June 19, 2017

Regulatory Analysis and Development
PPD, APHIS, Station 3A–03.8
4700 River Road Unit 118,
Riverdale, MD 20737–1238

Re: Docket No. APHIS-2015-0057. Evaluation of Existing Regulations; Importation, Interstate Movement, and Environmental Release of Certain Genetically Engineered Organisms

Dear Sir or Madam:

The Biotechnology Innovation Organization (BIO) is pleased to submit these comments in response to the USDA Animal and Plant Health Inspection Service's (APHIS') request for public input on the proposed revisions to its biotechnology regulations in 7 CFR Part 340.[1] Thank you for the opportunity to provide input as APHIS considers revision of its regulations. We provided similar comments in April 2016 in response to a request for public input on the agency's Notice of Intent (NOI) to prepare an Environmental Impact Statement (EIS) in connection with possible regulatory revisions.[2]

BIO is the world's largest 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 healthcare, agricultural, industrial and environmental biotechnology products. BIO represents the majority of agricultural biotechnology product developers in North America, including companies developing products subject to APHIS oversight.

For the past 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, 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, feed, and fiber 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 science-based, pre-market regulatory oversight of these products under the auspices of the

[1] 82 FR 7008-7039 (January 19, 2017).
[2] https://www.regulations.gov/document?D=APHIS-2014-0054-0096

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Coordinated Framework for the Regulation of Biotechnology.[3] 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. APHIS should be commended 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.

Today, biological breakthroughs are enabling farmers to confront the grand challenge for agriculture: doing more with less. Society still faces the challenge of feeding an ever-expanding population, which will reach an estimated nine billion by 2050 and require at least a 70 percent increase in food, feed, fiber, and fuel production on less arable land.[4] Advancing the adoption of innovations and technology for agricultural production and long-term, sustainable rural development is a key goal in the White House's recently published directive promoting U.S. agriculture and rural prosperity.[5] A regulatory climate that fosters innovation in agricultural biotechnology will be an important component in meeting that goal, which will require a set of precise yet flexible tools for meeting the challenges facing US farmers today and into the future.

APHIS is to be commended for its efforts to achieve a better regulatory system for agricultural biotechnology and for recognizing the long history of scientific evidence and safety associated with agricultural biotechnology and plant breeding. We appreciate the strong position APHIS is providing on products of newer techniques like genome editing, and the similarity of many products derived from these techniques to conventional plant breeding. However, APHIS' proposed revisions to its 7 CFR Part 340 regulations have shortcomings significant enough that we are unable to support the revisions as proposed. Our close examination of the APHIS proposal reveals issues that must be addressed before APHIS will be able to achieve its innovation-related goals. Some of those issues include:

- Lack of predictability and clarity in scope of regulation
- Increased regulatory burden and uncertainty imposed on research and development phases of product innovation
- Challenges for the agency in implementing the proposed regulatory system on a scale compatible with current research and development activity, potentially leading many products to be trapped in regulatory limbo

[3] 51 FR 23352-23366 (June 26, 1986).
[4] United Nations Food and Agriculture Organization. 2009. *How to Feed the World in 2050.*
[5] https://www.whitehouse.gov/the-press-office/2017/04/25/presidential-executive-order-promoting-agriculture-and-rural-prosperity

- Potential inconsistency with other APHIS programs implementing the same regulatory authority
- Unintended consequences for other regulatory agencies in the Coordinated Framework (FDA and EPA) and for domestic and international markets

These issues will have a significant negative impact on innovation, particularly for small companies and universities hoping to develop agricultural products for specific regional or environmental needs or to develop minor use crops important domestically and internationally. We believe that problems with APHIS' proposed regulatory system are significant enough that APHIS will need to substantially revise the proposed rule and solicit additional public input in order to address them. APHIS can better meet its goals with fewer risks and disruptions by modifying its proposed approach.

Appended to this letter, we provide more detailed documentation of our analysis of the strengths and weaknesses of the APHIS proposal, along with our recommendations for a more practical way forward. In short, we believe that APHIS will be best able to improve its regulatory system successfully by making more focused changes to the current regulatory framework, strategically focused on addressing specific issues, rather than by undertaking a radical departure from the current system.

Our key recommendations for APHIS include:

- Abandon its "up front" regulatory status evaluation concept and instead specify clear, risk-based criteria defining the scope of regulation.

- 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.

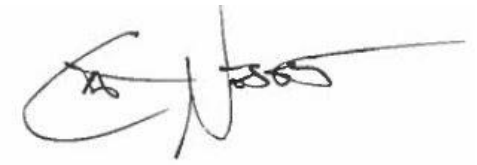
- Rather than incorporating redundant noxious weed provisions into 7 CFR Part 340, if necessary propose revisions to APHIS noxious weed regulations (7 CFR Part 360) to identify specific categories of GE plants (if any) that pose a noxious weed risk and need further evaluation.

The current regulatory system has operated quite successfully for decades and has resulted in no adverse plant health impacts to U.S. agriculture. Yet APHIS has an opportunity to incorporate its 30 years of experience and make its oversight more risk-proportionate. In the end, we believe that making targeted strategic improvements to the current regulatory system will engender broader support, prove easier to implement, and have a much more immediate impact with fewer unintended consequences.

Finally, because consistent policies globally for products of plant breeding innovation such as gene editing are essential to advancing agriculture, promoting innovation, and harmonizing trade regimes, we urge the U.S. government agencies to actively engage with our trading partners as soon as possible to work toward consistent, science-based policies across countries.

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

Sincerely,



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BIO Analysis of Proposed Revisions to 7 CFR Part 340

This document provides a detailed analysis of APHIS' proposed revisions to its regulations in 7 CFR Part 340,[1] prepared by the Biotechnology Innovation Organization. We first briefly summarize the principles we believe represent effective rulemaking, and analyze APHIS' proposal against these benchmarks. While we commend the agency for proposing innovative concepts in modernizing its pre-market regulatory system, our analysis leads us to conclude that APHIS' proposed revisions are inconsistent with many of these principles, making the agency unlikely to be successful in accomplishing its regulatory goals. We believe the shortcomings of the proposed rule are significant enough that the agency will need to substantially revise its proposed regulatory revisions in order to address them and publish the revised proposal for additional public input.

We believe APHIS will be best able to successfully improve its pre-market regulatory system by making strategic changes to the current regulatory system focused on addressing specific issues, rather than by proposing a radical departure from the current system. While some reform is needed, the current regulatory system has operated quite successfully for decades and has resulted in no adverse plant health impacts to U.S. agriculture. We believe that making targeted, strategic improvements to the current regulatory system would engender broader support, prove easier to implement, and have a much more immediate impact with fewer unintended consequences.

PRINCIPLES OF GOOD REGULATION

A diversity of Executive Orders, agency memoranda, and other Executive Branch directives and materials establish best practices and guiding principles for effective rule-making and regulation in general. A number of these are specific to oversight of biotechnology. We briefly describe some of these directives here, and will later use these as benchmarks to discuss the strengths and weaknesses of the regulatory revisions that APHIS has proposed.

Importantly and most recently, the White House directed 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."[2] We believe that this directive sets forth a key goal against which any biotechnology-related policies and regulations should be measured.

Several additional Executive Orders direct agencies to follow certain principles and requirements in rulemaking.[3] In 2011, the White House published a memorandum to the heads of executive

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[1] 82 FR 7008-7039 (January 19, 2017).
[2] https://www.whitehouse.gov/the-press-office/2017/04/25/presidential-executive-order-promoting-agriculture-and-rural-prosperity
[3] E.O. 12866, E.O. 13258, E.O. 13422, E.O. 13563, E.O. 13497, E.O. 13610.

departments and agencies, describing guiding principles for regulation of emerging technologies in particular.[4] Based upon these rulemaking principles, regulations should be:

- 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 with minimal 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 with regard to 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 for the Regulation of Biotechnology, which established how Federal agencies would exercise oversight of products of the then-emerging technology.[5] Those foundational principles were later reiterated in 1992, when OSTP 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.[6]

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[4] https://www.whitehouse.gov/sites/default/files/omb/inforeg/for-agencies/Principles-for-Regulation-and-Oversight-of-Emerging-Technologies-new.pdf
[5] 51 FR 23352-23366 (June 26, 1986).
[6] 57 FR 6753-6762 (February 27, 1992).

These principles were recently reaffirmed by OSTP in a review of the Coordinated Framework published in early 2017.[7]

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

ANALYSIS OF PROPOSED RULE

Noxious Weed Authority

Central to the agency's proposed regulatory revisions is incorporation into 7 CFR Part 340 of the noxious weed authority derived from the Plant Protection Act of 2000 (PPA). APHIS argues that this revision is necessary in order to enable the agency to evaluate the potential noxious weed risk of GE organisms, and that it currently does not have regulatory systems in place to address this risk. We disagree. APHIS has not provided a clear justification that its current noxious weed regulations in 7 CFR Part 360 are inadequate to protect U.S. agriculture from noxious weeds. We do not support the incorporation of the noxious weed authority into 7 CFR Part 340 for the reasons described below.

The PPA provides APHIS with the authority to protect U.S. agriculture from the harmful impacts of plant pests and noxious weeds. Plant pests are defined as:

> "…any living stage of any of the following that can directly or indirectly injure, cause damage to, or cause disease in any plant or plant product:
> (A) A protozoan.
> (B) A nonhuman animal.
> (C) A parasitic plant.
> (D) A bacterium.
> (E) A fungus.
> (F) A virus or viroid.
> (G) An infectious agent or other pathogen.
> (H) Any article similar to or allied with any of the articles specified in the preceding subparagraphs."[8]

[7] https://www.epa.gov/sites/production/files/2017-01/documents/2017_coordinated_framework_update.pdf
[8] 7 USC 7702 Sec 403(14)

Noxious weeds are defined as:

> "…any plant or plant product that can directly or indirectly injure or cause damage to crops (including nursery stock or plant products), livestock, poultry, or other interests of agriculture, irrigation, navigation, the natural resources of the United States, the public health, or the environment."[9]

The PPA, in relevant part, authorizes the Secretary of Agriculture to oversee the detection, control, eradication, suppression, prevention, or retardation of the spread of plant pests. Pursuant to that broad authority, the Secretary of Agriculture may prohibit or restrict the importation, entry, exportation, or movement in interstate commerce of any plant pest, plant, plant product, or article capable of harboring a plant pest as necessary to prevent the introduction of a plant pest into the United States or the dissemination of a plant pest within the United States, and also may determine that certain articles, plants, and plant products are not plant pests and are not subject to prohibitions or restrictions on movement in interstate commerce.

APHIS currently has three parallel sets of regulations implementing these authorities: plant pest-related regulations in 7 CFR Part 330, noxious weed-related regulations in 7 CFR Part 360, and the regulations in 7 CFR Part 340, which cover certain GE organisms (including plants) which are plant pests, were created using plant pests, or which incorporate genetic sequences from plant pests. APHIS provides no justification why this three-part system provides inadequate oversight of GE organisms which may pose a risk of being noxious weeds. APHIS has routinely considered weediness in its plant pest risk assessments in support of determinations of non-regulated status, providing the agency with an opportunity to identify plants needing additional scrutiny as potential noxious weeds under 7 CFR Part 360. Indeed, based upon the existing review process APHIS concluded in the preamble of the proposed rule that:

> "Most GE plants that APHIS has regulated in the past, such as varieties of corn and soybeans modified with common agronomic traits, do not qualify as 'noxious weeds.'"

Further, APHIS alludes to consideration of noxious weed potential in numerous responses to "letters of inquiry," letters intended to clarify regulatory jurisdiction under 7 CFR Part 340.[10] Clearly, APHIS uses both of these mechanisms to identify new plant varieties which may need further assessment under APHIS noxious weed regulations. Additionally, the public has the ability

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[9] 7 USC 7702 Sec 403(10)

[10] https://www.aphis.usda.gov/aphis/ourfocus/biotechnology/am-regulated/regulated_article_letters_of_inquiry/regulated_article_letters_of_inquiry See for example, APHIS BRS response to Ceres Inc. (February 28, 2017): "If APHIS determines that a plant poses a noxious weed risk, APHIS would consider regulating the plant under the noxious weed regulations, 7 CFR part 360. APHIS has the option to regulate plants under 7 CFR 360 regardless of whether or not they meet the definition of a regulated article under 7 CFR 340".

under 7 CFR Part 360 to petition APHIS to consider listing a plant, including GE plants, as a noxious weed, and has used the opportunity to do so on several occasions. Notably, in response to public petitions and of its own initiative, APHIS has evaluated the noxious weed potential of GE plants under the existing regulations in 7 CFR Part 360 multiple times in the last few years.[11]

In short, while 7 CFR Part 340, in isolation, does *not* provide the agency the authority to evaluate the noxious weed risk of GE plants, APHIS has not provided adequate reasons the agency could not continue to assess the noxious weed risk of GE plants under the current noxious weed regulations. Not only has the agency provided no compelling argument supporting a need to incorporate this review into 7 CFR Part 340, the agency's own actions demonstrate that incorporation of the noxious weed authority into 7 CFR Part 340 is not required to evaluate any potential noxious weed risk of GE plants.

Incorporation of the noxious weed authority into 7 CFR Part 340, as proposed, would create two parallel regulatory systems to evaluate the same risk, under the same statutory authority, in potentially inconsistent ways. APHIS does not clearly articulate why it needs a second, *different* risk assessment system to evaluate noxious weed risk under a revised 7 CFR Part 340 from the one it already uses to evaluate the same potential risk under 7 CFR Part 360. This creates the potential for a scenario in which a "noxious weed" under 7 CFR Part 340 may not be subject to the same standard as a noxious weed under 7 CFR Part 360.

Finally, the proposed regulatory system goes against a foundational tenet of the Coordinated Framework dating back to 1986: that oversight should be based upon the risk of the product, and not merely due to the process used in its development. The system proposed by APHIS would require that *all* GE plants be evaluated as potential noxious weeds. APHIS is, without basis, proposing a system that a priori treats all GE plants as equally likely to pose a noxious weed risk, merely because of the technology used to develop them. This action is contradicted by APHIS' own statements that most agricultural crops have few if any weedy characteristics prior to genetic engineering, that none of the GE plants evaluated to date have been determined to be noxious weeds, and that evaluating them "solely for plant pest risk has not been problematic."[12]

Conversely, APHIS argues that developers increasingly may be developing plants with preexisting weedy characteristics to have traits that may further enhance the plant's weediness, thus creating a "correspondingly higher risk that such a plant may be genetically engineered into a noxious

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[11] For example, GE corn, soy, creeping bentgrass, and others. See https://www.aphis.usda.gov/aphis/ourfocus/planthealth/plant-pest-and-disease-programs/pests-and-diseases/sa_weeds/sa_noxious_weeds_program/ct_riskassessments/!ut/p/z0/fYzLDsIgEEW_pR9gBoxBXZJqWh91TdmQiSKSWiAMPj7fRvfu7jk5uaBBgQ749A6LjwHvE_damBOvG7Za8GOz3XAm2_Xu0C4Fq5mAPej_wfQwz13dOdAJy23mwzWCIjQvay_0XSG-fXzQz5iUo8s4gjoXkz0NSGSJRhsKQRp0L2VVfQA1I5Y1/

[12] 82 FR 7008-7039 (January 19, 2017).

weed." However, the agency provides little scientific basis, specificity or concrete examples of the kinds of GE plants it would consider to pose a noxious weed risk and that could *not* be regulated under existing noxious weed regulations. If APHIS believes that such GE plants exist which are not currently adequately regulated under 7 CFR Part 360, then APHIS should: 1) identify the specific, risk-based criteria defining such plants and the introduced traits that elevate noxious weed risk,[13] and 2) if needed, propose revisions to 7 CFR Part 360 to incorporate appropriate regulatory criteria and assessment mechanisms to consider regulating such plants as noxious weeds.

BIO recommends:

- *APHIS should not incorporate the noxious weed authority into 7 CFR Part 340, but instead continue to use its noxious weed regulations in 7 CFR Part 360 to regulate risks related to noxious weeds.*

- *If APHIS has a reason to believe that its current noxious weed regulations in 7 CFR Part 360 are inadequate to capture certain products of biotechnology legitimately posing a noxious weed risk, APHIS should:*

    1. *Identify the specific, risk-based criteria defining such plants and the introduced traits that create an elevated noxious weed risk, and,*

    2. *If needed, propose revisions to 7 CFR Part 360 to incorporate appropriate risk-based regulatory criteria and assessment mechanisms to consider* regulating such plants as noxious weeds.

Scope of Regulation

APHIS is to be commended for its efforts to refine its scope of regulation to be better aligned with plant health risk. However, APHIS is proposing a significant and complex expansion to the way in which it determines which organisms are subject to regulation under 7 CFR Part 340. The proposed rule simultaneously expands the definitions of genetic engineering, narrows the scope of organisms considered to pose a plant pest risk, broadens the scope of organisms considered to potentially pose noxious weed risk (effectively all GE plants), and then leaves the ultimate regulatory status determination to two different complex risk assessment models (plant pest and noxious weed risk).

[13] For example, in its 2017 notice, APHIS solicits public input on how to adequately oversee risks posed by plants producing certain pharmaceutical or industrial compounds. In its 2008 proposed rule, however, APHIS appeared to argue that it *did* have the authority to regulate such plants, impliedly because such plants might be considered toxic or pose a public health risk, a characteristic of noxious weeds (73 FR 60008-60048, October 9, 2008). The agency has provided no explanation for this change in interpretation in its authority.

We appreciate that the agency intends that such a system would likely result in APHIS determinations that many plant-trait combinations would not be regulated, as illustrated by the agency's "Regulatory Status Under Proposed 340" table.[14] However, we believe the proposed system is unnecessarily complicated and lacks clarity and predictability about the kinds of organisms that would actually be subject to regulation. We believe that the most effective regulatory system should 1) provide clear, risk-based criteria to identify organisms that are exempt from pre-market oversight and those needing further risk assessment, and 2) include mechanisms by which organisms within the initial risk-based scope can be efficiently assessed for risk and, if appropriate, determined to pose no plant pest risk.

The scope of organisms subject to APHIS' current regulations is defined to be:

> "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."[15]

This definition dates to a time when there was concern that using genetic sequences from plant pests and creation of GE plants using plant pest vectors could pose an increased risk of creating or disseminating plant pests. As a result, many GE plants have been subject to APHIS oversight merely because of the presence of harmless viral sequences, such as the common 35S promoter derived from Cauliflower Mosaic Virus (CMV), and transformation 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.

In the proposed rule, APHIS argues that the current definition of a regulated article is outdated:

> "This reflects the concern from the 1980s that if an organism was modified using genetic material taken from a plant pest, or a plant pest was used as a vector or vector agent to carry genetic material in an organism, the resulting GE organism could also be a plant pest… Based upon APHIS' experience evaluating field trials data from thousands of permits that authorize environmental releases of regulated organisms, as well as more than 150

[14] https://www.aphis.usda.gov/aphis/ourfocus/biotechnology/biotech-rule-revision/2016-340-rule/reg-status-table
[15] 7 CFR 340.1

petitions for non-regulated status, that has not proven to be the case… The use of plant pests in these ways either as donors or regulatory sequences or for vectoring genetic material into a recipient organism has a long history of safe use and does not result in disease or injury to the recipient organism."

We agree with the agency that the current regulatory trigger is a poor indicator of risk, unnecessarily including a significant number of products which are very unlikely to pose a plant pest risk, and is in need of reconsideration. However, we also feel that substituting the proposed plant pest triggers for the current definition of a regulated article may have significant unintended consequences. We believe that the best approach is to refine the current scope of regulation by progressively removing from pre-market regulation categories of species-trait combinations and products meeting certain risk-based criteria, and recognize that products that are indistinguishable from those that could be developed using conventional breeding or found in nature should not be subject to differential treatment based on the method used in their development. This approach would also help the agency to continually refine its regulatory scope as new scientific information becomes available. We propose a new mechanism for accomplishing this approach below.

BIO recommends:

- *APHIS should refine its current scope of regulation by progressively removing from pre-market regulation categories of species-trait combinations and products meeting certain risk-based criteria, and recognize that products that are indistinguishable from those that could be developed using conventional breeding or found in nature should not be subject to differential treatment based on the method used in their development.*

APHIS proposes to exclude from the definition of "genetically engineered organism" many organisms identical or nearly-identical to organisms created using genetic engineering or newer gene editing techniques that could have been created via traditional plant breeding and chemical or radiation-based mutagenesis. We agree with this approach— most of these kinds of organisms are not currently subject to APHIS' 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 risk as plant pests (or noxious weeds), there is no evidence to suggest that they pose a greater plant pest or noxious weed risk than organisms developed via traditional breeding or mutagenesis, neither of which are subject to APHIS pre-market regulations. Consistent with foundational principles of the Coordinated Framework, we believe that plant varieties developed through plant breeding innovations, such as gene 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.

In reviewing the current regulatory process under Part 340, every effort should be made to adopt reforms that will promote agricultural innovation in accordance with the President's Executive Order, Promoting Agriculture and Rural Prosperity in America,[16] and the mission of the recently established White House Office of American Innovation. The benefits to agriculture that have resulted from, and will continue to result from, the development and commercialization of innovative plant products, including crops developed using gene editing and other precision breeding methods, should be available to all of our nation's farmers. 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 excluded from premarket review.

Consistent policies globally for products of plant breeding innovation, however, are essential to harmonizing trade regimes. The US Government should make a clear, positive statement on the importance of innovation in agriculture, including innovation in plant breeding, and should adopt consistent policies across regulatory agencies. U.S. government agencies should be encouraged to actively engage with our trading partners around these policies as soon as possible to work toward consistent, science-based policies across countries.

BIO recommends:

- *The US government should adopt consistent policies regarding products of plant breeding innovation, and should actively engage in international leadership to work toward consistent, science-based policies among our important trading partners.*

Finally, we acknowledge that any regulatory scope criteria, however risk-based and scientifically defensible, will always bring within regulatory scope organisms which, upon further, more detailed assessment, do not in fact pose the risk they were initially presumed to pose. Therefore, any effective regulatory system needs additional mechanisms to assess efficiently the potential risk posed by organisms within the scope and, if appropriate, determine are not plant pests. APHIS' current regulations have two such mechanisms, but both have limitations. The petition process (7 CFR Part 340.6) allows developers to petition APHIS to determine an organism is not a plant pest based upon its lack of plant pest risk, but this mechanism has been unnecessarily limited to evaluation of individual organisms (generally a single event, although one or more individual organisms or events can be included in a single petition). The more streamlined extension process (7 CFR Part 340.6(e)) allows the agency to remove an organism from oversight based upon its

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

similarity to a previously deregulated organism, but again, not only has the process been unnecessarily limited to individual organisms, it is also limited because consideration is tied to assessments of previously-evaluated organisms.

We believe that there will be many instances in which it is more scientifically justifiable to assess the regulatory status of whole categories of organisms, such as those of the same combination of species and trait. Such a mechanism would allow the agency to efficiently assess the plant pest risk of, and remove from oversight if appropriate, whole classes of organisms without having to assess each individual member of the class separately. This would prevent the agency from having to perform redundant analyses of multiple examples of nearly-identical organisms, and could dramatically increase agency efficiency by instead making regulatory determinations on broader categories. APHIS could accomplish this either by adding a novel mechanism to the existing 7 CFR Part 340 regulations, or by modifying the existing petition/extension processes, to more easily allow evaluation of broader species-trait combinations or other appropriate categories. For example, APHIS could use the new process to grant nonregulated status to many of the categories of species-trait combinations listed in the agency's "Regulatory Status Under Proposed 340" table.[17] Further, the agency could use the same mechanism to refine the scope of regulation by exempting from regulation organisms that meet certain criteria, such as those modified using disarmed *A. tumefaciens* or which incorporate specific sequences from plant pests. The use of such a mechanism would allow the agency both to assess broad categories of crop-trait combinations and to progressively refine its scope of regulation, without the associated complexities and unintended consequences of the system described in the proposed rule.

BIO recommends:

- *APHIS should add a new mechanism to its regulations (or modify the existing petition processes in 7 CFR 340.6) 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.*

"Up Front" Regulatory Status Evaluation

We agree with APHIS that, based upon its 30 years' experience, the agency has sufficient scientific evidence and familiarity to justify that broad categories of GE organisms with a demonstrated history of safety need no longer be regulated as either plant pests or noxious weeds. The agency's "Regulatory Status Under Proposed 340" table[18] includes many of the products for which we agree

[17] https://www.aphis.usda.gov/aphis/ourfocus/biotechnology/biotech-rule-revision/2016-340-rule/reg-status-table
[18] Ibid.

further regulation as potential plant pests is no longer scientifically justified. However, the "up front" regulatory status evaluation system the agency proposes to use to reach these determinations is inefficient, non-transparent, and unlikely to have the capacity to keep up with scale of research and development of new products.

Despite the agency's assertions that most GE organisms do not pose risks as plant pests or noxious weeds, the risk assessment system proposed by APHIS represents a one-size-fits-all system that subjects every category of GE organism to the same level of review, regardless of the actual risk posed by the organism. This results in a regulatory system that is profoundly inefficient because, even by the agency's own admission, the vast majority of organisms assessed by the up-front system pose little risk of being pests or weeds. The agency is in essence proposing a needle-in-a-haystack regulatory system, in which each piece of straw is subjected to the same elaborate scrutiny, with no efficient means to focus the agency's limited resources on identifying the actual "needles," resulting in inefficiency and waste.[19] Additionally, in shifting the timing of its risk assessments from the back end of the product development cycle, when only a handful of products are likely to be released on a broad commercial scale, to the front end, when tens of thousands of experimental research lines are first brought to the field, APHIS will needlessly expend limited resources preparing risk assessments on products the vast majority of which will never be brought to market nor have any justifiable plant pest or noxious weed risk.

Another significant weakness of defining regulatory scope with an "up front" regulatory status evaluation is that such a system provides little clarity and transparency about which organisms will actually be subject to regulation. The public cannot independently review the agency's risk assessment instructions[20] in order to determine which products are regulated with any degree of certainty. APHIS has not articulated any clear decision-making criteria of how the agency will use its risk assessment to decide which organisms will be regulated and which will not, and whether they would be regulated, or even assessed, as plant pests, noxious weeds, or both. The lack of clarity and transparency about decision-making criteria has the potential to lead to a system that is arbitrary. [21] Further because regulatory status evaluations are based upon data submitted to the agency by the developer in early stages of development, some of the data requirements would be

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[19] The Noxious Weed Program currently implemented by APHIS does not prepare noxious weed risk assessments for every plant species; instead, the program focuses its limited resources on those species for which the agency has some plausible reason to believe them to be more invasive, harmful, etc. In comparison, the system being proposed by APHIS requires the agency to prepare a risk assessment for every crop-trait combination, regardless of actual risk. This leads to significant inefficiencies, such as having to prepare lengthy assessments to determine whether even non-GE corn, soybeans, and cotton (38, 48, and 50 pages long, respectively) are noxious weeds: https://www.aphis.usda.gov/aphis/ourfocus/biotechnology/biotech-rule-revision/2016-340-rule/sample_wra

[20] https://www.aphis.usda.gov/biotechnology/downloads/340/draft_wra_work_instructions_v4-1-2.pdf

[21] We also note that from a scientific perspective, the validity of using weed risk assessment models to inform policy decisions, particularly regarding cultivated crops, is not without controversy. See Smith et al. 2015. Predicting Biofuel Invasiveness: A Relative Comparison to Crops and Weeds. *Invasive Plant Science and Management* 8:323–333.

cost-prohibitive, may include highly confidential business information, and would be of questionable value in risk assessments. Additionally, the system appears unable to determine the regulatory status of future, hypothetical products, and, unlike the current regulations, developers could not learn the regulatory status of their products until long after they have invested in the development of a new product.

APHIS provides itself no timelines for reaching regulatory status evaluations for new crop-trait combinations, but suggests it may take "a matter of months." Based upon our experience with similar processes, we estimate that the time it will take the agency to review data submitted by a developer, prepare a lengthy risk assessment, prepare and publish a notice in the *Federal Register* to solicit public comment, incorporate comments, and post the final determination on the web will take realistically six months or more.[22] This does not account for the additional time required for developers to prepare and submit an application under the new process. In the meantime, products are caught in regulatory limbo—waiting for the agency to provide a regulatory status determination and unable to be imported, moved interstate, or released into the environment until the agency concludes its process.[23] We believe that the inability to read the regulations and know with any certainty which products will be subject to them will have a significant, adverse impact on business decisions about investment in research and development, stifling innovation.

An additional significant weakness of the "up front" regulatory status evaluation is that the agency is unlikely to have the capacity to implement such a system on a scale capable of keeping pace with real-world research and development. In 2016 alone, APHIS authorized field trials representing more than 150 different species and 50,000 species-trait combinations.[24] The majority of these were authorized within 30 to 120 days, consistent with current APHIS regulations. Under the proposed system, the regulatory status of those 50,000 species-trait combinations— plus *many more* not included within the scope of current regulations[25]— would be initially unknown. Based upon our analysis, we believe APHIS has significantly underestimated the resources necessary to implement its proposed "up front" regulatory status evaluation system.

Because the APHIS proposal is ambiguous about how broadly each individual risk assessment would be (narrow, event-by-event vs broad, phenotypic categories), it is difficult to estimate the

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[22] Additionally, APHIS does not articulate how it intends to implement the requirements of the National Environmental Policy Act (NEPA) under this system. Implementation could add additional delays to the proposed system.

[23] The APHIS proposal indicates that in some limited circumstances, the agency would consider authorizing permits for importation or interstate movement (but not field testing) of organisms that had not yet undergone a regulatory status evaluation, but that such organisms would be considered to pose a high degree of risk and permitting requirements would be significantly more stringent.

[24] Based upon public communications from the agency and the publicly-available APHIS database at: https://www.aphis.usda.gov/brs/status/BRS_public_data_file.xlsx

[25] Organisms which meet the proposed definition of "genetically engineered organism" but which do not meet the definition of "regulated article" under the current regulations.

number of risk assessments the proposed system would entail. According to its Regulatory Impact Analysis, APHIS estimates that the risk assessment component of its proposed system would require preparation of an estimated 50-500 risk assessments per year.[26] We assume the agency may envision that the number of risk assessments will be substantially lower than the number of actual species-trait combinations for two reasons: 1) the agency may intend to prepare risk assessments on broader categories of organisms that include multiple species-trait combinations per risk assessment, and 2) the number of species-trait combinations will gradually decline over time as the agency removes more and more organisms from oversight. We are unable to independently evaluate the agency's capacity estimates, however, because no justification for these estimates is provided.

We estimate that the total number of risk assessments necessary for the first year following implementation could be anywhere from approximately 1200 if the agency makes determinations based on broad phenotypic categories[27] to 50,000 individual risk assessments if the agency makes determinations narrowly, event-by-event.[28] To put this in perspective, while the 65 species-trait combinations proposed not to be regulated by APHIS[29] may represent a substantial percentage of the total number of authorized field trials (because field trials of corn, soy, cotton, etc. are much more common), the list represents only a very small fraction of APHIS' actual risk assessment workload that would be required under the proposed system. And to date, APHIS has published only *sixteen* draft risk assessments in support of the proposed not-regulated list.[30]

We believe that not only has APHIS underestimated the number of regulatory status evaluations the agency would have to prepare under such a system, it has also underestimated the resources needed to implement the system. APHIS estimates that the risk assessment component of its proposed system would require only five to nine full-time employees (FTEs), at a cost of $700,071 to $1,265,036, respectively, to implement, based upon the agency's need to prepare 50-500 risk assessments per year. Even if we accept APHIS' estimates, it seems unlikely that five to nine FTEs would be sufficient to prepare 50-500 lengthy risk assessments annually. This represents as many as 100 assessments per staff member per year, and because applications are typically seasonal, workload would not be evenly distributed throughout the year. We believe that not only has APHIS underestimated the number of FTEs necessary to prepare 50 to 500 risk assessments, as described

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[26] Regulatory Impact Analysis, Table 6, Footnote 6. https://www.aphis.usda.gov/biotechnology/downloads/340/340_ria.pdf

[27] According to APHIS' public database, in 2016, APHIS granted authorizations for approximately 150 different species with more than 800 different "phenotypes" in nearly 1200 different species-phenotype combinations. "Phenotypes" in the APHIS public database appears to represent relatively broad categories of traits (e.g. "HT - herbicide tolerance," "Agronomic Property – abiotic stress tolerance"), as opposed to single genes or specific modes of action. We have used 1200 as a ballpark low-end estimate for the number of regulatory status evaluations the agency, if APHIS intends to make regulatory determinations based upon broad categories like those in the APHIS public database.

[28] The number of species-trait combinations the agency authorized in 2016.

[29] https://www.aphis.usda.gov/aphis/ourfocus/biotechnology/biotech-rule-revision/2016-340-rule/reg-status-table

[30] https://www.aphis.usda.gov/aphis/ourfocus/biotechnology/biotech-rule-revision/2016-340-rule/sample_wra

above, APHIS may have significantly underestimated the number of risk assessments necessary to keep up with the annual scale of research and development. In contrast, under the current regulations APHIS has demonstrated that it has more than enough capacity to authorize field trials of all 50,000 species-trait combinations, in the 30-120 days required by current regulations, n a manner that addresses the potential for plant pest risk, with the majority of those authorizations being concentrated in the few months leading up to spring planting season.

In short, we believe the agency has significantly underestimated the capacity needed to prepare "up-front" risk assessments on a scale commensurate with today's scale of research, and that this mismatch represents a critical flaw in the regulatory system being proposed by the agency. The dramatic disconnect between agency capacity and the scale (and timing) of real-world research will likely lead to staggering regulatory gridlock, bringing innovation to a halt. Further, because academic and small business researchers are more likely to be field-testing *new* applications for research purposes than institutions breeding previously-assessed traits into commercial varieties, smaller institutions will be disproportionately affected by the inefficiencies of the proposed risk assessment system. In contrast to the current notification and permitting processes, which are able to authorize field trials in 30-120 days, under the proposed system, in order to take a single research plant to the field, academic researchers would be required to submit a lengthy application, wait for the agency to prepare, publish, and solicit public comment on its risk assessment, and publish a final determination—a process that could take potentially six months or more— and then (if regulated) consider issuance of a permit. We predict that most outdoor academic research would be impossible under such a system. APHIS should retain the current permitting and notification procedures, because these processes enable science-based, predictable, quick and efficient assessment of proposed field trials for all researchers and developers that adequately addresses the potential for plant pest risk.

To summarize, we believe that the "up-front regulatory status evaluation" proposed by the agency is in effect a case-by-case regulatory system that provides little regulatory clarity and gives the agency the ability to make potentially arbitrary decisions about what is subject to regulation. Because of the proposed system's significant inefficiencies in the use of limited agency resources, the lack of transparency and clarity about regulatory status of individual products, and the likelihood that the agency will not have sufficient capacity to keep up with the scale of research, we do not support the use of an up-front risk assessment-based "regulatory status evaluation" system as a means to determine whether an organism is subject to regulation. Instead (as we also discussed in the context of regulatory scope above) APHIS should develop specific risk-based criteria that clearly and transparently describe the scope of regulation.

BIO recommends:

- *APHIS should abandon its "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.*

- *APHIS should retain the current permitting and notification procedures, because these processes enable science-based, predictable, quick and efficient review and authorization of proposed field trials for researchers and developers that adequately addresses the potential for plant pest risk.*

NEPA ANALYSIS AND PROGRAMMATIC ENVIRONMENTAL IMPACT STATEMENT

In addition to the proposed rule itself, APHIS published a programmatic environmental impact statement (EIS) which analyzes the possible impact of the proposed regulatory changes on the human environment. First, the lack of clarity or transparency about precisely which organisms will ultimately be subject to regulation and the criteria used to reach those determinations limits our ability to evaluate independently the proposal's impacts and benefits to the human environment. We believe that a revised rule with clearer regulatory criteria will help to address questions about its environmental analysis.

Secondly, APHIS has not articulated how it intends to implement NEPA for individual agency actions to be undertaken under the proposed rule. 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 helps inform consideration of the feasibility of the regulatory program APHIS is proposing. The burden on agency resources would be even greater if for example, APHIS intends to prepare individual NEPA analyses to accompany each "up front" regulatory status evaluation. To address this, APHIS should clearly articulate how it intends to implement the requirements of NEPA under a proposed rule, and to publish accompanying draft revisions to APHIS NEPA-implementing regulations (7 CFR Part 372) for public input.[31]

BIO recommends:

- *APHIS should clearly articulate how it intends to implement the requirements of NEPA under any proposed rule, and to publish accompanying draft revisions to APHIS NEPA-implementing regulations (7 CFR Part 372) for public input.*

[31] APHIS proposed revisions to its current NEPA implementing regulations on July 16, 2016 (81 FR 47051-47071), but those proposed revisions did not reflect the proposed regulatory revisions to 7 CFR 340 the agency published on January 19, 2017. APHIS should ensure that the two sets of regulations are consistent.

UNINTENDED CONSEQUENCES

We commend the agency for making bold, creative moves in attempting to modernize its regulatory system. However, we are concerned that because the agency's proposal represents such a significant departure from the current regulatory system, the agency may be unintentionally creating more problems than it is solving. In addition to the issues we raised above, we briefly outline some of the other possible unintended consequences the agency's proposal may have.

Regulatory Impact

APHIS suggests that its proposed rule would result in substantial regulatory relief for developers. Some aspects of the rule do indeed provide regulatory relief, but other aspects are likely to increase regulatory burdens substantially. First, shifting risk assessment from the "back end" (petitions and extensions) to the "front end" (up-front regulatory status evaluation) dramatically increases the regulatory burden imposed on developers with products in early stages of research and development. Whereas outdoor research with these early-stage products can currently be authorized via notification and permits— intended to be relatively simple processes which take 30-120 days— under the proposed rule, these early-stage products would be required to undergo a lengthy, petition-like process, including data submission, complex risk assessment, and public comment, before even being eligible to apply for a permit (a process we estimate could take six months or more). This new burden would be imposed on thousands of individual research organisms that have not been shown to have any plant pest risk, many of which would never be brought to market. We believe that this shift in burden alone is likely to have a significant negative effect on early stages of research, potentially making outdoor research impractical. The impact on small and public sector researchers may be even more profound.

Secondly, for those organisms that complete the regulatory status evaluation and are determined *not* to be subject to further APHIS regulations, some regulatory relief could be created. However, this reduction in regulatory burden is largely administrative and is unlikely to be as significant as the agency envisions, because it is likely to have little impact on already established industry stewardship practices. Even if these early-stage research organisms are not regulated by APHIS, the stringency of field trial stewardship will not likely appreciably diminish.

We are concerned that APHIS has failed to justify the proposal's up-front risk assessment provision from a cost-benefit perspective. As stated previously in these comments, we are skeptical of APHIS's estimate of the number of up-front risk assessments that will need to be performed on a yearly basis and the true resource implications of this policy change. Even if we accept APHIS's estimate of 500 risk assessments per year at a cost to the Federal government of $1,265,036, this cost represents only one component of the full cost of this regulatory change. APHIS has not

considered the full social costs of the up-front risk assessment requirement— i.e. the foregone value of public and private resources expended to comply with and implement the provision, and from reductions in output that could result from product development delay or disapproval. APHIS states in the Regulatory Impact Analysis that, "neither the pace of commercialization nor volume of GE products commercialized is expected to change dramatically from current levels; nor is the biotech developer's control over the development process expected to be materially altered as a result of this rule. " However, we anticipate many products currently under development would be subject to the proposed up-front regulatory status evaluation process, resulting in significant delay or possibly prohibiting these organisms from reaching the commercial market altogether. The uncertainty and delay associated with the up-front risk assessment approach is likely to lead to stranded assets and even project cancellations for product developers. We firmly believe that if APHIS were to consider the real resource implications of the up-front risk assessment provision for product developers then the rule would easily pass the threshold of $100 million in costs per year, triggering the analytical requirements of OMB Circular A-4 for "Economically Significant" rules.

In addition, we are concerned that the regulatory impact analysis for the proposed rule fails to estimate the marginal social benefits and marginal social costs of each of APHIS' proposed requirements. Many of the proposed requirements are costly and provide few, if any, risk-reduction benefits. APHIS should comply with the relevant Executive Orders and OMB guidance in Circular A-4 to estimate the marginal social benefits and social costs for each of its proposed requirements. Furthermore, we are concerned that despite its analysis of various regulatory alternatives in its NEPA analysis, APHIS only analyzed the costs and benefits of one alternative relative to the proposed rule in its Regulatory Impact Analysis, an approach inconsistent with OMB Circular A-4. In summary, we believe strongly that APHIS has failed to fully analyze the costs and benefits of the proposal in its Regulatory Impact Analysis, and in particular the up-front risk assessment provision. Before proceeding with a final action APHIS should fully comply with the requirements of EO 12866 and Circular A-4 by demonstrating the net social benefits of its proposed regulatory changes.

Impacts on Other Federal Agencies

APHIS acknowledges that its proposed rule may create significant complications for the two other Coordinated Framework agencies that oversee agricultural products, FDA and EPA, and asks the public for input in addressing these problems. The APHIS proposal creates significant uncertainties about how FDA and EPA might adjust their regulatory programs to accommodate the changes to the APHIS regulatory system, making it even more difficult for us to provide substantive input on the full ramifications of the regulatory changes APHIS has proposed. We encourage APHIS to develop a regulatory system that more fully and clearly articulate how the updated system relates to the regulatory programs of FDA and EPA, reflecting clearer coordination with and support of those agencies.

Impacts on Markets and Trade

It is important for the agency to consider carefully whether any proposed regulatory changes impact marketing of products of agricultural biotechnology. APHIS should engage with a broad range of stakeholders, both domestically and internationally, to explain its proposed regulatory revisions and their implications. APHIS and other U.S. government agencies should be encouraged to actively engage with and provide strong leadership to our trading partners around proposed new policies, and identify ways to transition to new regulatory systems that harmonize trade regimes. APHIS should consider adopting regulatory approaches which are measured and facilitate an orderly transition and global acceptance. We believe that the recommendations we have made here— in particular the addition of a new mechanism allowing APHIS to progressively remove from regulation broad categories of crop-trait combinations— will help to facilitate such a transition.

CONCLUSION: SUMMARY OF BIO RECOMMENDATIONS

We commend APHIS for thinking "outside the box" by considering bold, new improvements to its existing system of regulation. However, we believe the shortcomings of the proposed rule are significant enough that the agency will need to substantially revise its proposed regulatory revisions in order to address them and to re-propose those revisions for public input. We believe that APHIS will be best able to improve its regulatory system successfully through strategically-focused changes addressing specific issues, rather than by undertaking a broad, significant departure from the current system. In the end, making targeted strategic improvements to the current regulatory system will engender broader support, prove easier to implement, and have a much more immediate impact with fewer unintended consequences.

In summary, we believe that APHIS should pursue regulatory change through the following actions:

- *APHIS should not incorporate the noxious weed authority into 7 CFR Part 340, but instead continue to use its noxious weed regulations in 7 CFR part 360 to regulate risks related to noxious weeds.*

- *If APHIS has a reason to believe that its current noxious weed regulations in 7 CFR Part 360 are inadequate to capture certain products of biotechnology legitimately posing a noxious weed risk, APHIS should:*

    1. *Identify the specific, risk-based criteria defining such plants and the introduced traits that create an elevated noxious weed risk, and,*

2. *If needed, propose revisions to 7 CFR Part 360 to incorporate appropriate risk-based regulatory criteria and assessment mechanisms to consider* regulating such plants as noxious weeds.

- *APHIS should refine its current scope of regulation by progressively removing from pre-market regulation categories of species-trait combinations and products meeting certain risk-based criteria, and to recognize that products that are indistinguishable from those that could be developed using conventional breeding or found in nature should not be subject to differential treatment based on the method used in their development.*

- *The US government should adopt consistent policies regarding products of plant breeding innovation, and should actively engage in international leadership to work toward consistent, science-based policies among our important trading partners.*

- *APHIS should add a new mechanism to its regulations (or modify the existing petition processes in 7 CFR Part 340.6) 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.*

- *APHIS should abandon its "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.*

- *APHIS should retain the current permitting and notification procedures, because these processes enable science-based predictable, quick and efficient review and authorization of proposed field trials for researchers and developers that adequately addresses the potential for plant pest risk.*

- *APHIS should clearly articulate how it intends to implement the requirements of NEPA under any proposed rule, and to publish accompanying draft revisions to APHIS NEPA-implementing regulations (7 CFR Part 372) for public input.*