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Re: Request for Information re Section 8 of Executive Order 14081: Identifying Ambiguities, Gaps, Inefficiencies, and Uncertainties in the Coordinated Framework for the Regulation of Biotechnology (87 Fed. Reg. 77900 (Dec. 20, 2022)), APHIS-2022-0076.

The Biotechnology Innovation Organization (BIO) is pleased to respond to the Office of Science and Technology Policy's Request for Information re: Section 8 of Executive Order 14081 (EO)[1], specifically requesting input as to how regulations underpinning the Coordinated Framework for the Regulation of Biotechnology can better facilitate the use of biotechnology to stimulate the economy and to enable products that further societal goals related to health, climate change and energy, food and agricultural innovation, resilient supply chains, and innovative scientific advances.

BIO represents more than 1,000 members in a biotech ecosystem with a central mission – to advance public policy that supports a wide range of companies and academic research centers that are working to apply biology and technology in the agriculture, energy, manufacturing, and health sectors to improve the lives of people and the health of the planet. BIO is committed to speaking up for the millions of families around the globe who depend upon our success.

BIO applauds the EO's recognition that in order to meet the challenges of a changing climate and sustainably increase production to feed a growing world, it is crucial to lead with science and U.S. innovation. Climate change is already impacting agricultural production. According to research by Nature Climate Change,[2] 21 percent of global agriculture production, including livestock, tree farming, and traditional crops such as corn and soybeans, has been negatively impacted by climate change, a slowdown that is equivalent to losing the last seven years of productivity growth.

To meet this challenge, we must incentivize the adoption of innovative, sustainable technologies and practices; and streamline and expedite regulatory pathways for breakthrough technology solutions.[3] The adoption of biotechnology in agriculture and the development of biobased technologies has

[1] Advancing Biomanufacturing and Biotechnology Innovation for a Sustainable, Safe, and Secure Bioeconomy, https://www.whitehouse.gov/briefing-room/presidential-actions/2022/09/12/executive-order-on-advancing-biotechnology-and-biomanufacturing-innovation-for-a-sustainable-safe-and-secure-american-bioeconomy/
[2] https://www.nature.com/articles/s41558-021-01000-1
[3] Jennifer Doudna, Crispr Wants to Feed the World, https://www.wired.com/story/crispr-gene-editing-climate/.

already contributed to food security, sustainability, and climate change solutions. The acceptance of biotechnology has enabled large shifts in agronomic practices that have led to significant and widespread environmental benefits. Ensuring that policies and regulations continue to advance innovative breakthroughs will be critical. Increasing the use and acceptance of these technologies can reduce greenhouse gas emissions throughout agricultural supply chains and strengthen producers' resiliency to climate change while increasing and diversifying production and helping tackle hunger by bringing more nutritious offerings to all tables.

The U.S. has led the way in developing these innovations due to thoughtful, bipartisan public policy. This has created a favorable climate in which to undertake the lengthy and risky job of investing in and developing the next biotech breakthroughs; allowing producers to use new technologies; and ensuring a pathway to market for new products. However, America's continued success and leadership are not guaranteed, and its global leadership is slipping away.

BIO urges the Administration to prioritize clarity and efficiency in regulating biotechnology and to demonstrate an understanding of the potential for biotechnology to provide solutions for issues that are also priorities for this Administration.

I. Administration's Continued Support of Biotechnology

BIO encourages the Administration to continue the consistent theme of support for biotechnology in previous administrations, as outlined in Executive Order 14081.

The original Coordinated Framework and its recent modernization build upon a foundation established by a number of earlier Executive Orders across multiple Administrations directing agencies to adhere to important principles and requirements in rulemaking and administrative governance. In 2011, the White House published a memorandum to the heads of executive departments and agencies, describing guiding principles for regulation of emerging technologies in particular.[4] These rulemaking principles, which remain critical today, are aimed at ensuring that regulations are:

- Protective of health and the environment while promoting innovation.
- Based on the best available scientific and technical information.
- Cost-effective and commensurate with risk.
- Flexible and adaptable to accommodate new evidence and learning.
- Simple, clear, transparent, and minimize uncertainty.
- Adopted through a public and transparent process.
- Coordinated with other federal agencies, state authorities, a broad array of stakeholders, and the international community.

[4] Memorandum for the Heads of Executive Departments and Agencies (March 11, 2011), *available at* https://obamawhitehouse.archives.gov/sites/default/files/omb/inforeg/for-agencies/Principles-for-Regulation-and-Oversight-of-Emerging-Technologies-new.pdf

To ensure America is able to respond to future challenges in cleaner, more efficient ways, maintain its global leadership, and allow its farmers, ranchers, sustainable fuel producers, and manufacturers to have access to cutting edge technologies, the United States must invest in new technologies and have risk-proportionate regulations that spur biological innovations, including implementation of domestic policies that facilitate access to innovation in spite of non-science-based and politicized foreign regulatory systems and policies.

The government should also focus on removing barriers and assisting beginning and socially disadvantaged farmers and ranchers in accessing and utilizing these technologies, so all producers can adapt to the challenges ahead. Key to these principles is accessibility and transparency of the regulatory processes and key personnel at the agencies. BIO therefore asks that each Coordinated Framework agency consistently make available organizational charts, periodically updated, so that all stakeholders have equal visibility as to personnel assignments and contact information. In addition, BIO asks that the U.S. government ensure that all agencies, are sufficiently staffed and with appropriate scientific expertise to address new technologies and new applications of technology.[5] By taking coordinated steps to accelerate and deploy innovation, the Coordinated Framework agencies can ensure that the American bioeconomy is resilient, self-sustaining, and strong.

II. Animal Biotechnology

Using biotechnology to improve the genetics of animals has the potential to address a broad array of societal issues important to this Administration – adapting to climate change; increasing the sustainability of animal agricultural production; improving animal health and welfare; improving human health and nutrition; and responding effectively to zoonotic disease. The success of these innovations is critically dependent on regulatory systems that incentivize development and commercialization of innovation.

BIO believes that an effective regulatory framework for the oversight of biotech animals should be based upon the following principles:

1. Oversight must protect animal health and welfare, ensure the safety of food, feed, or pharmaceuticals derived from the animals, and consider the possible impacts of the animals on the environment.
2. Implementation of oversight must be clear, transparent, efficient, predictable, timely, and based upon the best available science.

[5] *See* Preparing for Future Products of Biotechnology, National Academies of Science (2017), available at https://www.nationalacademies.org/our-work/future-biotechnology-products-and-opportunities-to-enhance-capabilities-of-the-biotechnology-regulatory-system.

3. Risk assessment must be proportionate to the actual risk posed by the specific species/trait combination. Lower-risk, more-familiar traits, including traits that impart health benefits to humans and animals, should be given expedited review.
4. And, as to animals used for food production, once all appropriate safety reviews are completed, the approved animals should be allowed to be treated as any other farm animal in production and commerce. Ongoing post-market regulatory requirements imposed on such animals, even after they have been determined to be as safe as conventional animals, strongly disincentivizes development and commercialization.

Currently, opportunities to implement these principles are stalled given the current impasse between the Food and Drug Administration's (FDA's) Center for Veterinary Medicine (CVM) and the United States Department of Agriculture's Animal and Plant Health Inspection Service (USDA-APHIS). CVM currently regulates "intentional genomic alterations" in animals utilizing the new animal drug authority under the Federal Food, Drug, and Cosmetics Act (FFDCA), as described in draft "Guidance for Industry #187" (Guidance 187). In early 2021, USDA-APHIS published an Advanced Notice of Proposed Rulemaking in which it discussed its intention to assume regulatory jurisdiction over certain biotech animals used in agriculture.[6]

In the intervening period, BIO understands that FDA has proposed revisions to Guidance 187 that would make improvements to regulatory transparency and efficiency, among other improvements. But those revisions have not yet been made available for public review and comment. Given that the Guidance 187 is equally applicable to biopharmaceutical animals, whose oversight FDA would retain even if USDA-APHIS's proposal were finalized and implemented, BIO asks that the Office of Management and Budget (OMB) allow the Food and Drug Administration (FDA) to promptly publish its revised Guidance 187 in draft form for public review and comment. Stakeholder input on proposed changes to FDA's regulatory framework for animal biotechnology is critical to facilitating an effective and streamlined regulatory pathway for both agricultural and non-agricultural animals produced using biotechnology. Prompt publication of FDA's draft guidance enables animals solely within FDA's jurisdiction to benefit from any improvements to FDA's framework. Publication would have the added benefit of further informing the necessity and scope of a potential regulatory role for USDA. The current impasse is simply untenable and is actively discouraging U.S.-based innovation and the accessibility of new tools for farmers and for human and animal health.

Following release of the guidance, FDA and USDA should collectively identify opportunities for collaboration and coordination in a way that keeps the food supply safe but stimulates innovation by getting safe products into the market as expeditiously as possible. Careful consideration must be given to the treatment of animal products that could potentially come under the purview of both federal agencies at different points in the development and commercialization timeline. For example, developers of products already approved by FDA would likely strongly oppose any requirement to later restart an entirely new review at USDA. Similarly, developers with products currently in review at FDA that transition to the USDA system would not want to lose progress on FDA reviews, be

[6] 85 Fed. Reg. 84269 (Dec. 28, 2020).

forced to repeat experimental studies already developed or reviewed by FDA or experience other delays or inefficiencies. Developers in such situations would incur significant, burdensome costs if regulatory studies must be redesigned or repeated due to even small differences between FDA and USDA expectations. If a dual agency regulatory framework were adopted, BIO would strongly encourage meaningful inter-Agency collaboration on formal mutual recognition between USDA and FDA, so that approvals already granted by FDA can be recognized by USDA, and regulatory data provided to FDA could be recognized by USDA so that developers do not lose their significant investment in time and research in the transition.

Time is of the essence. Last year, extreme heat across the Great Plains killed thousands of cattle. It was also the worst bird flu outbreak in U.S. history with nearly 58 million birds dying and egg prices increasing by 120 percent. Innovations in animal biotechnology may be able to help prevent, prepare for, and respond to future outbreaks of infectious diseases, while helping livestock producers adapt to climate changes. However, continued uncertainty about these agencies' overlapping jurisdictions will stifle innovation at a critical time for the technology, farmers, and the planet. BIO remains committed to continuing to work collaboratively with USDA, FDA, and other Executive Branch offices on the urgent need to improve the regulatory system for products of animal biotechnology that continues to ensure the safety of the animals, consumers, and the environment while fostering innovation and expedited commercialization of beneficial improvements to animals produced using biotechnology.

III. Microbial Biotechnology

Technology developers utilize microorganisms improved using biotechnology to create high-performing agricultural inputs that can be used alone or in conjunction with conventional products to provide more sustainable solutions to meet grower needs. These sustainable solutions are being developed to help address the impacts of climate change on agriculture, as well as reduce use of energy-consuming synthetic fertilizers, which are responsible for 2.4 percent of global greenhouse gas emissions[7] and a major factor on the inflationary pressures felt by producers and consumers around the globe. Developing and deploying microbial technology in crop production can result in reduced nutrient run-off, increased nutrient use efficiency, increased crop resilience to biotic or abiotic stress, and enhanced soil health, among other agricultural and environmental benefits.

Regulatory agencies should continue to communicate with stakeholders so that microbial product developers of all sizes are able to understand and clear any necessary regulatory hurdles and reach the market as efficiently as possible. BIO encourages the U.S. government to ensure that all of the Coordinated Framework agencies with oversight over microbial products, including those at USDA-APHIS, FDA, and the Environmental Protection Agency (EPA), are adequately staffed with the appropriate scientific expertise so that regulatory oversight aligns with the good governance principles in Section I.

[7] https://www.researchsquare.com/article/rs-1007419/v1

While USDA-APHIS's recently revised Part 340 Rule has the potential to streamline the deployment of innovative plant technologies, it has created uncertainty for microbial technology developers. Absent from Part 340 are clear regulations that enable an appropriate and predictable path to testing biotechnology-derived microorganisms in the field or bringing them to the commercial marketplace. Developers of such products therefore experience uncertainty-related delays in identifying and testing these products, which leads to no clear path for commercializing new products.

BIO requested in its comments on the proposed Part 340 rule that USDA develop, propose, and implement a plan to facilitate research, development, and commercialization of non-plant biotechnology-derived organisms, including microbes and insects. As we noted at the proposed rule stage, continued failure to do so will create a significant competitive disadvantage for these products, slow research and development, and delay introduction to the market of innovative products with the potential to be an additional solution for some of agriculture's most pressing challenges. Other key agricultural markets have clearer regulatory pathways for these products, which provides those countries with a competitive advantage in developing and adopting enhanced microbial products.

BIO appreciates USDA-APHIS's work on its recently released Questions & Answers – Working with Microorganisms Developed Using Genetic Engineering Under 7 C.F.R. §340 – August 2022, relevant to non-plant organisms potentially under its jurisdiction. BIO was also pleased to hear during USDA-APHIS's Biotechnology Regulatory Services' (BRS') recent stakeholder meeting that BRS is preparing for a March 2023 release of a guidance document offering additional clarification on the regulatory pathway for microbes under Part 340. BIO strongly encourages BRS to continue devoting expert resources to that guidance document to meet this anticipated timeline, and to microbial technologies more generally. BIO also strongly encourages BRS to release the guidance document in draft form for public review and comment before a final guidance document is issued in the coming months. In conjunction with that soon-to-be-released guidance, BIO also asks that USDA-APHIS to reinstate the former Am I Regulated (AIR) process or establish a similar consultative process so that developers have a formal mechanism to obtain regulatory clarity under 7 C.F.R. part 340 for microorganisms developed using biotechnology, while the Agency contemplates further clarification. BIO further requests that any rulemaking contains "futureproofing" provisions that would enable developers and other stakeholders to petition the agency for additional exemptions or other opportunities to streamline regulatory processes as science further develops.

USDA should further ensure coordination between APHIS-PPQ and EPA so that regulation of microbial products not regulated under Part 340 is transparent, efficient, and not unnecessarily duplicative. For those products that fall under EPA's jurisdiction, the agency should ensure that the risk assessment is proportionate to any actual risk posed by the microbe. Where the need for registration of a particular product as a pesticide is not clear, an expeditious review under the M009 process should be provided and the agency should likewise allow similar products to be grouped for review without imposition of multiple fees.

Separately, BIO notes that USDA-APHIS in its proposed Part 340 revisions indicated it would "maintain a list of taxa that contain plant pests on its website and would be available for consultation by developers to help them determine whether or not their GE non-plant organism is or is not a plant pest." 84 Fed. Reg. 26521. The previous list of taxa, that was codified in the prior 7 CFR Part 340 regulation at section 340.2(a), helped provide a degree of regulatory clarify that was unfortunately lost with the revision to Part 340. To BIO's knowledge, USDA-APHIS has not yet made a new list public or otherwise available for public comment. Furthermore, the agency has not proposed processes for removing taxa/genera from the list or modifying the list as taxonomic designations change over time. Additional clarity is needed from the Agency on how the list will be relevant to Part 340 generally. BIO asks that APHIS make these clarifications or disclose its current thinking regarding the list, if different from its proposal, as soon as possible.

BIO also urges USDA to identify ways within USDA and with its sister agencies to define this product class and study how plant biostimulant products can contribute to soil health. Plant biostimulants can improve a plant's natural nutritional processes, which results in enhanced tolerance to abiotic and other environmental stresses and improves overall plant health, growth, quality, and yield. In doing so, these products can increase the uptake and utilization of existing and applied nutrients. Plant biostimulants also can increase yield and quality without increasing applied fertilizer, water, or expanding planted acres, thus, sustainably enhancing the efficient use of these inputs and natural resources. Comprehensively, these technologies will not only result in a significant reduction in agriculture's climate and water-quality footprint, but it is a win-win for farmers, as the costs for their crop inputs and labor needs would decrease.

Regarding EPA's oversight over microbial technology under the Toxic Substances Control Act (TSCA), BIO's members request that EPA's Office of Pollution Prevention and Toxics develop a template and/or other guidance to identify and harmonize the specific components to be included in the data package developers are required to submit for a Microbial Commercial Activity Notice (MCAN) under TSCA. Providing clear, easily accessible guidance will streamline developers' preparation of MCAN packages and will create new efficiencies on the part of agency reviewers.

Additionally, microbial biotechnology procured through aquaculture is yielding breakthrough discoveries. For example, novel marine microbes were discovered that produce new natural chemicals that outperform existing antimicrobials to control surface contamination and biofouling, to kill bacteria and fungi at concentrations too low to trigger resistance, and to act as biostimulants for agri/aquaculture. This innovation does not fall into any current category for U.S. grant funding or other support, which is holding back the development and commercialization of the technology in the U.S. Innovators making discoveries in microbial biotechnology are forced to look for support overseas. The oceans are an untapped resource for remediating the pollution in our waters and soils and providing cures for antimicrobial-resistant (AMR) bacteria and fungi – the "Superbugs" for which there is no other cure.

IV. Plant Biotechnology

A regulatory climate that fosters innovation is a crucial component to ensuring the development and deployment of tools producers will need for meeting the agricultural and environmental challenges in the future. In 2022 CropLife International commissioned AgBioInvestor[8] to conduct a time- and cost-to-market study. The study notes that the first widespread commercial cultivation of a biotechnology-derived genetic trait in commercial agriculture was in 1992. Since then, because of the demonstrated benefits, the number of genetically modified (GM) traits used in crops has increased significantly, which in turn has increased the number of crop species and geographic area where these crops are produced and used. The primary aim of this study was to provide an up-to-date view on the cost and duration associated with the discovery, development, and authorization of a new GM trait that has received cultivation approval in at least two countries and import approvals in at least five countries. The study builds upon the time- and cost-to-market study conducted in 2012 to examine how certain metrics have changed over time.[9]

Key take-aways from the 2022 study include:

- The cost of discovery, development and authorization of a new GM trait has declined $21 million over the past 10 years (from $136 million in the 2008–2012 period to the current value of $115 million). It should be noted that the regulatory phase of the process accounted for 51.1% of the total costs, compared to 36.7% in the 2012 study.
- More importantly, the time to market has increased from 13.1 years to 16.5 years. This represents a 26% increase over 2008-2012 when this study was last performed. The increase comes primarily in the regulatory phase, as developers are having to overcome more barriers and countries are regulating on less consistent timelines, increasing their data requirements, while also taking longer to approve products.
- The regulatory process alone now takes almost as long as the entire R&D process took in the previous study. This results in an additional 40 months of lost commercial revenue for product developers, meaning a reduction of the window for recouping a return on its investment.
- In general, the increased timelines and increased costs of the regulatory process contradicts the increasing experience with safety assessments of GM traits and the benefits of their cultivation and use globally.

a. USDA-APHIS

USDA's final Part 340, which BIO supports, aims to ensure that regulations keep up with innovation. Historically, USDA has had an excellent track record regulating plant biotechnology based on science and risk. The final rule acknowledges a history of safe use of plant biotechnology and the similarity of many genome-edited plants to those derived from conventional breeding techniques,

[8] https://croplife.org/wp-content/uploads/2022/05/AgbioInvestor-Trait-RD-Branded-Report-Final-20220512.pdf
[9] https://croplife.org/wp-content/uploads/pdf_files/Getting-a-Biotech-Crop-to-Market-Phillips-McDougall-Study.pdf

which itself has a long history of safe use. However, there are several areas in which USDA-APHIS-BRS can improve to further facilitate deployment of innovative products.

To safeguard consistency across regulatory reviews under the new Part 340, BIO recommends that USDA employ additional training to agency personnel, and develop streamlined, consistent, and science-based permit templates and review processes that are not overly prescriptive in developer implementation. These steps should be designed to ensure that reviewers are treating similar requests similarly and are consistent from year to year so that predictability is increased, and that permit conditions are proportional to potential plant pest risk, while remaining flexible so that agency and developer resources are used as efficiently as possible. BIO also encourages additional coordination between BRS and APHIS's staff working assessments under the National Environmental Policy Act to ensure an appropriate understanding of agriculture and consistent approach across offices. Finally, BIO encourages USDA-APHIS to take steps to ensure that decision-making for permits is on a timeline that more closely resembles notifications under the prior Part 340 rule, and carried out in a way that is transparent for developers. As an example, USDA-APHIS has completed only seven Regulatory Status Reviews (RSRs) as of today since the revised Part 340 rule became final in May 2020, with likely dozens still in the queue for review. Of the RSRs reviewed, the agency has consistently exceeded the timelines laid out in the regulations. USDA should also provide additional information regarding the scientific rationale and basis that may trigger the factors BRS uses when moving from an Initial Review to a Plant Pest Risk Assessment stage of regulatory status review.

USDA should continue to evaluate the agency's approach to exemptions to ensure that regulatory burden is consistent with plant pest risk. Specifically, BIO asks the agency to reconsider its current, restrictive approach to exemptions for gene edits in polyploid plants and gene edits stacked using molecular methods (also called simultaneous or multiplexed edits). This approach is overly restrictive especially compared to science-based and pragmatic frameworks adopted by other agencies in the Americas, resulting in increased opportunity for innovative product development.[10] Further, USDA should produce a timeline for finalizing additional exemptions under consideration.

In addition, BIO urges USDA to work with its counterparts in other agencies globally as they develop or update regulations addressing agricultural biotechnology, including the establishment of exemptions for certain products developed using the tools of genome editing. Such consistency across agencies will be of great importance to developers working to bring products to the U.S. market.

Finally, BIO encourages USDA to work collaboratively with FDA on new applications or products relevant to FDA's jurisdiction over food, but to ensure that any such collaboration does not result in duplicative or unnecessarily burdensome regulatory approaches or otherwise pose obstacles to development and commercialization of new technologies and products that are firmly within USDA's jurisdiction.

[10]Whelan (2020), Gene Editing Regulation and Innovation Economics https://pubmed.ncbi.nlm.nih.gov/32363186/

b. USDA-AMS

BIO encourages USDA's Agricultural Marketing Service (AMS) to develop a process by which product developers can voluntarily seek from AMS product-specific confirmation of whether or not a food is a bioengineered food subject to the National Bioengineered Food Disclosure Standard (BE Standard). As developers create new biotechnology products, whether plant, animal, or microbial, AMS does not currently provide developers with guidance or assistance in assessing whether food from such products would be subject to disclosure under the BE Standard. Knowing whether food from new biotech products is or is not subject to disclosure under the BE Standard can be useful in supporting innovation and investment in the agricultural biotechnology sector.

Additionally, BIO strongly recommends that AMS reconsider its prohibition on using genetically modified organisms in the manufacture of organic products when the genetically-modified organism and all nucleic acids (the genetically modified portion of the organism) are completely removed from the final product. For example, new technologies have emerged for the creation of peptide-based biopesticides, involving the manufacture of peptides through fermentation in a food-grade yeast where the yeast and all of its nucleic acids are removed from the final product. The final product is an effective pesticide with the ease of use of traditional chemical pesticides but with more favorable health, safety, and environmental profiles. Nevertheless, these peptides are precluded from organic certification solely because of the manufacturing process. As a result, organic farmers lack the ability to find effective pesticides, which increases the cost of organic produce. Peptide-based biopesticides could represent a significant opportunity for U.S. organic growers to reap more effective pest control and lower production costs, which could mean more ready access to lower cost, high quality produce for consumers.

c. EPA

On October 9, 2020, the U.S. Environmental Protection Agency (EPA) proposed regulatory revisions which would clarify the oversight and exemptions for certain "plant incorporated protectants" ("PIPs") – pesticide-like substances produced in plants – when developed using modern biotechnology in ways similar to conventional breeding or found in nature. BIO supports EPA's initiative to modernize EPA's regulations under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) to exempt from FIFRA certain PIPs in genome-edited plants, which came at a unique and critical time for technology developers and society. BIO is broadly supportive of the objectives of the proposed revisions to EPA regulations and the intent to expand the existing exemptions to include similar products developed using newer, more precise methods to introduce genetic variation in plants. We believe that the rationale behind the proposal is well-justified scientifically, will not result in any novel risks to the environment or to human health, and has the potential to facilitate the development of innovative applications of cutting-edge genetic tools in a wide variety of crops and economically important plant species.

BIO is concerned, however, that requirements of the proposed rule are needlessly prescriptive and unnecessarily restrictive. In particular, the requirement that exempt substances be identical to native substances, combined with the difficulty of demonstrating expression levels across a panoply of tissues, developmental stages, and genotypes, will make it exceedingly difficult for a developer to demonstrate eligibility for the proposed exemptions, which will significantly limit their utility in the U.S. without any safety benefit. Despite EPA's acknowledgement that plants developed using innovative plant breeding techniques are similar to those developed from conventional breeding and have a long history of safety (and that breeding is unlikely to lead to novel hazards or exposures), we believe that EPA's proposal still holds PIPs produced via biotechnology to a much different standard than the same plants produced via conventional plant breeding—an approach that is scientifically unjustified and fundamentally at odds with the principles of effective regulation laid out in the Coordinated Framework. In BIO's comments on the PIPs proposal, it encouraged EPA to ensure that its proposed exemptions are, to the greatest extent possible, consistent with similar exemptions adopted by USDA.

BIO recommends that EPA further clarify in the final rule that the scope of regulation of PIPs under 40 CFR Part 174 is limited to pesticidal substances intended to prevent, destroy, repel, or mitigate a pest through a specific toxic mode of action that acts directly on a pest. This clarification will help to better draw a distinction between 1) substances which are considered PIPs but are exempt from certain FIFRA requirements in 40 CFR Part 174, versus 2) substances which are not considered PIPs in the first place, and therefore not subject to 40 CFR Part 174 or FIFRA more generally.

BIO further recommends that EPA adhere to the good governance principles discussed herein when addressing its plant regulator authority as it relates to innovative products of biotechnology. The term "plant regulator" means "any substance or mixture of substances intended, through physiological action, for accelerating or retarding the rate of growth or rate of maturation, or for otherwise altering the behavior of plants or the product thereof" (40 CFR 174.3). Despite EPA's authority to oversee the safety of substances applied to plants intended to regulate their growth through physiological action, stretching the concept of "plant regulators" into the context of genetic alterations in plants is not supported under EPA's FIFRA authority and would establish a scope of regulation disproportionate to actual risk. Genetic modification is often aimed at changing a plant's characteristics that may in some way relate to its altering growth, development, or behavior, despite the absence of any of the kinds of toxic chemical substances originally intended to be overseen by FIFRA. BIO strongly opposes the attempted extension of FIFRA to require premarket review and registration for genetic changes that alter the plant's growth, development, or other physiological characteristics. Similarly, in light of the extensive experience and scientific understanding gained by EPA in reviewing certain categories of PIPs, such as the Bacillus thuringiensis proteins, and the excellent safety record of those products, the agency is now in a position to expedite processing of future like products by reducing data requirements for registration and, for food use crops, granting broader tolerance exemptions. Requests for guidance under the M009 process should likewise allow similar products to be grouped for review without imposition of multiple fees.

Finally, we encourage EPA to consider including in any amended PIP regulation a mechanism by which EPA may add new categories of exemptions for low-risk PIPs, either of their own initiative or in response to public petition. This will help EPA to future-proof its regulations and increase the agency's ability to adapt and respond to changes in science and continued innovation. USDA adopted a similar mechanism in its recent revisions to 7 CFR Part 340, and we would encourage EPA to consider doing the same. BIO further asks that EPA ensure that its Science Advisory Panel is sufficiently staffed and with appropriate scientific expertise to address new technologies and new applications of technology.

BIO looks forward to further engagement with EPA and with the Office of Management and Budget on these and other issues when the rule reaches an appropriate phase of the process under Executive Order 12866.

d. FDA

It is crucial that the government establish risk-proportionate, transparent regulations that spur biological innovations while protecting health and the environment in a timely manner. BIO strongly encourages FDA to promptly release its long-pending guidance on genome editing in plants and encourages FDA to ensure that the guidance (i) reconfirms principles from the 1992 policy statement on new plant varieties,[11] (ii) demonstrates regulatory consistency across all federal agencies, and (iii) aligns with the policies of like-minded key trading partners, like Canada.

Increased federal funding and coordination between agencies will be critical to maintain America's leadership and ensure its farmers and producers will have access to cutting edge agricultural technologies. BIO therefore urges the U.S. government to provide FDA with the necessary resources to support the issuance of the above-referenced guidance for industry on foods derived from plants produced using genome editing and to modernize and improve the timeliness and predictability of the Plant Biotechnology Consultation Program under FDA's 1992 Statement of Policy – Foods Derived from New Plant Varieties. The formal FDA consultation process on new plant biotechnology products has, in the past several years, slowed to a point where it consistently takes two to three years to complete, even for products with very familiar traits. Such extended reviews for products that FDA has concluded repeatedly are as safe as foods developed using traditional techniques is scientifically unjustified. Staffing at appropriate levels is crucial to ensuring that reviews—including those unattached to statutory user fees and mandatory timelines—are completed on a timeline that does not impede investment or disincentivize use of the voluntary consultation programs. Moreover, fundamental streamlining and efficiency gains in the processes are needed for FDA to keep pace with other agencies, including consolidation of agency divisions that are unnecessarily duplicative and waste agency resources. BIO also encourages FDA to clarify that for products derived from plant-trait-mode of action combinations having already cleared voluntary consultation, no further consultation is needed.

[11] *See* FDA, Statement of Policy: Foods Derived from New Plant Varieties (1992), *available at* https://www.fda.gov/regulatory-information/search-fda-guidance-documents/statement-policy-foods-derived-new-plant-varieties.

Finally, BIO is aware of and concerned about FDA's prejudicial and troubling approach to certain technologies, including new and innovative ways of producing in plants animal proteins for use in human food, *i.e.*, plant-grown proteins—a technology that was specifically called out in the RFI. BIO understands that FDA staff intend to use limited resources to pursue an obstructive, precautionary strategy that would block certain technologies altogether, rather than relying on the fundamental principles of risk assessment, recognition and trust in sister agencies' regulatory authorities, and collaborative and productive engagement with the developer, to facilitate careful, step-wise progress toward commercialization. We encourage FDA to promptly revise its approach to better align with good governance principles, and we look forward to engaging further with the agency on this issue.

Relatedly, BIO encourages FDA to fill out its staff with personnel having the requisite scientific expertise able to handle new and novel technologies and the application of those technologies in novel ways to produce innovative food products. BIO further encourages the government to look carefully at the recently issued report by the Reagan Udall Foundation. In it, FDA is encouraged to develop policies that enable its scientific staff to attend scientific conferences to learn about innovative technology, among other recommendations intended to improve the culture among FDA's food regulators. The Agency should do all it can to encourage its regulators to approach new technologies with an agnostic, open mind, a firm commitment to the good governance principles outlined herein, and a willingness to work collaboratively and transparently with product developers toward a goal of commercializing products, rather than stifling innovation.

A critical gap in FDA's ability to assess new drug candidates is knowledge of bacterial and fungal biofilm. Although biofilm is a fundamental aspect of animal and human microbiology and microbial resistance, FDA does not require that new drug candidates be tested for efficacy against biofilm during pre-clinical trials, which could ultimately result in significant financial losses to both the grantor agencies and taxpayers. FDA sends new drug candidates making antibiofilm claims to the EPA as "antimicrobial pesticides," rather than facilitating their use as therapeutics for humans and animals. Finally, FDA not created reimbursement codes for therapeutics and prophylactics making antimicrobial claims. This gap is costing healthcare systems the burden of over 2.7 million cases of biofilm-related infections per year, many fatal.

V. Synthetic Biology

Increasing research in synthetic biology will unlock innovations in agriculture and food productions, energy, and manufacturing. Biotechnology companies have identified opportunities to incorporate synthetic biology[1] in groundbreaking advances in industrial biotechnology manufacturing processes. Companies have begun using science to optimize the processes for producing renewable chemicals, biobased products, and biofuels. With synthetic biology techniques, industrial biotechnology companies can save time by shortening the number of steps used in traditional processes, reducing costs while developing new products. They can also reduce the products' impact on the environment. With proper support, synthetic biology can transform our economy.

[1] https://www.bio.org/blogs/synthetic-biology-innovation-industrial-biotechnology

Because of strong federal support, the United States is a leading nation in the development of synthetic biology. This success and high research productivity are not lost on foreign governments, including China, who are trying to kick-start their biomanufacturing sectors to catch up to, or even leapfrog, the U.S. Our continued growth will be fueled by robust scientific research, strong intellectual property rights, well-functioning technology transfer, dynamic capital investment, science- and risk-based regulation that minimizes obstacles, and public support that embraces the positive influence of biotechnology.

Supportive grants for research and development and startup will provide significant advances in foundational tool development and practical applications ranging from bioenergy, biomanufacturing, to biomedicine. The recommendations put forward by the National Academies of Sciences Engineering Medicine report, *Safeguarding the Bioeconomy*[2] can give further guidance in advancing the bioeconomy for the betterment of the U.S. and society.

BIO also supported the inclusion of the *Bioeconomy Research and Development Act* in the *CHIPS and Science Act of 2022* to strengthen and unifying engineering biology by establishing an initiative to advance research and development, advance biomanufacturing, and develop the future bioeconomy workforce. The Department of Defense Synbio Manufacturing MII[12] initiative also has great potential for collaborative, pro-innovation opportunities to expand American leadership in biotechnology.

VI. International

U.S. leadership in biotechnology is a cornerstone of U.S. economic and national security and provides a platform from which to exercise global leadership on key issues. Executing thoughtful and creative trade strategies is among the most effective means to enhance global science-based collaboration while growing the U.S. bioeconomy.

For over twenty years, the U.S. has successfully and safely led the world in the commercialization of biotechnology to enable increased production, sustainable farming, and industrial practices. These innovations reduce greenhouse gas emissions throughout agricultural supply chains, delivering environmentally friendly products and processes to the market and more nutritious offerings to consumers.

To ensure that agriculture can continue to be a solution to domestic and global climate and sustainability challenges and improve food security, the U.S. must continue to address acute and systemic trade barriers to innovative biotechnology tools in important export markets. To fully

[2] https://www.nap.edu/resource/25525/interactive/
[12] https://www.defense.gov/News/Releases/Release/Article/2388087/dod-approves-87-million-for-newest-bioindustrial-manufacturing-innovation-insti/

leverage the potential of technology to address these challenges, a level-playing field globally will be essential.

To do so, the United States must reassert its influence within the global trading system by leading efforts to place science and technology at the core of its global economic and strategic interests. As such, BIO encourages the administration to reengage with the World Trade Organization (WTO) to reform the institution and lead efforts to launch new initiatives focused on liberalizing trade and establishing rules to enable a revolution in science and technology. Particularly when it comes to new opportunities and initiatives that can resent WTO agricultural negotiations.

Further, while trade agreements can help establish science-based regulatory systems that can promote the development of, and access to, disruptive and transformative biotechnologies, they are only effective if the U.S. uses the mechanisms within to agreement to enforce those rules. Currently, BIO is particularly concerned that Mexico is failing to live up to its U.S. – Mexico – Canada Agreement (USMCA) obligations to facilitate trade and provide a science-based regulatory process for biotech products. BIO urges the administration to follow USDA Secretary Tom Vilsack and recognize there is "no reason to compromise[13]" on Mexico's failure to adhere to its commitments under USMCA. This is especially true for any proposal that that limits market access for corn, or other biotech crops grown by U.S. farmers, to the Mexican market on a non-science based distinction between food and feed products. We request the administration seek consultation regarding Mexico's USMCA violation of agricultural biotechnology to provide developers and producers provide a framework and timeline to resolve Mexico's treatment of agricultural biotechnology.

It is also necessary that the U.S. hold China to its commitments to implement critical market-based reforms, intellectual property protection, and science-based regulations. Regarding agricultural biotechnology, BIO urges the U.S. government to continue to engage with China to fully comply with the 'Phase One' commitments, including finalizing biotech risk assessments within two years. Honoring these commitments will help China implement a transparent, predictable, efficient, science- and risk-based regulatory process.

The U.S. should also proactively engage Europe on science-based climate and sustainable agricultural solutions, asserting the valuable and proven role of biotechnology to achieve food security and climate-positive successes in these sectors.

Finally, as noted earlier, BIO is concerned the U.S. regulatory policy for genome-edited plants, microbes, and animals is out of alignment with other countries and at risk of falling behind countries in South America, and Asia in R&D and commercialization. BIO members are actively leveraging genome editing techniques to develop plants, animal and microbes that are more resilient to pests, diseases, and extreme weather, and reduce usage of agricultural inputs. Several agricultural producing countries, such as Argentina, Brazil, Colombia, have established reasonable regulatory

[13] https://www.agri-pulse.com/articles/18695-vilsack-no-compromise-with-mexico-on-gm-corn

pathways for products derived through genome editing. However, other countries, such as Mexico and South Korea, both countries that have free-trade-agreements with the United States, have no regulatory framework for these emerging technologies. It is crucial that the U.S. leverage all multilateral and bilateral mechanisms to encourage the promulgation of gene editing regulations with all of our trading partners to facilitate commercial availability and acceptance of these emerging biotech products.

Conclusion

By proactively advancing biotechnology, we can take bold action to tackle issues of the highest priority for this Administration. BIO is committed to working with OSTP and the administration and welcomes the opportunity to meet with you and relevant Cabinet officials to further discuss how we can advance pioneering technology breakthroughs to improve the health and prosperity of our nation and the world.

Sincerely,

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