August 5, 2019

Dr. Alan Pearson
Assistant Deputy Administrator
Biotechnology Regulatory Services
Animal and Plant Health Inspection Service (APHIS)
4700 River Road
Unit 98
Riverdale, MD 20737-1238

Re: Docket No. *APHIS-2018-0034, Movement of Certain Genetically Engineered Organisms*[1]

Dear Dr. Pearson:

On behalf of the Biotechnology Innovation Organization (BIO), thank you for the opportunity to provide comments to the United States Department of Agriculture on its June 6, 2019 Proposed Rule regarding the movement of certain genetically engineered (GE) organisms.

BIO is the world's largest life sciences trade association representing nearly 1,000 biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States and in more than 30 other nations. BIO members are involved in the research and development of innovative biotechnology products that will help to solve some of society's most pressing challenges, such as managing the environmental and health risks of climate change, sustainably growing nutritious food, improving animal health & welfare, enabling manufacturing processes that reduce waste & minimize water use, and advancing the health and well-being of our families.

For over two decades, the products of agricultural biotechnology have been commercially available and widely used by a growing number of farmers around the world. In the United States, more than 90 percent of corn, cotton, canola, papaya, soybean, and sugar beet seeds planted contain at least one biotechnology-derived trait. Farmers use these products because they enable the production of more food and feed on fewer acres using less energy and reduced pesticide applications.

The research, development, and widespread commercialization of the current set of agricultural biotechnology products occurred as U.S. government agencies, including APHIS, conducted pre-market regulatory oversight of these products under the auspices of the Coordinated Framework for Regulation of Biotechnology (Coordinated

[1] 84 Fed. Reg. 26514 (June 6, 2019).

Framework).[2] The United States' science-based regulatory approach enabled technology developers to generate and commercialize many highly beneficial products, while assuring consumers and markets that such products have received appropriate pre-market regulatory scrutiny and are as safe and nutritious as their conventional counterparts. BIO commends APHIS for its efforts to improve its regulatory system over the years, from the addition of the streamlined notification process in 1993 and its improvement and addition of the extension processes in 1997, to more recent improvements to the petition process, new guidance for extensions, and clarification of the letter of inquiry process.

During that time, plant breeding techniques have continued to develop and now include more targeted and precise tools, which are the subject of significant agricultural research and development effort as they offer exciting potential to address growing challenges in agriculture and society generally. As noted in the Report to the President of the United States from the Task Force on Agriculture and Rural Prosperity (Rural Task Force Report),[3] global food demand will continue to increase, while availability of arable land will continue to decrease.[4] Innovation in agriculture has the potential to provide solutions and tools that can increase crop yields, improve crop quality, nutritional value, and food safety; increase resistance to pests and diseases; reduce water use; improve carbon sequestration; enhance tolerance to changes in climate and other environmental conditions; reduce food waste; improve health and wellness; decrease reliance on costly crop inputs; and bolster animal welfare.

Advancing and facilitating the adoption of innovations and technology for agricultural production and long-term, sustainable rural development has been a key goal of this Administration and many others, as recently addressed in the White House's Executive Order on Modernizing the Regulatory Framework for Agricultural Biotechnology Products (E.O. 13874).[5] As described in that Executive Order:

> In order to realize these potential benefits, however, the United States must employ a science-based regulatory system that evaluates products based on human health and safety and potential benefits and risks to the environment. Such a system must both foster public confidence in biotechnology and avoid undue regulatory burdens.

A regulatory climate that fosters innovation in agricultural biotechnology will be an important component in meeting that goal and ensuring development of a set of precise yet flexible tools for meeting the challenges facing U.S. farmers today and into the future. The challenges faced by farmers reflect challenges faced by society at large.

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[2] 51 Fed. Reg. 23352-23366 (June 26, 1986).

[3] https://www.usda.gov/sites/default/files/documents/rural-prosperity-report.pdf

[4] United Nations Food and Agriculture Organization. 2009. *How to Feed the World in 2050.*

[5] https://www.whitehouse.gov/presidential-actions/executive-order-modernizing-regulatory-framework-agricultural-biotechnology-products/

Practical, workable regulations are key to harnessing the resources necessary to address these challenges, and to providing opportunities for economic growth, job creation, and environmental benefits. The U.S. has been and continues to be an innovation leader in biotechnology and the development of modern breeding techniques.

BIO is committed to maintaining a strong partnership with the Agency to ensure the development and implementation of risk-proportionate regulations that underpin a workable, predictable, legally defensible, durable, and science-based regulatory system that facilitates innovation for all innovative biology-based products. In addition to working with the Agency on its proposed revision to Part 340, BIO is also committed to partnering with USDA and other appropriate agencies on identifying and implementing solutions to regulatory challenges for animal products of biotechnology, including those produced using more advanced breeding tools, to ensure that those products also have a predictable pathway to market.

At the same time, BIO recognizes that long-term innovation successes are driven by more than just sound regulatory policy. Public and marketplace support matter a great deal in the successful introduction of new products. BIO is committed to proactive transparency measures, including driving authentic dialogues with stakeholders and consumers to identify shared values and energize public understanding about innovation in food and agriculture.

Below, we (i) outline a set of principles and best practices for rulemaking and development of regulations to which the federal government has committed itself during the current and past Administrations; and (ii) provide more detailed feedback on APHIS's proposed revision to Part 340, and, where possible offer recommendations for improvement in the final rule. In addition, we note that consistency between the U.S. regulatory system and the systems of our trading partners (where possible) are essential to the smooth movement of products in the global supply chain. BIO therefore encourages the Agency to continue the work it has undertaken to actively engage with our trading partners and to continue working toward consistent, science-based regulatory policies across countries.

BIO agrees with and supports many aspects of APHIS's proposed revision, and has also identified areas for further improvement that will ensure that the final rule conforms to the principles of good regulation outlined below. BIO asks that, before finalizing the regulation, APHIS carefully consider these comments set out below to ensure that the final rule addresses *all* GE organisms, engenders broad support, and proves easier to implement.

I. PRINCIPLES OF GOOD REGULATION

A number of Executive Orders, Agency memoranda, and other Executive Branch directives and materials establish best practices and guiding principles for effective rulemaking and regulation in general. A number of these are specific to oversight of biotechnology and other innovative technologies applicable to agriculture. We briefly

describe some of these directives here to assist with providing context for our feedback on APHIS's proposal.

Importantly and most recently, the White House issued E.O. 13874, directing the U.S. Department of Agriculture, among other agencies, to review their respective agricultural biotechnology regulatory systems in an effort to streamline processes and remove regulatory barriers that restrict societal access to beneficial innovations. That Executive Order is consistent with White House directives issued earlier during this Administration asking executive branch agencies to identify legislative, regulatory, and policy changes, that, among other goals, "advance the adoption of innovations and technology for agricultural production and long-term, sustainable rural development."[6] BIO believes that these directives establish benchmarks against which any biotechnology-related policies and regulations should be measured.

The most recent Executive Order builds upon a foundation established by several earlier Executive Orders directing agencies to follow important principles and requirements in rulemaking.[7] 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.[8] These rulemaking principles 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.

We believe strongly that government policy regarding the products of biotechnology should be based upon these core "good governance" principles.

Regarding oversight of biotechnology in particular, in 1986, the U.S. White House Office of Science and Technology Policy (OSTP) first published the Coordinated Framework, which established how Federal agencies would exercise oversight of products of the then-emerging technology.[9] OSTP then reiterated those foundational principles in 1992

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[6] https://www.whitehouse.gov/the-press-office/2017/04/25/presidential-executive-order-promoting-agriculture-and-rural-prosperity

[7] E.O. 12866, E.O. 13258, E.O. 13422, E.O. 13563, E.O. 13497, E.O. 13610.

[8] https://obamawhitehouse.archives.gov/sites/default/files/omb/inforeg/for-agencies/Principles-for-Regulation-and-Oversight-of-Emerging-Technologies-new.pdf

[9] 51 Fed. Reg. 23352-23366 (June 26, 1986).

when it published a memorandum outlining "fundamental scope principles" to aid Coordinated Framework agencies in determining the scope of regulation:

1) A determination to exercise oversight within the scope of discretion afforded by statute should not turn on the fact that an organism has been modified by a particular process or technique, because such a fact is not alone a sufficient indication of risk.

2) A determination to exercise oversight in the scope of discretion afforded by statute should be based on evidence that the risk presented by introduction of an organism in a particular environment used for a particular type of application is unreasonable.

3) Organisms with new phenotypic traits(s) conferring no greater risk to the target environment than the parental organisms should be subject to a level of oversight no greater than that associated with unmodified organisms.[10]

These principles were reaffirmed by OSTP in a review of the Coordinated Framework published in early 2017.[11]

In the sections that follow, we analyze APHIS's proposed regulatory revisions through the lens of all these guiding principles for development of effective regulation.

II. ANALYSIS OF THE PROPOSED RULE

BIO commends APHIS on the extensive process it has undertaken with respect to its proposed revision to Part 340, which included stakeholder outreach and communication, and in particular, efforts to reach small companies and academics. APHIS's efforts provided an ample opportunity for stakeholders with an interest in research and development related to the application of new, innovative technologies to agriculture to provide input.

The fruits of that outreach and the resources the agency marshaled to develop it are apparent in the proposed rule. BIO commends APHIS for its efforts to improve the regulatory system for agricultural biotechnology and for recognizing the long history of scientific evidence and safety associated with agricultural biotechnology and plant breeding. BIO also appreciates the position APHIS has taken on products of newer breeding techniques like genome editing, and its recognition of the similarity of products derived from these techniques to products produced using conventional plant breeding. Attached to this comment is an Appendix identifying the numerous scientific studies, articles, and literature reviews that support the Agency's thinking on this point. APHIS's

[10] 57 Fed. Reg. 6753-6762 (February 27, 1992).

[11] https://www.aphis.usda.gov/biotechnology/downloads/2017_coordinated_framework_update.pdf

proposed framework also provides additional flexibility for plant product developers navigating the regulatory pathway for new products, enabling regulatory certainty during the research and development process. As described more fully below, APHIS should work to ensure that developers of non-plant GE organisms are afforded the same flexibility and opportunity for regulatory certainty.

In addition to presenting a practical and risk-based approach to new, innovative agricultural products, the proposed rule also contains a number of significant, material improvements over the Agency's January 2017 proposal[12] to revise Part 340. In our comments to that earlier proposal, BIO recommended that APHIS:

- Move away from the concept of an "up front" regulatory status evaluation and instead specify clear, risk-based criteria defining the scope of APHIS's pre-market oversight.
- Add a new mechanism to its regulations to allow the agency to assess and potentially remove from regulation broader categories of familiar species-trait combinations or organisms that meet certain criteria.
- Avoid incorporating into 7 C.F.R. Part 340 noxious weed assessments that are duplicative of assessments conducted under 7 C.F.R. Part 360.

Accordingly, BIO was pleased to see the Agency, in its most recent proposal:

- Clarify the regulatory status of a product before it undergoes the newly proposed regulatory status review process.
- Amend its approach with respect to its noxious weed authority to prevent unnecessary regulatory duplication.
- Move away from event-by-event regulation.
- Provide flexibility and certainty to GE plant developers by making permits available while the plant is completing the new regulatory status review process.

All these positive changes demonstrate that the Agency took seriously its commitment to undertake a "fresh look"[13] at Part 340 and has made positive changes that provide additional clarity for developers of new, innovative agricultural products.

While there is much to like in the proposal, BIO has also identified areas for further improvement that will ensure that the final rule meets the goals of being workable, predictable, legally defensible, durable, and science-based.

[12] 82 Fed. Reg. 7008-7039 (January 19, 2017).
[13] https://www.usda.gov/media/press-releases/2017/11/06/usda-re-engage-stakeholders-revisions-biotechnology-regulations

A. Scope of Regulation of Plant Products.

BIO commends APHIS for its significant efforts to refine its scope of regulation to be better aligned with plant pest risk. As noted in the proposal, APHIS's current regulations cover:

> Any organism which has been altered or produced through genetic engineering, if the donor organism, recipient organism, or vector or vector agent belongs to any genera or taxa designated in §340.2 and meets the definition of plant pest, or is an unclassified organism and/or an organism whose classification is unknown, or any product which contains such an organism, or any other organism or product altered or produced through genetic engineering which the Administrator, determines is a plant pest or has reason to believe is a plant pest.[14]

This definition dates to a time when using genetic sequences from plant pests and creation of GE plants using plant pest vectors was commonplace and provided a rationale for regulating such plants on a presumption that they could pose an increased risk of creating or disseminating plant pests. As a result, many GE plants have been subject to APHIS oversight based on the presence of harmless viral sequences, such as the 35S promoter derived from Cauliflower Mosaic Virus (CMV), or transformed using a disarmed version of the soil bacterium *Agrobacterium tumefaciens*, while nearly identical GE plants created without viral sequences, or engineered via other mechanisms, are not subject to APHIS oversight.

BIO was pleased to see the Agency rethink this regulatory approach first in its January 2017 proposal. In BIO's view, the most effective regulatory system for biotechnology should (i) provide clear, risk-based criteria to identify organisms that are exempt from oversight and those needing further risk assessment, and (ii) include clear, transparent, and defensible mechanisms by which organisms within the initial risk-based scope can be efficiently assessed for risk and, if appropriate, removed from further oversight. It was therefore BIO's view in connection with the Agency's proposal in 2017 that the best approach was to refine the existing scope of regulation by progressively removing from regulation categories of species-trait combinations and products meeting certain risk-based criteria. As BIO noted in 2017, that approach would help the agency to continually refine its regulatory scope as new scientific information becomes available.

In the proposed rule, APHIS has retained the view that a rethinking of regulatory scope is in order. Specifically, the Agency has acknowledged its "three decades of experience in evaluating GE organisms for plant pest risk," 84 FR at 26525, and that "[t]he Agency's evaluations to date have provided evidence that genetically engineering a plant with a plant pest as a vector, vector agent, or donor does not in and of itself result in a GE plant that presents a plant pest risk." 84 FR at 26515. As a substitute, APHIS has formulated a new scope of regulation for plants that is focused on properties of the GE

[14] 7 C.F.R. § 340.1

organism, rather than on the method used to produce it. The precepts are compatible with the good governance principles cited above, and BIO supports them and provides additional feedback and, in some cases, further refinement, including a request that the Agency promptly fill the gap left in its proposal related to non-plant GE organisms.

B. Approach to Plant Products of Genome Editing.

We commend the Agency for recognizing that any revision to Part 340 should "prepare the Agency for future advances" in the technology subject to its oversight. 84 FR at 26516. BIO notes that the Agency has done just that with respect to plant products developed using the "newer toolset" to expedite development of a plant with a desired genotype and/or traits. 84 FR at 26519. Specifically, APHIS proposes that "certain categories of modified plants would be exempted from the regulations in part 340 because they could be produced through traditional breeding techniques and thus are unlikely to pose a plant pest risk." 84 FR at 26517. As noted by the Agency, "[t]raditional breeding techniques generally involve deliberate selection of those plants with desirable traits either from existing population genetic variations or from new genetic variations created through artificial hybridization or induced mutations, and have been used since the advent of sedentary agriculture." 84 FR at 26519. Such plants, according to the Agency, "are likely to pose no greater plant pest risk than their traditionally bred comparators." 84 FR at 26519.

BIO strongly agrees with this approach for two reasons. First, the plants that would be subject to these exemptions are not currently subject to APHIS's definition of a regulated article, and we believe there is no risk-based justification for changing that status. Not only are such organisms unlikely to pose a plant pest risk, there is no evidence to suggest that they pose a greater plant pest risk than organisms developed via traditional breeding, which are not subject to APHIS pre-market regulations. As the Agency has concluded, "given the accepted safety of traditionally bred crops, and the principle that the use of recombinant DNA does not itself introduce unique risks, it is logical and appropriate to exempt from our regulation plants produced by any method if they could have been produced by traditional breeding." 84 FR at 26517, 26519.

Consistent with foundational principles of the Coordinated Framework, plant varieties developed through plant breeding innovations, such as genome editing methods, should not be subject to the additional pre-market regulatory review if they are similar to or indistinguishable from varieties that could be produced through conventional plant breeding.[15]

[15] Attached to these comments is an Appendix providing additional support for the Agency's conclusion on these important points. We encourage the Agency to review and incorporate these resources in connection with promulgation of the final rule and its further development of the draft Environmental Impact Statement published alongside the proposed rule.

Second, in updating the current regulatory process under Part 340, every effort should be made to promote agricultural innovation in accordance with the Rural Task Force Report, E.O. 13874, and their numerous predecessors from past Administrations. The benefits to agriculture that have resulted from, and will continue to result from, the development and commercialization of innovative products, including products developed using genome editing and other precision breeding methods, should be widely available to all our nation's farmers and to consumers more broadly. Given USDA's experience in operating under a comprehensive and coordinated federal regulatory process for oversight of new plant products since 1986, where the science demonstrates that a product or category of products could have been produced using conventional breeding methods or in nature, such products should be exempt from pre-market review.

To implement these exemptions from pre-market regulation under the proposed revised Part 340, the Agency has proposed Section 340.1(b), which provides that "[t]he regulations in this part do not apply to plants modified such that they belong to one of the categories listed below:

> (1) The genetic modification is solely a deletion of any size; or (2) The genetic modification is a single base pair substitution; or (3) The genetic modification is solely introducing nucleic acid sequences from within the plant's natural gene pool or from editing of nucleic acid sequences in a plant to correspond to a sequence known to occur in that plant's natural gene pool; or (4) The plant is an offspring of a GE plant that does not retain the genetic modification in the parent.

BIO generally agrees with the exemptions proposed by the agency above. These exemptions are broadly consistent with the categories of plants that the Secretary identified in 2018 as not subject to current regulations, nor for which the agency had any plans to regulate in the future.[16] APHIS has sufficient experience and familiarity reviewing plants in these categories of products using the existing "Am I Regulated" process. For example, as of September 2017, APHIS had authorized 333 field trials for plants edited using CRISPR, 29 using TALENs, 25 using zinc-finger nucleases.[17]

While we agree that it is helpful for the agency to clarify that plants that are offspring of GE plants that do not retain the genetic modification of the parent (aka "null segregants") are not subject to Part 340, we feel that their inclusion on a list of exempted plant modifications is somewhat confusing and redundant, because such plants do not carry any modifications. We recommend striking this particular category from the exemption list.

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[16] https://www.aphis.usda.gov/aphis/ourfocus/biotechnology/brs-news-and-information/2018_brs_news/pbi-details

[17] *See* https://www.aphis.usda.gov/biotechnology/downloads/Meetings/2017_sh_mtg/Stakeholder_Meeting_Presentation_2017.pdf

Additionally, the four exemptions described above are relatively narrow and do not fully encompass the spirit of the Secretary of Agriculture's March 28, 2018 statement that USDA does not plan to regulate plants that "could otherwise have been developed through traditional breeding techniques," 84 FR at 26519. Techniques commonly used by plant breeders today are capable of creating a much broader array genetic modifications than the limited exemptions proposed. As acknowledged by the Agency in its 2018 statement, these traditional plant breeding techniques have a long-demonstrated history of safety. See Appendix. Accordingly, BIO requests that the Agency revise the language in proposed Section 340.1(b)(3) in the final rule to better align with the Secretary's intent, and recommends that proposed Section 340.1(b) read as follows:

> (1) The genetic modification is a deletion of any size; or (2) The genetic modification is a single base pair substitution; or (3) The genetic modification is introducing nucleic acid sequences from with the plant's natural gene pool or from editing nucleic acid sequences in a plant to correspond to a sequence from that plant's natural gene pool or otherwise accessible through traditional breeding methods such as induced or somaclonal mutagenesis, tissue culture, protoplast, cell or embryo fusion, wide and bridging crosses, or other methods that enable efficient movement of genes from unadapted to elite varieties.

Whether or not the Agency chooses to adopt the exemption language proposed above, we recommend that the Agency make clear in the final rule that it has ability to add additional exemptions through an expedited process (e.g. via guidance). Adopting a mechanism to add new exemptions over time ensures the regulatory system stays up-to-date and keeps pace with scientific knowledge.

C. "Confirmation" Process under Proposed Section 340.1(d).

In addition to providing specific exemption criteria, the Agency has proposed Section 340.1(d), under which a developer could voluntarily seek from the Agency a "confirmation" that a GE plant fits one of the categories identified in proposed Section 340.1(b) or is a product with a plant-trait-mechanism of action (MOA) combination that the Agency has evaluated and determined poses no plant pest risk, under proposed Section 340.1(c). BIO appreciates that the Agency considered and responded to stakeholder feedback that APHIS's process should include a means for a product developer to seek confirmation regarding a product's regulatory status. As confirmed through BIO's conversations with stakeholders, written confirmation provides several valuable benefits to developers and other interested parties including awareness for grain handlers, processors, and exporters; food manufacturers and retailers; consumers and public advocacy groups; and others regarding what products are in the marketplace.

BIO encourages the Agency to include in the final rule a process by which a developer is required to notify the Agency of a GE plant which the developer has determined meets one of the exemptions in proposed 340.1(b) or (c) prior to placement on the market. BIO looks forward to working with the Agency on implementing guidance that achieves

transparency without limiting innovation in either commodity or specialty crops. In the meantime, we recommend the following provide the backbone of such guidance:

1. Notification should be required no later than 90 days before initial placement on the market, however, a developer would not be precluded from submitting the notification earlier;
2. Notification should provide the plant species and information for exempted product(s) sufficient to show the applicability of an exemption under 340.1(b) or (c):
    a. For exemptions under 340.1(b) sufficient information could be the developer, the species, and confirmation that the genome-editing technique used and resulting plant(s) meets a specific 340.1(b)exemption,
    b. For exemptions under 340.1(c) sufficient information could be the developer, species, and identification of the antecedent product of the same species with a similar trait-mechanism of action that was earlier determined to be unlikely to pose a plant pest risk;
3. The Agency would have 60 days from the date of a submission to review the information in the notification and to contact the developer with any questions or requests for further clarification on the notification. However, no Agency action is required and no response from the Agency within the 60-day timeframe shall be the equivalent to no objections;
4. If desired, the developer may request a written confirmation, as described in the voluntary confirmation process in proposed 340.1(d). The Agency shall provide confirmation within 60 days;
5. Information required to be submitted under mandatory notification would be posted to an Agency web-resource for public and stakeholder transparency upon notification;
6. Additional, voluntary information provided in the notification and associated Agency responses would also be posted to an Agency web-resource, but are subject to APHIS withholding of confidential business information (CBI) in accordance with proposed Section 340.7.

This approach would be consistent with the direction given to the USDA, FDA, and EPA in the June 11, 2019 Executive Order. It would also take into account the direction that our international trading partners are taking. Importantly, it would offer the possibility of more consistency among the US regulatory agencies. To encourage efficiency and prevent redundant regulation, we would strongly recommend that USDA and other agencies, where appropriate, enter into a Memorandum of Understanding recognizing the notification process at USDA. The mandatory notification process and website posting would have the additional benefit of providing public notice and transparency about new products intended for placement on the market.

***D. Definitions*.**

"Genetically engineered organism." Throughout the proposed rule and preamble text APHIS uses the term "genetically engineered organism" or "GE organism" but has not proposed a formal definition for that term. While in the current proposal the Agency defines "genetic engineering," *see* proposed Section 340.3, the Agency does not make clear how that definition applies to the definition of "GE organism." This approach departs from APHIS's January 2017 proposed rule, in which the Agency defined "GE organism," providing a clear and transparent means for developers and other stakeholders to ascertain precisely which organisms are and are not subject to pre-market oversight under Part 340.

It is BIO's view that the omission of a definition for "genetically engineered organism" makes the rule less clear and less transparent and more difficult for developers to implement with respect to the scope of regulation. Accordingly, BIO asks that the Agency include in the rule a definition for "GE organism" using the framework from January 2017 and incorporating the exemptions set forth in proposed Section 340.1(b), as amended in accordance with the discussion above. The text would read as follows:

> Genetically engineered organism (GE organism). An organism developed using genetic engineering. For the purposes of this part, an organism will not be considered a genetically engineered organism if the organism meets one or more of the exemptions in Section 340.1(b).

Other Definitions. In addition to providing a definition for "genetically engineered organism," the Agency should also consider making modifications to several other proposed definitions.

The Agency has proposed to define "genetic engineering" as "[t]echniques that use recombinant or synthetic nucleic acids to modify or create a genome," proposed Section 340.3, suggesting that "[t]his proposed definition is clearer than the existing one" by avoiding use of the term "recombinant DNA techniques," a term it notes "is not defined in the regulations." 84 FR 26522.

But the same can be said for APHIS's use in the current proposal of the term "synthetic," which is not widely understood in the context of biotechnology and for which the Agency has provided no explanation, other than to note that the Agency intends "synthetic DNA" to be captured. Accordingly, BIO requests that the Agency clarify that "synthetic" nucleic acids for purposes of Part 340 are those that are non-naturally occurring. This additional information will provide developers and other stakeholders with a clearer picture of what products the Agency intends to include within the scope of the regulations.

BIO also notes that, in several places in the proposed rule and its preamble related to non-plant organisms, the Agency uses the phrasing "used to control" in the context of a product intended to be used to address a plant pest. For example, in Part 340.2(d), in

describing the types of products the Agency expects would require a permit prior to movement, the Agency identifies "a microorganism used to control plant pests or an invertebrate predator or parasite (parasitoid) used to control invertebrate plant pests and could pose a plant pest risk." *See also* 84 FR at 26520, 26522, 26522, 26524. The proposed rule does not include a definition for "used to control." As drafted, "used to control" has the potential to be broad in scope, because it could be interpreted to include both intentional and *unintentional* use and thereby introduces disharmony with the Federal Insecticide, Fungicide, and Rodenticide Act's definition of "pesticide," which turns on intended use of a product. *See* 7 U.S.C. § 136(u). To ensure that APHIS's regulatory scope is consistent with and does not exceed EPA's, BIO requests that the Agency clarify that by "used to control" plant pests, the Agency is referring to products *intentionally* used to control plant pests.

Throughout the proposed rule, APHIS discusses the regulatory end-point for regulation of GE plants as "could pose a plant pest risk" or "could pose a potential plant pest risk". APHIS proposed to define plant pest risk as "possibility of harm to plants resulting from introducing or disseminating a plant pest or exacerbating the impact of a plant pest". The language proposed by the agency is inconsistent with the Plant Protection Act (PPA). We recommend that APHIS use the language more consistent with PPA to determine whether a GE plant is a plant pest and thus should be regulated. Sec 411(e)(3)(B) uses the end-point of "may pose a significant risk of causing injury to, damage to, or disease in any plant or plant product".

E. Regulatory Status Review.

In its current proposal, the Agency has indicated that it will implement a new "regulatory status review" (RSR) process for evaluating GE plants for plant pest risk under which APHIS would consider the following information "in combination and individually" (i) The basic biology of the plant prior to modification; (ii) the trait that resulted from the genetic modification; and (iii) the mechanism of action, rather than the method by which the organism is genetically engineered. 84 FR at 26524. If the Agency finds that the plant-trait-MOA combination is unlikely to pose a plant pest risk and is therefore not subject to Part 340, "the developer could proceed with product development and marketing activities free from regulation under part 340." 84 FR at 26524. Developers not wishing to immediately proceed with the RSR process, or uncertain about whether a product is similar to a previously-evaluated crop-trait-MOA eligible for exemption, would have the option of applying for a movement permit under the regulations. *Id*.

The Agency has also proposed that the Agency will compile a "comprehensive list" of products having completed the regulatory status review and make information pertaining to the results of all completed reviews publicly accessible on the APHIS website. 84 FR at 26517. In addition, APHIS has proposed that it would exempt from the regulations in part 340 "GE plants with plant-trait-mechanism of action (MOA) combinations" it has "already evaluated by conducting a regulatory status review and found to be unlikely to pose a plant pest risk," including "GE plants for which we have made determinations of nonregulated status under the petition process." 84 FR at

26517. The Agency proposes that developers would have the ability to "self-determine" whether a product is subject to such an exemption, relying on the information made publicly available on APHIS's website. *Id.*

The Agency's approach is consistent with BIO's comments to the Agency's 2017 Part 340 proposal, in which we recommended that APHIS (i) add a new mechanism to its regulations to allow the agency to assess and potentially remove from pre-market regulation broader categories of species-trait combinations or organisms that meet certain criteria based on familiarity and past reviews; and (ii) abandon the "up front" regulatory status evaluation concept, and develop regulatory revisions to define specific risk-based criteria that clearly and transparently identify the categories of organisms the agency believes should be within scope and in need of pre-market regulatory scrutiny.

BIO strongly supports APHIS's efforts to refine the existing scope of regulation by progressively removing from regulation categories of species-trait combinations and products meeting certain risk-based criteria, thereby ensuring that Agency resources are allocated commensurate with risk and clearing potentially unnecessary regulatory hurdles for products capable of addressing challenges in agriculture. BIO also offers below a handful of comments and potential opportunities for improvement, clarification, or both with respect to this proposed new RSR framework.

Initial Review and Plant Pest Risk Assessment. The Agency has proposed a two-tier system for the RSR process, beginning with an Initial Review process followed, if necessary, by a more comprehensive RSR that would be accompanied and supported by a Plant Pest Risk Assessment. Specifically, the Agency has indicated that the Initial Review phase would be "objective, rapid, and based on transparent predetermined criteria" and would result in "a finding of whether a GE organism[18] is subject to the regulations in Part 340," a process having "functional similarity" to the current "Am I Regulated" (AIR) process. 84 FR at 26527. APHIS proposes that its Initial Review would consider whether "alterations in the GE plant are likely to pose a plant pest risk, based on analysis of the following factors:

> I. The biology of the comparator plant and its sexually compatible relatives; II. The trait and mechanism-of-action of the modification(s); and III. The effect of the trait and mechanism-of-action on: a. The distribution, density, or development of the plant and its sexually compatible relatives; b. The production, creation, or enhancement of a plant pest or a reservoir for a plant pest; c. Harm to non-target organisms beneficial to agriculture; and d. The weedy impacts of the plant and its sexually compatible relatives.

[18] While the Agency uses the term "GE organism" here to describe the RSR process, it has proposed that the process is exclusively available only to plants, thereby leaving an incomplete and uncertain regulatory pathway for non-plants, as set forth in Section II.G, below.

84 FR at 26526. APHIS has proposed making available on its website a list of plant-trait-MOA combinations having successfully cleared the Initial Review phase of the RSR. 84 FR at 26527.[19]

In circumstances where, through the Initial Review process, APHIS "identifies potential plant pest risks," the Agency proposes it would conduct "a PPRA [plant pest risk assessment], a more robust analysis than the initial review, to evaluate the factor(s) of concern and to determine the likelihood and consequences of the potential plant pest risks identified in initial review." 84 FR at 26527. The Agency proposes that the RSR as supplemented by the PPRA process could result in a finding (i) that the plant-trait-MOA combination is not subject to the regulations, or (ii) that additional information is needed to evaluate potential plant pest risks. 84 FR at 26527. APHIS proposes that, in cases where a plant product undergoes the more "robust" RSR with the PPRA process, the results of both the Initial Review and the PPRA would be made public and subject to public comment. 84 FR at 26527. Such plant products would either be found unlikely to pose a plant pest risk and not subject to regulation under Part 340 or, without such a finding, continue to be subject to movement under permit. 84 FR at 25427. [See also discussion of "plant pest risk" under Other Definitions, above]

BIO requests that the Agency provide additional detail in the final rule, and in the associated final Environmental Impact Statement, concerning the dividing line between the Agency's RSR under the Initial Review and the criteria the Agency would use in determining that the more "robust" RSR with PPRA process is warranted under the circumstances. APHIS uses the term "factor(s) of concern," but provides no additional information regarding specific factors to be addressed or evaluated and what general types of information may be necessary to APHIS's review of "the likelihood and consequences of the potential plant pest risk." Proposed Section 340.4(b)(3)(1); 84 FR 26527. BIO requests that APHIS clearly define the criteria it intends to use and how those criteria will be applied to various plant types, including but not limited to how APHIS intends to determine "distribution, density, or development of the plant and its sexually-compatible relatives" and weediness across plant types. Proposed Section 340.4(b)(1)(iii)(A), (D). Additional clarity in the rule and in the final EIS will ensure that the Agency's decision-making criteria are clear and transparent, leading to predictable, defensible determinations concerning plant pest risk. *See also* Section II.I, below.

In addition, BIO notes that the AIR process has provided APHIS with plant-trait-MOA information for a number of products and that APHIS has reviewed and considered that information in rendering its regulatory determinations under the current process. BIO encourages APHIS to use and rely on information it has gained through the AIR process in undertaking RSR assessments to prevent unnecessary duplication and ensure efficient use of regulatory resources.

[19] To date, APHIS has not made the list available, precluding the opportunity for comment on how APHIS defines the mechanisms of action for previously deregulated products.

Status of Products Subject to Determination of Non-Regulated Status. The Agency has also indicated that products having obtained a Determination of Non-Regulated Status will be identified on APHIS's website for use by developers in assessing whether a particular product is eligible for exemption under the plant-trait-MOA exemption. However, the Agency has not provided adequate clarification regarding the status of those deregulated products under the new framework, *e.g.*, whether the previous determinations of no plant pest risk will remain under the new framework and/or be subject to a grandfathering provision, or whether the Agency will reassess those products using the new RSR process. Without clarification, the regulations could be interpreted to require new, redundant evaluations of products having completed the existing Part 340 process. Accordingly, BIO asks that the Agency make clear in the final rule, in section 340.2, that the regulations do not apply to GE organisms that have been granted nonregulated status pursuant to former regulations under Part 340.

Information Requests for RSR. The Agency has provided some initial detail regarding the information it plans to require in connection with an RSR related to a GE plant and its plant pest risk potential. Proposed Section 340.4(a)(4)(ii); 84 FR at 26525. Included in the Agency's characterization of the information it expects to receive is "the genotype of the modified plant including a detailed description of the difference in genotype between the modified and unmodified plant." 84 FR at 26525. As currently drafted, the regulation may be misinterpreted to imply that the Agency expects significantly more sequence information, *i.e.*, whole genome sequencing, than is necessary for the Agency to conduct its assessment of plant pest risk. In order to ensure that the Agency's request for information is calibrated to the Agency's need for information, and to facilitate the protection of developers' valuable CBI and trade secrets, BIO requests that the Agency clarify that the information needed is limited to sequence information for the specific genetic modification in the plant, rather than for the entire plant, by revising Section 340.4(a)(4)(ii) as follows:

> (ii) A description of the differences in genotype between the modified and unmodified plant;

In addition, BIO notes that, in the past thirty years, the Agency has not reviewed or deregulated any GE plants that would pose the kinds of plant pest risks APHIS proposes to evaluate, for example, in proposed Section 340.4(b)(1)(iii). BIO therefore asks that the Agency ensure that RSR data requirements are sufficiently flexible in conjunction with the specific nature of the particular product being evaluated so that developers have an ample opportunity to obtain the benefit of a reduced data submission and take advantage of APHIS's intention to reduce the need for field trial data.

Regarding APHIS's anticipated data needs related to the RSR, BIO notes that certain data categories appear to exceed what APHIS has asked for over the past 27 years of reviewing petitions, despite the fact that APHIS's current data requests have demonstrated their adequacy for purposes of assessing plant pest risk. Accordingly, BIO also requests that, to the extent possible, PPRA data requirements should align with the information the Agency had been seeking previously and should under no circumstances

increase a developer's data submission burden, as the current proposal appears to do. For example, APHIS has indicated that it will seek information regarding "production, creation, or enhancement of a … reservoir for a plant pest," although developers currently do not enumerate the level of plant pest presence in field trials. Proposed Section 340(b)(1)(iii)(B).

Protection of Confidential Business Information. APHIS has indicated that "[t]he general description of the plant-trait-MOA combination will not be eligible for CBI designation," but that "[c]ertain technical information that could be used to re-create an organism" may be eligible for CBI designation "under existing statutory authorities." 84 FR at 26526, 26533. BIO members are therefore concerned that APHIS's RSR process, as proposed, provides inadequate opportunity for developers to claim information submitted in support of that process as CBI. Without a clear and unqualified option for protecting valuable intellectual property and other proprietary information, developers would be unwilling to submit genotypic information to the Agency. If APHIS's aim is to encourage greater use of the RSR process, APHIS should ensure that proposed Section 340.7 extends to data submitted in connection with the RSR process. Otherwise, APHIS virtually assures that no developer would apply for the RSR process until a product has been selected for commercialization.

Consistent Use of Terminology. In describing its proposal related to crop-trait-MOA analyses, the Agency alternatively uses the terms "same" and "similar" to describe the types of products that could be subject to exemption under proposed Section 340.1(c) based on their use of a crop-trait-MOA combination that has already been assessed by the Agency and deemed not to be a plant pest risk. *See, e.g.*, 84 FR 26517, 26520, 26526 ("same"); 26516 ("similar"). Two products may have a "similar" crop-trait-MOA combination that is not necessarily the "same," creating the potential for ambiguity with respect to what is and is not exempted. BIO therefore asks for the Agency to ensure that the final rule clarifies the Agency's intention in this regard, both in the preamble and in the final rule text itself. It may also be helpful for the agency to provide more specific definitions of "mechanism of action" and "trait."

PMPIs*.* APHIS notes in the preamble to the proposed rule that certain plants genetically engineered to produce pharmaceutical and industrial compounds, also known as plant-made pharmaceuticals and industrials (PMPIs) could, under the proposed Part 340 framework, "could be grown outdoors without the need for APHIS permits and without APHIS oversight." 84 FR 26518. In response to APHIS's request for comment on "the best manner to address," this issue, *id.*, BIO agrees with APHIS that developers "have various legal, quality control and marketing motivations to maintain rigorous voluntary stewardship measures," and that "developers would continue to utilize such measures for field testing" of products, like PMPIs, where under the proposed regulatory framework USDA would not require a permit. 84 FR 26535. BIO also points APHIS to

Excellence Through Stewardship,[20] a resource that such a developer could use to guide field trials conducted without APHIS oversight.

F. Regulatory and Implementation Timelines.

Noticeably absent from APHIS's proposed rule are any concrete timelines for agency responses to confirmation requests under proposed Section 340.1(d), completion of Initial Reviews or PPRA processes under the RSR process (proposed Section 340.4); or permit applications. For example, while APHIS has characterized the Initial Review process as "rapid," it has suggested no specific timeline on which such a review would take place. As BIO has communicated to APHIS in the past[21], clear and predictable timelines are imperative for ensuring a clear and predictable regulatory system, without which innovation is stifled. BIO therefore asks that APHIS make clear in the final rule specific timelines for each of the components of the new framework and ensure that APHIS has adequate resources to consistently meet the timelines it sets from the time the rule takes effect and into the future.

Relatedly, APHIS has failed to provide any guidance regarding timing and transition from the current Part 340 framework to the new framework for developers of GE plants and non-plants. As APHIS is aware, developers are conducting numerous research and development activities under permits and notifications, are planning for next-phase activities for products in development and are awaiting APHIS action on pending petitions for non-regulated status. Given the significant volume of activities ongoing under the current system and the need to ensure an orderly transition to the new framework, BIO asks that the Agency provide in the final rule reasonable implementation and compliance dates that provide developers adequate time to plan for and adapt to the new framework and that ensure transparency regarding APHIS's plan for transitioning from the current to the new system.

BIO recommends that APHIS provide a 2-year transition period for organisms not currently subject to Part 340 to comply with the new regulations. For products currently under regulation, developers could elect to comply with the new regulation sooner. BIO recommends that the Regulatory Status Review and mandatory confirmation provisions become effective within thirty days of the rule's effective date. Regarding elimination of the notification process and implementation of new permit conditions, we recommend that currently-authorized permits and notifications be allowed to continue through the expiration date of the existing notification or permit.

BIO further points APHIS to the implementation and compliance timeline provisions recently promulgated in 7 C.F.R. Part 66, the final rule for the National Bioengineered

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[20] https://www.excellencethroughstewardship.org/

[21] BIO Comments on Docket No. APHIS-2015-0057, Evaluation of Existing Regulations; Importation, Interstate Movement, and Environmental Release of Certain Genetically Engineered Organisms (June 19, 2017), Appx. at 12.

Food Disclosure Standard, which provided entities regulated under that rule with a clear, transparent plan for transitioning to the new standard.

G. Regulation of Non-Plant GE Organisms

We commend the Agency for recognizing that any revision to Part 340 regulatory system should "prepare the Agency for future advances in the genetic modification of plants," but note that the Agency has done very little, if anything, with respect to preparing the Agency for future advances relevant to non-plant GE organisms, or ensuring a regulatory pathway for non-plant products currently under development. As set forth in detail below, BIO asks that the Agency marshal all necessary resources to promptly develop, propose, and implement a plan to facilitate research, development, and commercialization of non-plant GE organisms, including microbes and insects. Failure to do so will create a significant competitive disadvantage for these products and delay their introduction to the market.

In the proposed rule, the Agency has stated that "APHIS will continue to regulate … GE non-plant organisms that pose plant pest risks. Such organisms would require permits for movement. Other GE non-plant organisms that do not pose a plant pest risk would not fall under the scope of the regulations and therefore would not require permits for movement." 84 FR at 26516. BIO agrees that the Agency's focus on only those GE non-plant organisms that pose a plant pest risk is the appropriate scope for the Agency's regulatory oversight. Lacking from the proposal, however, is a clear and predictable regulatory framework for non-plant GE organisms potentially subject to Part 340—an uncertainty that has the significant potential to slow research, development, and commercialization of entire categories of innovative agricultural products with the potential to present novel and lasting solutions to some of agriculture's most pressing challenges.

The Agency's current regulatory framework provides developers of non-plant GE organisms with access to the AIR process to determine whether a particular non-plant GE organism is subject to regulation under Part 340 and, if so, the ability to apply for and obtain permits for movement or release.

As discussed above, the new regulatory process outlined in the proposed rule provides de facto corollaries for the AIR and petition for determination of non-regulated status processes, but only for plants. The Agency has made clear that only GE plants are eligible for exemption from Part 340 under proposed Sections 304.1(b) and (c) and that "the regulatory status review process would apply only to plants and not to genetically engineered plant pests or other genetically engineered non-plant organisms that fall within the scope of the regulations. 84 FR at 26517. This partial revision, with no corresponding process for non-plant GE organisms, creates regulatory uncertainty with respect to non-plant GE organisms by leaving such products subject to Part 340 with a single regulatory option: movement under permit. Developers of such products have no formal means by which to self-determine that they do not pose a plant pest risk, request confirmation from the agency regarding their regulated or non-regulated status, seek an

early consultation regarding the regulatory status of a particular product, or apply to the Agency for determination by risk assessment that its product does not pose a plant pest risk. The Agency's failure to provide any formal processes for non-plant products, or any timeline in which to develop such a process, has the potential to bring research and development of innovative non-plant products to a complete halt – a result that stands in stark contrast to the mandate set forth in the E.O. 13874 and good governance principles generally.

Accordingly, BIO urges the Agency to promptly develop and issue guidance in conjunction with the final rule on a process parallel to the proposed Section 340.1(d) confirmation process and the Regulatory Status Review for non-plant GE organisms potentially subject to regulation under Part 340, including:

(i) an opportunity for developers to self-determine whether they are subject to Part 340 and apply to the Agency for confirmation of regulatory status;
(ii) a process by which developers can consult with the Agency regarding products in a research and development pipeline for guidance on a proposed regulatory pathway;
(iii) a listing of non-plant organisms having been evaluated by APHIS and deemed unlikely to pose a plant pest risk; and
(iv) access to a regulatory status review process for use in assessing whether a particular organism or class of organisms is subject to Part 340 based on an assessment of whether the GE organism-trait-MOA combination poses a plant pest risk.

Without these critical tools, developers of non-plant GE organisms will lack any semblance of clear, predictable, risk-based regulatory options. In addition, APHIS should ensure that, in the final rule, any movement restrictions imposed on non-plant organisms, whether microorganisms or invertebrates, should be based on the fact that the organism itself poses plant pest risk and not on the fact that the non-plant is *used to control* plant pests.

In proposed Section 340.2, the section of the proposed rule addressing what GE organisms are subject to movement permit requirements, the Agency has proposed that permits would be required for, in relevant part, a GE organism that: "(c) Is not a plant but has received deoxyribonucleic acid (DNA) from a plant pest, as defined in § 340.3, and the DNA from the donor organism either is capable of producing an infectious agent that causes plant disease or encodes a compound that is capable of causing plant disease; or (d) Is a microorganism used to control plant pests or an invertebrate predator or parasite (parasitoid) used to control invertebrate plant pests and could pose a plant pest risk." These criteria are general, high-level, and provide little guidance to developers assessing the regulatory pathway for a particular non-plant GE organism potentially subject to these provisions. BIO therefore asks USDA to build out the high-level criteria identified in proposed Section 340.2(c) and (d) with examples and more specificity regarding the basis for regulation.

To address this request, the Agency should follow its own model with respect to plant products and develop clear criteria for a developer of non-plant GE organisms to use in ascertaining whether its product is subject to regulation. For guidance on what criteria to use, the Agency should look to current oversight of "intergeneric" microorganisms under other federal programs, a concept initially developed in the Coordinated Framework to identify microorganisms formed by combining genetic material from microorganisms of different genera.[22] Using clear, transparent, risk-appropriate criteria will ensure that the Agency harmonizes its regulatory framework with its framework for plants, provide regulatory oversight for non-plant GE organisms where appropriate to do so, and ensure that products that do not pose a plant pest risk are not subjected to unnecessary regulatory scrutiny.

BIO also notes that, as drafted, implementation of the proposed revisions to Part 340, and in particular in proposed Section 340.2, may create opportunities for duplicative regulation of products under Part 340 by USDA-APHIS-BRS and under Part 330 by USDA-APHIS-PPQ. BIO therefore asks that APHIS provide in the final rule clear dividing lines between BRS's and PPQ's individual scopes of regulation. Given the Administration's directive to agencies to reduce regulatory burdens on products that will enable innovation in agriculture, every effort should be made to ensure that BRS is regulating in a way that is consistent with its mission but that also ensures that regulatory resources are not unnecessarily duplicated by other branches of USDA.

APHIS proposes that it "will 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 FR 26521. APHIS has not yet made the list public or otherwise available for public comment, and has not proposed processes for removing taxa/genera from the list, modifying the list as taxonomic designations change over time, or how the list will be relevant to Part 340 generally. BIO asks that APHIS make these clarifications.

As described above in Section II.F, APHIS should also provide implementation and compliance timelines and direction regarding a transition plan as it relates specifically to non-plant GE organisms subject to regulation under this part.

H. Permitting

Obtaining authorization to conduct field trial research is a critical part of agriculture research and development programs. BIO supports APHIS's proposal to allow field trials to be conducted under permit without needing to first complete a RSR.

Permitting Versus Early Regulatory Status Review. Industry research programs regularly test thousands of crop/trait/MOA combinations, the vast majority of which never enter a formal research program. Some field tests are intended strictly for

[22] See, *e.g.*, 62 Fed. Reg. 17910-01 (April 11, 1997).

research purposes aimed at scientific advancement while others are intended to produce a future product. Seeking RSR for thousands of unique GE organisms annually would create a significant and unnecessary burden on industry and APHIS for GE organisms that may never move beyond the first field trial. This aspect of research and development, in combination with lack of specific timelines for RSR completion and inadequate protections for CBI associated with the process (discussed below), will incentivize BIO members to continue to make extensive use of the permitting process for most field trials. We are concerned that APHIS may have significantly underestimated the number of field trials that developers will elect to conduct under permit.

Permitting Process and Timelines. APHIS has proposed to remove the notification process and instead allow regulated activities only under permits. APHIS has justified its discontinuance by claiming that the notification process makes it difficult for APHIS to conduct inspections and determine compliance with the performance standards. BIO understands the Agency's theoretical concern but notes that these challenges have not been borne out in practice. Following the USDA Office of the Inspector General audit in 2005, APHIS has requested that companies submit Design Protocols for Agency review. Field trials conducted under notifications or permits were all conducted subject to the Design Protocols, essentially transforming the majority of notifications into the regulatory equivalent of permits.

The primary advantage of the notification process is not flexibility in how the trials are conducted but rather the certainty for developers of relatively short timelines to obtain authorization. APHIS has done a remarkable job of acknowledging notifications by the required timelines of 10 days for interstate movement and 30 days for importation and field release; whereas permits are approved within 120 days.

Predictable timelines are extremely important to developers because of the planning needed to conduct field research on a seasonal basis. Early planning is needed to identify field trial locations and secure contracts with landowners, introduce new constructs into the research pipeline, and select lines for research advancement. Uncertain and possibly longer regulatory timelines require developers to select more sites and consider more constructs for inclusion on permit applications. In turn, APHIS must conduct more critical habitat assessment for compliance with the Endangered Species Act and risk assessments on the plant/phenotype/genotype combination.

We therefore recommend that APHIS establish clear, relatively short timelines for issuance of permits under the new rule.

Amendments of Permits. BIO commends the Agency for recognizing the need to amend permit locations and proposing this allowance in the regulation. The ability to amend locations is critical when weather or other unforeseen circumstances necessitate a change in location. In addition to locations, the Agency has proposed that applicants name the researcher at each field trial location. Because of employee attrition, role changes, project changes, and changes to trial location, the researcher at the trial site

may change throughout the life of the permit from planting to completion of volunteer monitoring. BIO therefore requests that APHIS explicitly allow for changes in researchers through a notification process to the Agency. A formal permit amendment should not be necessary because no additional evaluation is required by the Agency.

Request for Clarification. With respect to proposed Section 340.5 generally, BIO requests that APHIS identify the standard permit conditions that would be applicable to all GE organisms regulated by APHIS. If a standard condition only applies to GE plants, instead of microorganisms or insects, the Agency should make that clear.
The Agency should also be specific regarding which, if any, Department of Transportation (DOT) packaging requirements are applicable to shipment of products subject to Part 340. As drafted, there is a general reference to DOT regulations at 49 C.F.R. Part 178 comprising an extensive set of requirements related generally to the transport of hazardous waste. As worded, the proposal could be viewed as adoption of a position by the Agency that GE organisms are the equivalent of hazardous materials, a position for which there is no basis, scientific or otherwise.

"Additional Information." In proposed Section 340.5(b)(4), APHIS has indicated that it would "require additional information as needed" for permit applications and, in preamble text, indicated that APHIS "proposes to routinely request … multiple GPS coordinates for requested acreage, as well as multiple GPS coordinates for actual release acreage to appropriately describe the approved area." 84 FR at 26528. Asking for GPS coordinates for field releases for "requested" acreage presents a number of implementation problems. For example, developers may not yet be aware of exact locations for where field trials will be planted at the time of the permit application and is often subject to change based on weather, field conditions, or other changes. If APHIS's goal is to track information regarding the actual location of seeds, collecting information regarding actual acreage shortly after planting would adequately satisfy that goal without imposing additional unnecessary burdens on developers.

I. Draft EIS and Revisions to National Environmental Policy Act Regulations.

In addition to the proposed rule itself, APHIS published a draft programmatic environmental impact statement (EIS), which analyzes the possible impact of the proposed regulatory changes on the human environment, and certain modest changes to its NEPA-implementing regulations (7 CFR Part 372), all for public input.

In the draft EIS, APHIS has provided information regarding how it intends to implement NEPA for individual agency actions to be undertaken under the proposed rule. *See, e.g.*, EIS at 4-106 – 4-108. BIO agrees with the Agency's current articulation regarding the interplay between the new processes established in the proposed rule and the Agency's administration of its NEPA obligations in connection with those new processes. BIO has attached to this comment an Appendix containing a number of references and resources that will assist the Agency as it completes its analysis.

BIO looks forward to reviewing APHIS's additional analysis in the final programmatic EIS regarding the Agency's assessment of potential environmental impacts associated with its proposed new framework and processes. Providing this information would be helpful not only to help the public understand how the general impacts being analyzed in the programmatic EIS relate to subsequent, action-specific NEPA analyses, but also would help inform implementation of the regulatory program APHIS is proposing. APHIS should clearly articulate how it intends to implement the requirements of NEPA under the final rule in the final EIS and ensure that its revisions to APHIS NEPA-implementing regulations (7 CFR Part 372) adequately conform to the proposed changes.

J. Other Issues.

While BIO appreciates of the complexity of the proposed rule's new framework, BIO has several suggestions it asks APHIS to consider related to implementation.

Early Consultation. Neither the confirmation process under proposed Section 340.1(d) nor the regulatory status review processes under proposed Section 340.4 provide a clear means by which a product developer could approach APHIS for consultation on a hypothetical product, *e.g.*, a GE organism (plant or non-plant) at the most preliminary stage of research and development, for regulatory guidance regarding how that product, if developed, may fit into the Part 340 regulatory framework. BIO asks that APHIS ensure that non-binding guidance accompanying the final rule provides for such a process, including processes for the protection of developer's confidential business information, to enable developers to gain an initial understanding of APHIS's thinking to help inform the developer's product pipeline development efforts and to ensure an efficient allocation of research and development dollars.

Information collection generally. In a number of places in the proposed rule, the Agency has suggested that it will provide "additional information" on its website that it has not yet disclosed in connection with this proposed rule. *See* 84 FR 26521, 26525, 26528. As BIO has communicated to the Agency in connection with recent proposed changes relevant to field trials, the Agency should clearly communicate the substance of any such guidance to stakeholders well in advance of implementation and provide an opportunity for stakeholder feedback. Doing so will help the Agency better accomplish its goals by allowing stakeholders to identify unanticipated implementation issues, thereby avoiding potential unintended consequences; use the input to improve proposals and build a strong record to support changes; and provide a better sense regarding the ease, or lack thereof, of implementation of the new requirements and help set appropriate expectations regarding the time needed to implement such changes. Accordingly, BIO asks that APHIS revise in the final rule Section 340.4(a)(4) to state as follows:

> (4) Information submitted in support of a request for a regulatory status review or re-review must meet the requirements listed in this paragraph. Additional non-binding guidance on how to meet these requirements may be found on the APHIS website.

Small-scale testing (<10 acres) of Plant Incorporated Protectants (PIPs). The Agency has asked for comment on the fact that, under its proposed rule, outdoor plantings of ten acres or less of "GE plants developed using a plant pest as a vector, vector agent or donor of genetic material would not necessarily be regulated" and that such plant would be regulated "only if it had a plant-trait-MOA combination that the Agency has not yet evaluated for plant pest risk or if it was evaluated and found to pose a potential plant pest risk." 84 FR at 26519.

As the Agency has noted, "PIPs fall under the regulatory oversight of EPA," 84 FR at 26528, which maintains a well-supported exemption from its regulatory framework for field trials of less than 10 acres, provided there is "adequate containment to prevent the PIP from entering the food and feed supply." 40 C.F.R. § 172.3. As stated in EPA guidance, "[a]n EUP is generally not required for testing at or under 10 acres, because such tests are generally presumed not to involve unreasonable adverse effects."[23] APHIS has noted that, in response to APHIS's new approach to field trials, EPA "may decide to require experimental use permits for all, some, or none of such PIPs and may conduct inspections of all, some, or none of those PIPs under permit." 84 FR at 26529. APHIS has accurately reflected EPA's regulatory exemption for PIP field trials under ten acres,[24] and BIO encourages APHIS to allow EPA to address any issues it may anticipate related to regulation of these types of field trials. A potential change in regulation by USDA does not change the fundamental requirements on developers to comply with the provisions of EPA's PIPs regulations.

Certain Exemptions from Permitting Requirements. In proposed Section 340.5, APHIS has proposed extending its existing exemptions from permitting requirements for movement of certain GE organisms to include disarmed *Agrobacterium tumefaciens*, under certain movement conditions. 84 FR at 26529. BIO strongly supports this additional exemption.

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[23] PRN 2007-2: Guidance on Small-Scale Field Testing and Low-level Presence in Food of Plant-Incorporated Protectants (PIPs), April 30, 2007.

[24] BIO notes that, if EPA were to shift its approach and regulate PIPs field trials of less than ten acres in the same way it regulates PIPs field trials of more than ten acres, the shift in approach would impose costly and unnecessary burdens on developer, resulting in significant negative impacts on the development of innovative products.

Thank you for the opportunity to provide comments on proposed revisions to APHIS's biotechnology regulations. Please feel free to contact me directly if you have any questions about our comments.

Sincerely,

Dana O'Brien
Executive Vice President
Food and Agriculture Section
Biotechnology Innovation Organization

Biotechnology Innovation Organization

Appendix

<u>Part 1</u>:
Exemptions for Plants That Could Otherwise Have Been Produced Through Traditional Breeding Techniques.

The Agency has proposed that "certain categories of modified plants would be exempted from the regulations in Part 340 because they could be produced through traditional breeding techniques and thus are unlikely to pose a plant pest risk" and "are likely to pose no greater plant pest risk than their traditionally bred comparators." 84 Fed. Reg. at 26517. The Agency has further noted that, "given the accepted safety of traditionally bred crops, and the principle that the use of recombinant DNA does not itself introduce unique risks, it is logical and appropriate to exempt from our regulation plants produced by any method ***if they could have been produced by traditional breeding***." *Id*. at 26517, 26519. The following information supports the Agency's proposal.

I. Plant Breeding has a long history of developing safe, efficacious varieties for growers and consumers

Plant genomes are not static; each individual plant has a unique genetic makeup. Breeders have leveraged various techniques to utilize and introduce genetic variation into their breeding populations since the early part of the 20th century (Moose and Mumm 2008). It wasn't until the use of the tools of molecular biology became commonplace that researchers began to understand and characterize the genetic variation underlying visible traits (phenotypes), and molecular markers were developed that could be used to follow their segregation and inheritance. During selection, breeders leverage molecular markers to follow the segregation of markers for genes that correlate with the desired phenoytpes. Often breeders will use many markers that span the genome and correlate with specific traits in their breeding populations. By the mid 1980s genetic maps of entire genomes could be made using observations of marker cosegregation (Moose and Mumm 2008). Markers have been used to speed up the process of elite line selection and allows the breeder to simultaneously enrich for favorable alleles while selecting away from alleles that are associated with undesired traits.

In addition to introducing new alleles, genes, and traits from crossing within elite lines or bringing in diversity via breeding with wild relatives of crops, breeders have also introduced new variation into breeding populations via different methods of induced mutagenesis. Mutagenesis can be induced by exposing a plant to physical (e.g. ionizing radiation such as gamma or X-rays), chemical or biological agents (e.g. exposure to pathogens, or some gene editing tools) that trigger DNA "breaks". These "breaks" are then "repaired" by naturally occurring DNA repair and recombination processes in the cells to result in the introduction of different types of DNA changes in the genome of an organism. At molecular level, induced mutations are comparable to spontaneous mutations occurring due to the action of physical agents (e.g. natural radiation or UV light) or biological factors (e.g. errors of DNA replication, recombination, movement of

transposons). The main reason for breeders to use induced mutagenesis is that such tools increase the chance that a desired mutation can be generated with a higher frequency and speed. In the last century thousands of plant products on the market have been developed using various selective breeding techniques; mutagenesis breeding [1] alone has resulted in over 3,200 varieties derived from 214 different species that have been safely produced and consumed (Ahloowalia, et al. 2004). Thus, production and consumption of food crops derived from plant breeding programs which leverage the plasticity of plant genomes have a long history of safe use.

1A. Overviews of Breeding Processes/Safety of Breeding:

ASTA (2016) Common practices of plant breeders. American Seed Trade Association, Alexandria, VA

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1C. Genome Editing Tools are an Extension of Breeding Resulting in Variation Similar to that Observed via Traditional Breeding

Genome editing is used to introduce specific and intended changes to the DNA in the genome of an organism and is a targeted and more efficient form of mutation breeding. Methods of genome editing take advantage of naturally occurring DNA repair and recombination processes to introduce desired targeted changes. Genome editing can result in a broad range of outcomes from changes of a few nucleotides (deletions, insertions, substitutions) to the integration of DNA sequence. These types of mutations are considered equivalent to those which arise via either spontaneous mutations or through the use of "conventional" breeding tools, e.g. induced mutagenesis (irradiation or chemical). Induced mutagenesis techniques generate mutations such as deletions ranging in size from tens to millions of base pairs, and rearrangements that include inversions and chromosomal translocations. As noted above, induced mutagenesis techniques have been used for many decades to develop over 3200 cultivars in more than 200 plant species.

Regardless of the breeding method used for the generation and introduction of specific traits (*e.g.* wide cross hybridization, chemical or radiation mutagenesis, genome editing), before being released, commercial plant varieties go through an extensive process of testing, backcrossing and selection. The development of a new plant variety generally requires the qualitative (visual for outward phenotypes) and quantitative (yield, disease scoring, molecular markers) evaluation of hundreds of thousands of plants, over the span of 6-9 years and 10-100 geographic locations, ultimately resulting in the selection of few new varieties that show the desired collection of characteristics and are safe for production and consumption.

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Part 2:
Exemptions of GE Plants with Plant-Trait-Mechanism of Action Combinations Found to Be Unlikely to Pose a Plant Pest Risk.

The Agency has proposed to exempt from the regulations in part 340 "GE plants with plant-trait-mechanism of action (MOA) combinations" it has "already evaluated by conducting a regulatory status review and found to be unlikely to pose a plant pest risk," including "GE plants for which we have made determinations of nonregulated status under the petition process." 84 Fed. Reg. at 26517. The following information supports the Agency's proposal.

Over the past 27 years APHIS has made over 130 determinations of non-regulated status[2] for GE plants possessing a range of crops, traits and modes of action. Many of these products have been used in the development of commercial plant varieties and hybrids that have been grown on billions of combined acres in the US and around the world. These GE products have also been evaluated by dozens of regulatory agencies in other countries reaching conclusions very similar to those reached by APHIS in their PPRA and NEPA analysis that such products pose no additional risks to humans or the environment relative to their conventional counterparts. A database maintained by

[2] See: https://www.aphis.usda.gov/aphis/ourfocus/biotechnology/permits-notifications-petitions/petitions/petition-status

ISAAA[3] tracks the hundreds of authorizations that have been granted to GE crops based on reviews conducted by thousands of expert scientific evaluations.

In addition, a subset of the products that have been reviewed and deregulated by USDA have also been evaluated by EPA. As is noted in the pEIS (pg 3-106), EPA's assessment of PIP-containing plant products are conducted under the authority in FIFRA. To grant a registration, the agency must conclude that the product does not pose unreasonable adverse effects to man or the environment under normal conditions of use. The 37 previously evaluated PIP products registered for Section 3 commercial use are listed by EPA on their website[4].

APHIS has stated (pg. 4-41) in its draft pEIS that "A recent review by the National Academy of Sciences, examining the past 20 years of data on these GE crop types, found that overall, there is no evidence of cause-and-effect relationship between GE crops and environmental problems (NAS 2016a)." This cited NAS study is perhaps one of the most comprehensive evaluations of the impact GE crops have had over the initial two decades of commercial planting of these crops.

The following additional references further support the agencies' assertions and conclusions regarding the environmental impact and other aspects of GE plant-trait-MOA combinations that have previously been evaluated and deregulated by the agency.

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