November 1, 2016

National Science and Technology Council:
Emerging Technologies Interagency Policy Coordination Committee
Office of Science and Technology Policy
1650 Pennsylvania Avenue NW
Washington, DC 20504

Submitted Electronically via Federal eRulemaking Portal (http://www.regulations.gov)

Re: Food and Drug Administration Docket No. FDA-2015-N-3403; Clarifying Current Roles and Responsibilities Described in the Coordinated Framework for the Regulation of Biotechnology

Dear Sir or Madam:

The Biotechnology Innovation Organization (BIO) is pleased to submit these comments in response to the Notice of Request for Public Comment published by the National Science and Technology Council, Science and Technology Policy Office[1]. BIO is the world's largest biotechnology trade association, representing more than 950 biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States and in more than 30 other nations. Our members are involved in the research and development of healthcare, agricultural, food, industrial and environmental biotechnology products, and BIO represents the majority of the biotechnology product developers in North America.

The Coordinated Framework for Regulation of Biotechnology (Coordinated Framework) has made it possible for BIO members to develop products that have improved the productivity of plant and animal agriculture while decreasing their environmental impacts, enhanced food safety and quality, increased the use of renewable resources and decreased manufacturing costs and energy use. Consequently, BIO is especially interested in the Administration's efforts to clarify the roles and responsibilities described in the Coordinated Framework[2], and we appreciate the opportunity to provide comments.

[1]81 FR 65414 September 22, 2016. Available at https://www.gpo.gov/fdsys/pkg/FR-2016-09-22/pdf/2016-22802.pdf
[2]Executive Office of the President. Office of Science and Technology Policy. Coordinated Framework for Regulation of Biotechnology, 51 FR 23302, June 26, 1986. http://www.aphis.usda.gov/brs/fedregister/coordinated_framework.pdf

1201 Maryland Avenue SW
Suite 900
Washington DC 20024
202.962.9200 P
202.488.6306 F
bio.org

In a series of Executive Orders (EOs) and memos, most notably EO 13563, EO 13610 and its memo on principles for regulation and oversight of emerging technologies[3], the Administration has clearly described the importance of appropriate regulation to economic growth and innovation, while continuing to meet the requisite objectives of protecting the health of humans, animals and the environment. BIO members concur with the Administration's view that "regulation and oversight should avoid unjustifiably inhibiting innovation, stigmatizing new technologies, or creating trade barriers."[4] As such, BIO supports the objectives of this initiative, as articulated in the 2 July 2015 memorandum from the Executive Office of the President (EOP)[5], which are to:

- ensure public confidence in the regulatory system, and
- prevent unnecessary barriers to innovation, while continuing to protect health and the environment.

BIO is pleased that the Administration continues to reaffirm the principles of good regulation in the document on which comments are requested, *Modernizing the Regulatory System for Biotechnology Products: An Update to the Coordinated Framework for the Regulation of Biotechnology* (*Draft CF Update*)[6]. If innovation is to flourish, then these principles, which were originally articulated in the 1986 Coordinated Framework and amplified in the 1992 "Federal Oversight" document[7], must continue to guide the agencies as they consider approaches to appropriate, science-based oversight of future biotechnology products.

Responses to Questions

The July 2015 EOP memo initiated a process with the following one-year tasks: "(1) development of an updated CF to clarify the roles and responsibilities of the agencies

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[3]EO 13563 (January 18, 2011) *Improving Regulation and Regulatory Review* http://www.whitehouse.gov/the-press-office/2011/01/18/executive-order-13563-improving-regulation-and-regulatory-review; EO 13610 (May 10, 2012) *Identifying and Reducing Regulatory Burdens* http://www.whitehouse.gov/the-press-office/2012/05/10/executive-order-identifying-and-reducing-regulatory-burdens; Memorandum (March 11, 2011) *Principles for Regulation and Oversight of Emerging Technologies* http://www.whitehouse.gov/sites/default/files/omb/inforeg/for-agencies/Principles-for-Regulation-and-Oversight-of-Emerging-Technologies-new.pdf

[4]*Principles for Regulation and Oversight of Emerging Technologies* http://www.whitehouse.gov/sites/default/files/omb/inforeg/for-agencies/Principles-for-Regulation-and-Oversight-of-Emerging-Technologies-new.pdf . March 11, 2011.

[5]Executive Office of the President. *Modernizing the Regulatory System for Biotechnology Products.* July 2, 2015. https://www.whitehouse.gov/sites/default/files/microsites/ostp/modernizing_the_reg_system_for_biotech_products_memo_final.pdf

[6]https://www.whitehouse.gov/sites/default/files/microsites/ostp/biotech_coordinated_framework.pdf

[7]57 FR 6753, February 27, 1992. *Exercise of Federal Oversight within Scope of Statutory Authority: Planned Introductions of Biotechnology Products into the Environment.* Available at https://www.whitehouse.gov/sites/default/files/microsites/ostp/57_fed_reg_6753__1992.pdf

that regulate the products of biotechnology; (2) formulation of a long-term strategy 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; and (3) commissioning an external, independent analysis of the future landscape of biotechnology products."[8]

The notice published in the 22 September Federal Register[9] asks for public comment on four specific questions related to the first task:

"1. What additional clarification could be provided regarding which biotechnology product areas are within the statutory authority and responsibility of each agency?

2. What additional clarification could be provided regarding the roles that each agency plays for different biotechnology product areas, particularly for those product areas that fall within the responsibility of multiple agencies, and how those roles relate to each other in the course of a regulatory assessment?

3. What additional clarification could be provided regarding communication and, as appropriate, coordination among agencies, while they perform their respective regulatory functions, and for identifying agency designees responsible for this coordination function?

4. What additional clarification could be provided regarding the mechanism and timeline for regularly reviewing, and updating as appropriate, the Coordinated Framework to minimize delays, support innovation, protect health and the environment and promote the public trust in the regulatory systems for biotechnology?" [10]

BIO offers the following comments on the questions posed.

1. *What additional clarification could be provided regarding which biotechnology product areas are within the statutory authority and responsibility of each agency?*

Determining if a biotechnology product is subject to regulation -- and, if so, the nature, extent, and likely costs and burdens of such regulation -- is one of the most fundamental questions a developer or investor must ask and answer before deciding to venture into a technically demanding, risky and expensive product development process.

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[8] *Ibid*
[9] 81 FR 65414 September 22, 2016.
[10] 81 FR 65414 September 22, 2016.

The inability to answer this question thwarts innovation before it can even begin, depriving society of beneficial products and stifling subsequent economic growth that could have been driven by that innovation.

The tables, figures and text in Section D of *Modernizing the Regulatory System for Biotechnology Products: An Update to the Coordinated Framework for the Regulation of Biotechnology*[11] (CF Update) are helpful in explaining the agencies' current regulatory roles and responsibilities in the pre-market stage of product development, as clearly as possible. Most developers of most biotechnology products should be able to determine the regulatory status of the product they hope to develop from the information in Section D. In addition, the public can see the breadth of biotechnology products that are regulated by federal agencies.

Table 1 in Section D identifies the authorizing statutes and corresponding protection goals relevant to each agency's current regulation of biotechnology products. BIO especially appreciates the inclusion of agency protection goals because they are essential to the problem formulation approach to risk assessment, which is key to science-based, risk-proportionate regulation. The protection goals are also useful in providing general insights into the categories of risks the agencies evaluate and, as such, will inform the public about the wide-ranging health, safety and environmental issues the agencies attend to. However, including additional information on specific risks that agencies evaluate should increase public confidence even further, because the stringency of the regulatory approval process for the products of biotechnology is exceptionally robust. Clear explanations of the specific risks being addressed by each agency and descriptions of how those risks are assessed will also be very helpful for product developers, especially small companies and academic scientists who are new to product development in a highly regulated environment. Transparent information on the agencies' methodologies and tools for determining a product's regulatory status and assessing its risk should be readily available and sufficiently self-explanatory for any product developer to gain an overview of the regulatory process without needing to contact the agencies. This will help agencies to conserve limited government resources and will make it easier for developers to estimate approximate regulatory costs. In addition, the risk assessment data that will be required can affect biotechnology product design in the earliest stages of product research and development.

In Table 2 in Section D, the role of FDA-CVM in regulating animal feed could be better defined, according to BIO members that develop both GE plants and GE microbes. Lack

[11] https://www.whitehouse.gov/sites/default/files/microsites/ostp/biotech_coordinated_framework.pdf

of clarity about CVM's role in regulating animal feed has created regulatory uncertainty and delays for some members.

With respect to the text and figures in Section D, BIO appreciates the *Draft CF Update* document's clarity in describing EPA's regulation of the plant incorporated protectant (PIP) molecules produced by "GE plants." In the past, the distinction between regulating the pesticidal substance (the PIP) and regulating the GE plant has not always been clearly understood or articulated by some stakeholders, governments and new PIP developers. Clearly describing the specific limits of EPA's authorities with respect to PIPs not only explains agency responsibilities for the regulated community and the public but also provides clarity for the agencies. As such, the clarification helps to guard against redundant and potentially inconsistent regulatory actions taken by one or more agencies, and against inappropriate, and at times inadvertent, expansion of regulatory scope.

Similarly, BIO welcomes the clarity of the Administration's description of FDA's regulatory authority with respect to "GE animals": FDA regulates the recombinant DNA construct inserted into animal's DNA, and not the animal itself.

BIO also appreciates the Administration's reaffirmation that "damage" in the Plant Protection Act refers to "biological, chemical, or physical damage, not damage due to market impacts, including those due to the presence of GE material".

However, Section D could be improved by including additional information that describes agency roles and responsibilities *after* a product has reached the marketplace, e.g., adverse event reporting requirements under FIFRA and FDA removal of adulterated products. Sharing this information would increase public confidence in the comprehensive nature of the regulatory system by sending the message that agency oversight does not end with product approval. It would also help product developers assess the regulatory requirements and associated costs throughout a product's life cycle. This information is essential for making sound investment decisions.

For biotechnology products that are *not* within the scope of agency pre-market approval authority, agencies could do a much better job of communicating with the public, including the media, to meet the objective of this initiative, "to ensure public confidence in the regulatory system"[12]. BIO suggests the following:

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[12]Executive Office of the President. *Modernizing the Regulatory System for Biotechnology Products.* July 2, 2015. https://www.whitehouse.gov/sites/default/files/microsites/ostp/modernizing_the_reg_system_for_biotech_products_memo_final.pdf

- Make it clear that all biotechnology products are subject to government regulation and oversight whether or not a specific product has been through a pre-market regulatory review and approval process. The regulatory agencies with oversight over biotechnology products have the authorities to remove products from the marketplace, as needed.

- Agencies should be more communicative about these products being acceptable for domestic use even if they have not been subjected to pre-market regulatory review and approval. Not all products warrant a pre-market review and approval by a federal regulatory agency simply because they are new to the marketplace.

- Be more explicit about products' being outside agency authorities, either because they do not pose the risk the agencies are responsible for overseeing, and/or because past experience indicates any risks are minimal and can be managed sufficiently using the agency's post-market regulatory authorities.

- Recognize that routine agency terminology is often misinterpreted by the public and media. When EPA 'drops from review' a material that it deems to be safe and compliant, the message often sent to laypersons unfamiliar with this terminology is that the federal government does not regulate that product. When APHIS confirms that a gene-edited product containing no plant pest genetic material is not a regulated article, the media often hear 'USDA is not regulating gene-edited products'.

- Consider broadening use of social media and email notices to correct important inaccuracies and misinterpretations about the regulatory system and agency decisions, like those just described, that are repeated frequently in the media.

Finally, we would be remiss if we failed to note that, in some cases, agencies have exceeded the limits on the scope of their oversight responsibilities described in the *Draft CF Update* document:

- Contrary to TSCA authorities as described on page 31, on at least some occasions, EPA has required industrial biotechnology companies to notify them about GE microbes that produce food ingredients.

- BIO members report that FDA-CVM asks for information that exceeds its scope of regulatory oversight for animal feed.

- Public and private sector developers have been deterred from developing products by unexpected expansions of scope that contradict an agency's published policy statements or are inconsistent with applicable regulations. For example, the

University of Florida ceased development of a delayed-ripening melon because EPA informed the researchers that it would be regulated as a pesticide.

If a goal of this initiative is to provide clarity to product developers, then an agency's interpretation of its oversight must align with the descriptions in the *Draft CF Update*, as well as with applicable laws, regulations and current policies and guidance documents that describe that agency's regulatory scope and processes.

2. What additional clarification could be provided regarding the roles that each agency plays for different biotechnology product areas, particularly for those product areas that fall within the responsibility of multiple agencies, and how those roles relate to each other in the course of a regulatory assessment?

The existing division of responsibilities among the three agencies is logical and consistent with each agency's mission, authority and expertise. Table 2 and the case studies in Section G provide useful descriptions of the offices within each agency or agencies that may have regulatory responsibility for a given class of biotechnology products. Perhaps more importantly, the table and case studies elucidate quite clearly the need for communication and coordination, to avoid delays and duplication, across agencies. Many BIO members have extensive experience shepherding products through the pre-market regulatory process, and they have repeatedly encountered areas of duplicative and overlapping reviews.

In the past, some agencies have unnecessarily delayed publishing their reviews and decisions until another agency published its review, even though the assessments and/or decisions are not interdependent. Agency reviews and publication of the results were delayed merely because other agencies were reviewing data pertinent to both decisions and were not due to science-based justification, supported by applicable statutory and regulatory authority. Allowing unnecessary interagency dependencies harms not just product developers, but all members of our society who benefit from scientific innovation, by creating unnecessary delays and regulatory uncertainty, as well as by causing public confusion. This problem seems to have abated recently. However, the apparent abatement may be due to a significant decrease in approval requests rather than to actual resolution of the problem.

A number of BIO members specifically mentioned FDA-CVM coordination problems, both within FDA (CFSAN, CDER/CBER) and with EPA and USDA.

Finally, BIO members recommend consideration of including more examples, such as a GE microbe, or its enzymes, used in a fermentation process to produce renewable chemicals or biobased products that may be subject to both EPA and FDA oversight.

3. What additional clarification could be provided regarding communication and, as appropriate, coordination among agencies, while they perform their respective regulatory functions, and for identifying agency designees responsible for this coordination function?

Appendix E describes the current mechanisms that enable communication and information- sharing among the three agencies: Formal and Ad Hoc Interagency Working Groups and Memoranda of Understanding. While knowing about these mechanisms may help a few product developers better navigate the regulatory process at points where poor communication and lack of coordination are impeding progress, a more pertinent question is how to use existing mechanisms to improve interagency communication and coordination. Our members have experienced unexpected regulatory delays, rooted in interagency miscommunication and lack of coordination, for a wide range of products from herbicide tolerant corn varieties to genetically engineered cyanobacteria and algae.

BIO is encouraged by the creation of the Interagency Biotechnology Working Group[13] (Biotechnology WG), under the auspices of the Emerging Technologies Interagency Policy Coordination Committee, which was precipitated by this update initiative, and we strongly recommend sustained support of the WG by subsequent Administrations. Similar interagency groups - the Domestic Policy Council Working Group on Biotechnology and the Biotechnology Science Coordinating Committee - played essential roles in creating and implementing the 1986 Coordinated Framework and ensuring its functionality. In more recent years, the absence of a functional interagency working group for biotechnology, operating under strong support and leadership provided by the White House, led to significant regulatory delays, uncertainty, lack of coordination and agency mission creep.

Without strong direction from the highest levels of government, the U.S. position as the global leader of biotechnology-based innovation is in jeopardy. One need only look to the scientific literature on the newest gene-based technologies to observe that many other countries are poised to displace the leadership position the U.S. has occupied.

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[13]Executive Office of the President. *Modernizing the Regulatory System for Biotechnology Products.* July 2, 2015. https://www.whitehouse.gov/sites/default/files/microsites/ostp/modernizing_the_reg_system_for_biotech_products_memo_final.pdf

EO 12866[14] provides useful structures and processes for White House leadership in maintaining a regulatory system that balances the goals of protection and innovation. In order to implement its specific regulatory review and planning functions, EO 12866:

- authorizes OMB-OIRA[15] to provide meaningful guidance and oversight to the agencies;
- directs the OIRA to chair and convene at least quarterly meetings of a Regulatory Working Group that serves as a forum to help agencies identify and analyze important regulatory issues;
- directs each agency to "designate a Regulatory Policy Officer, responsible for ensuring the development and implementation of its regulations are consistent with the philosophy and principles of EO 12866."

We encourage the White House to make use of these and any other available mechanisms to exercise sustained leadership that encourages interagency communication, coordination and cooperation.

With respect to "additional clarification … for identifying agency designees responsible for this coordination function," we were not able to locate any mechanism for identifying agency designees in the *Draft CF Update document.* BIO recommends careful consideration of options such as explicitly designating interagency coordination as a primary responsibility of certain key employees at all three agencies.

4. What additional clarification could be provided regarding the mechanism and timeline for regularly reviewing, and updating as appropriate, the Coordinated Framework to minimize delays, support innovation, protect health and the environment and promote the public trust in the regulatory systems for biotechnology?

Agencies should be strongly encouraged to publish clear guidance on the scope of regulations, data requirements, regulatory processes, and bases of decision-making, not only for regulatory reviews of proven products that are about to enter the marketplace, but also for oversight of field trials and other regulatory activities. Publication of clear guidance will greatly increase the transparency and predictability of the regulatory system, clarify the bases for decision-making, resist politicization, and reduce the likelihood that agency scope and practice will inadvertently change or drift over time.

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[14]EO 12866 (Sept 1993) *Regulatory Planning and Review*. http://www.archives.gov/federal-register/executive-orders/pdf/12866.pdf

[15]Office of Management and Budget – Office of Information and Regulatory Affairs

Agencies should also be encouraged to implement process improvement projects to identify ways to improve the timeliness, efficiency and predictability of their premarket regulatory processes. USDA conducted such a project in 2011, which resulted in significant improvements in the timeliness of its petition review process. The project was based entirely on data and information held by USDA about the internal functioning of its business process. All agencies could greatly benefit from similar efforts to improve other regulatory processes, as well. Agencies should set reasonable timelines for completion of their review processes, and implement process controls to ensure they are able to meet those timelines consistently.

Much of the inefficiency in the current regulatory system results from reviewing the same or similar products-- and the same or similar field trials-- over and over. Agencies should use their extensive experience to identify ways to reduce redundant data requirements or review of products with which the agencies are extremely familiar. This strategic use of experience and familiarity to improve the efficient use of limited agency resources should play a central role in the long-term plan for keeping the regulatory system up to date and in any considerations to exempt future products from review requirements when relevant risk assessments have been completed for the same or similar products.

Agencies can feel confident in acting on this evidence and making the appropriate adjustments when their decisions are paired with a robust stakeholder outreach and communications effort. Therefore, they should increase their external engagement, making stakeholder outreach a regular and ongoing activity -- not only to help stakeholders understand the regulatory systems, but to solicit feedback on the functioning of the regulatory system and its impacts on stakeholders.

Equally important, agencies should be more proactive in describing how their regulatory processes ensure protection of human and animal health and the environment and in defending the validity of their safety assessments and decisions. Agencies should strengthen their public-facing communication strategies so that each agency's regulatory determinations are more accessible to and understandable by the general public. Agencies should vigorously defend the rigor of their decisions, the risks evaluated, and the scientific bases for their conclusions. Additionally, a coordinated effort from the Administration, including White House leadership as well as leaders in EPA, FDA, and USDA - visibly and vocally supporting the quality of the regulatory process and confidence in the safety of individual products and processes that have been reviewed - will further the U.S. as a global leader and help to improve the global dialogue. Improved levels of public confidence from these efforts might, in turn, reduce the pressure that regulators are experiencing from some sources to increase regulatory scrutiny when it is not scientifically justified.

In summary, biotechnology's potential for driving innovation is virtually limitless. Realizing that potential depends not only on sound regulatory policy but also on strong and far-sighted leadership at the highest levels of government. BIO and its members appreciate the leadership shown by this Administration in encouraging regulatory approaches that protect health and the environment, while reducing regulatory burdens that impede innovation unnecessarily.

With Sincerest Regards,

James C. Greenwood
President and CEO