerability Assessments that scan information about plant, animal, and microorganism biotechnology research and development activities in other countries for biotechnology products that are in development pipelines and could be imported into the United States. These assessments identify products already in commercial production in other countries, but not yet authorized in the United States.

Future activities

During development of the proposed Update to the Coordinated Framework, the agencies identified a number of actions intended to improve predictability and efficiency. To this end, EPA, FDA, and USDA are committing to the following:

- **EPA, FDA, and USDA commit to interagency communication that helps with timely decisions on regulatory jurisdiction for biotechnology products, in order to help clarify for developers which of the regulatory agency(ies) might have oversight responsibility for a novel biotechnology product for a specific application.**
- **EPA, FDA, and USDA will continue to explore ways to enhance collaborations for the oversight of biotechnology products in an effort to optimize the review and use of scientific data or regulatory assessments**. Greater collaborations between agencies have the potential to reduce the cost, complexity, and time needed to bring safe, new products to market, which is especially important to small and mid-sized companies and academics. Enhanced collaboration and, where feasible, coordination, can also benefit developers and the public by ensuring that the best possible science, standards, and practice drive the regulatory process.
- **EPA, FDA and USDA will continue to examine their regulatory structures with the goal of clarifying how the U.S. Federal Government will regulate genetically engineered insects in an integrated and coordinated fashion to cover the full range of potential products.** The agencies are working to better align their responsibilities over genetically

engineered insects with their traditional oversight roles, for example, considering mechanisms that would enable EPA to regulate genetically engineered mosquitos under FIFRA when the developer claims they are intended to control population levels, and FDA to regulate them under FD&C Act when the developer makes a disease claim. USDA will continue to exercise its authorities for control of certain plant or animal pest insects.

- **EPA OPP is undertaking a reorganization of the EPA staff assigned to the regulation of biopesticides**, **including genetically engineered microorganisms and plant-incorporated protectants**. The reorganization is to facilitate interaction among the various experts needed to address novel products of modern biotechnology, and, thus, to facilitate EPA's ability to more efficiently address such products. The reorganization will also create efficiencies by centralizing review and regulation of plant-incorporated protectants (PIPs) into one group.
- **EPA OPP is modifying its approach to transformation event in product identification.** The "transformation event" is generally part of the identity of a PIP. EPA has historically assumed that a different transformation event means a different PIP even if the same vector is used in the engineering. Advances in techniques for the sequencing of genetic information now give EPA the ability to determine whether PIPs associated with different transformation events might be properly considered as "identical or substantially similar". Such a consideration could, for example, affect how the PIP is registered. The modified approach to transformation event would apply to PIPs in seed propagated and in clonally propagated plants, but would likely be most useful for companies developing PIPs in clonally propagated plants. More details will be made available to interested stakeholders at EPA OPP's September 29, 2016 "Plant-Incorporated Protectant (PIP) Data Requirements Symposium."
- **EPA OPP intends to clarify its approach to pesticidal products derived from genome editing techniques.** This clarification will be consistent with the principles for the regulation of biotechnology products articulated in the Coordinated Framework and the goals and objectives of the July 2015 EOP memorandum.
- **FDA intends to clarify its policy for the regulation of products derived from genome editing techniques, including, as appropriate, identifying and/or updating relevant existing guidance documents.** For example, FDA intends to update its Guidance for Industry 187, *Regulation of Genetically Engineered Animals Containing Heritable Recombinant DNA Constructs*, to clarify how developers of animals produced using emerging technologies (e.g., genome editing) may meet applicable statutory and regulatory requirements. This update will be consistent with the principles for the regulation of biotechnology products articulated in the proposed Update to the Coordinated Framework and the goals and objectives of the July 2015 EOP memorandum.
- **FDA intends to explore updating guidance regarding the consultation procedures for food derived from new plant varieties.** An update to these procedures, which date back to 1996, will help developers have a clearer understanding of what FDA expects during a

consultation. Any update to these procedures will be consistent with the principles for the regulation of biotechnology products articulated in the proposed Update to the Coordinated Framework and the goals and objectives of the July 2015 EOP memorandum.

- **FDA's Emerging Sciences Working Group will be used to identify science and technology trends of relevance to FDA's regulatory responsibilities, including those for biotechnology products.** For FDA to achieve its mission of protecting and promoting public health, it must be prepared for emerging issues and scientific advances that will affect regulated products, and it must be so prepared well in advance of formal FDA regulatory submissions. To help it realize this goal, FDA formed the Emerging Sciences Working Group. The group will provide an FDA-wide science-based forum to identify and communicate scientific regulatory approaches to anticipated high-impact emerging science and technology.

Supporting the Science that Underpins the Regulatory System

One of the key principles of the U.S. Federal regulatory system for biotechnology products is that regulatory reviews and decisions should be based on the best available science. EPA, FDA, and USDA/APHIS support such science through collaborations with Federal research agencies and through intramural and extramural research portfolios, when appropriate.

Examples of existing mechanisms and activities are listed below

- **FDA leverages its intramural and extramural research portfolios to support regulatory science.** Regulatory science, for FDA, is the science of developing new tools, standards, and approaches to assess the safety, effectiveness, quality, toxicity, public health impact, or performance of FDA-regulated products. FDA identified regulatory science as a cross-cutting strategic priority in its most recent Strategic Priorities document, issued in 2014. In addition, FDA developed a Strategic Plan for Regulatory Science that identified plans to close critical gaps in scientific knowledge required to support regulatory decision-making. As discussed in this plan, a science priority area is to ensure FDA readiness to evaluate innovative emerging technologies, including by coordinating regulatory science for emerging technology product areas. In addition, the Global Coalition of Regulatory Science Research, for example, is building a foundation of collaborative research, scientific exchange, and training as a basis for regulatory decision-making. As needed, FDA also engages in various extramural and intramural research activities to address scientific gaps and develop new methods, models, and approaches required to inform regulatory policy development and decision-making. For example, FDA has relationships with several academic institutions through its Centers of Excellence in Regulatory Science and Innovation (CERSI) as well as through several subject-specific Centers of Excellence. FDA regulatory science activities seek to employ or develop tools that are relevant to biotechnology products (e.g., with respect to food safety, research to

improve the understanding of allergens to help inform the assessment of the potential allergenicity of proteins; and research related to whole genome sequencing).

- **USDA leverages expertise and resources from USDA's research agencies, the Agricultural Research Service (ARS) and the National Institute of Food and Agriculture**. In cases where there is mutual interest, USDA funds can be directed towards research to inform regulatory activities. One mechanism for such coordination is the Biotechnology Risk Assessment Grants (BRAG) program, which supports the generation of new information that will assist Federal regulatory agencies in making science-based decisions about the effects of introducing biotechnology products into the environment. Investigations of effects on both managed and natural environments are relevant. Also, APHIS discusses research needs with ARS which, when mutual interests arise, uses intramural funds for projects that inform regulatory activities.

Future activities

- **EPA, FDA, and USDA will continue to explore mechanisms to enhance coordination with Federal research agencies to help support agencies' regulatory science needs.**

Implementation of the Strategy

As instructed in the July 2015 EOP memorandum, for at least five years, starting one year after the release of the S*trategy*, EPA, FDA, and USDA are expected to produce an annual report on the specific steps the agencies are taking to implement this *Strategy*. In their first annual report, the agencies may, if appropriate, provide a concrete list of regulatory and other activities and expected timeframes. The agencies will also include in that report any additional actions taken by the agencies to improve the transparency, predictability, and efficiency of biotechnology regulation and the coordination among the regulatory agencies. This report will be made available to the public by the Executive Office of the President.