From Farm to Table - The Future of GMO Plans and Animals

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#187

Guidance for Industry

Regulation of Intentionally Altered Genomic DNA in Animals

Draft Guidance

(This guidance is a revision of Guidance #187, "Regulation of Genetically Engineered Animals," which has been revised to update information concerning the products of different technologies used to produce such animals, and to provide new weblinks.)

Submit comments on this draft guidance by the date provided in the *Federal Register* notice announcing the availability of the draft guidance. Submit electronic comments to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852. All comments should be identified with the Docket No. FDA-2008-D-0394.

For further information regarding this document, contact Laura R. Epstein, Center for Veterinary Medicine (HFV-1), Food and Drug Administration, 7519 Standish Place, Rockville, MD 20855, 301-796-8558, email: Laura.Epstein@fda.hhs.gov.

Additional copies of this guidance document may be requested from the Policy and Regulations Staff (HFV-6), Center for Veterinary Medicine, Food and Drug Administration, 7519 Standish Place, Rockville, MD 20855, and may be viewed on the Internet at either http://www.fda.gov/AnimalVeterinary/default.htm or http://www.regulations.gov.

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Guidance for Industry

Regulation of Intentionally Altered Genomic DNA in Animals

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

I. Introduction and Background

FDA is issuing this draft revised Guidance for Industry to clarify its approach to the regulation of intentionally altered genomic DNA in animals. This guidance addresses animals whose genomes have been intentionally altered using modern molecular technologies, which may include random or targeted DNA sequence changes including nucleotide insertions, substitutions, or deletions, or other technologies that introduce specific changes to the genome of the animal.[1,2,3] This guidance applies to the intentionally altered genomic DNA in both the founder animal in which the initial alteration event occurred and the entire subsequent lineage of animals that contains the genomic alteration.

Recombinant DNA (rDNA) technology has been used for the past 40 years to intentionally alter traits in microorganisms, plants, and animals (Cohen and Boyer 1973). Various agencies across the US government (USG) have provided guidance and regulation to affected stakeholders

[1] FDA used the term "genetically engineered" (GE) to describe the animals within the scope of current Guidance for Industry #187. The term "GE" does not suit the discussion in this revised draft guidance because this draft guidance's scope includes animals whose genomes have been intentionally altered with new technologies. The term "transgenic" is also not used for the same reason, except for citation of earlier documents.

[2] In Draft Guidance for Industry #236, "Regulation of Mosquito-Related Products," FDA has proposed to clarify that the phrase "articles (other than food) intended to affect the structure or any function of the body of man or other animals" does not include articles intended to prevent, destroy, repel, or mitigate mosquitoes for population control purposes. Instead, such products are pesticides regulated by the Environmental Protection Agency (EPA) (http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM533600.pdf).

[3] The term "modern molecular technologies" does not include selective breeding or other assisted reproductive technologies, including random mutagenesis followed by phenotypic selection.

describing the regulation of these altered organisms and the products of those alterations. Historically, recombinant DNA (rDNA) techniques involved splicing DNA sequences from various sources and introducing them into animals[4] via techniques that resulted in random integration events. Animals whose genomes have been intentionally altered by rDNA technology have been produced since the early 1980s when Brinster et al. (1981)[5] and Palmiter et al. (1982)[6] reported on the development of mice altered in this manner. Not long thereafter, Hammer et al. (1985)[7] demonstrated that rDNA techniques could be used to intentionally alter the genomes of rabbits and pigs.

More recently, new technologies have emerged that are intended to alter the genomes of various organisms, including animals. Some of these include the use of "nucleases" or "genome editing technologies" including engineered nuclease/nucleotide complexes such as zinc finger nucleases (ZFN), transcription activator-like effector nucleases (TALENs), and the clustered regulatory interspersed short palindromic repeats (CRISPR) associated systems.[8] These nucleases are intended to introduce alterations at specific sites in the genome, rather than the more random changes associated with rDNA technology. The process of producing these targeted DNA sequence alterations is often referred to as "genome editing." We anticipate that other technologies intended to alter genomic DNA will arise over time.

Intentional genomic alterations may be heritable or non-heritable (e.g., those alterations intended to be used as gene therapy). Although much of this guidance will be relevant to non-heritable intentionally altered genomic DNA, this guidance primarily addresses heritable intentionally altered genomic DNA. For non-heritable genomic alterations, we recommend that sponsors contact the agency directly for further information.

This guidance is intended to clarify our requirements and recommendations for producers and developers ("sponsors," "you") of animals with intentionally altered genomic DNA. We note that the regulated article for such animals is the intentionally altered genomic DNA of the

[4] For purposes of this guidance, "animals" refers to non-human animals.
[5] Brinster, R.L., et al . (1981) Somatic expression of herpes thymidine kinase in mice following injection of a fusion gene into eggs. *Cell* 27: 223-231
[6] Palmiter, R.D., et al. (1982) Dramatic growth of mice that develop from eggs microinjected with metallothionein-growth hormone fusion genes. *Nature* 300: 611-615.
[7] Hammer, R. E. et al. (1985) Production of transgenic rabbits, sheep, and pigs by microinjection. *Nature* 315: 680-683.
[8] For a more complete description of genome editing techniques, see *Nature* Special Supplement Vol. 528, 2 December 2015.

animal. As a short hand in this guidance document, we sometimes refer to regulation of the article (i.e., the altered genomic DNA) in such animals as regulation of the altered animal.

Some animals with intentional alterations to their genomes are intended to produce medical and other products, such as human drugs or medical devices that are subject to regulation by other FDA centers. Where sponsors have developed animals that are intended to produce human medical products that are separately regulated by FDA's Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER), or Center for Devices and Radiological Health (CDRH), or a human food additive regulated by FDA's Center for Food Safety and Applied Nutrition (CFSAN), CVM will work closely with the other FDA Centers that regulate those products derived from these animals to ensure that our oversight is complementary and not unnecessarily duplicative.

In addition to this guidance, there are other guidelines and laws that may apply to animals with intentionally altered genomes:

- Existing guidances and other documents prepared by other FDA Centers including the Points to Consider in the Manufacture and Testing of Therapeutic Products for Human Use Derived from Transgenic Animals (1995) http://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/OtherRecommendationsforManufacturers/UCM153306.pdf, and

- Source Animal, Product, Preclinical, and Clinical Issues Concerning the Use of Xenotransplantation Products in Humans (2003) http://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Xenotransplantation/ucm092707.pdf.

- Medical Devices Containing Materials Derived from Animal Sources (Except for In Vitro Diagnostic Devices) - Draft Guidance for Industry and Food and Drug Administration Staff (2014) http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm381379.htm

- Federal laws, regulations, and guidelines for the humane care, handling, and slaughter of animals, as well as guidelines in place at your institution or establishment;

- Applicable Federal, State, local and tribal laws, regulations, and guidelines addressing environmental safety, including those NIH guidelines that apply to your institution or establishment;

- Applicable Federal, State, local and tribal laws, regulations, and guidelines pertaining to the importation, interstate movement, or release of wildlife;

- Federal laws, regulations, and guidelines governing the import or export of animals across US boundaries; and

- Other applicable Federal, State, or local laws, regulations and guidelines.

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word "should" in Agency guidances means that something is suggested or recommended, but not required.

II. Statutory and Regulatory Authority

A. The Regulated Article

FDA's authority over new animal drugs comes from the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 321 et seq.). The definition of a drug, in section 201(g) of the FD&C Act, includes "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals"; and "articles (other than food) intended to affect the structure or any function of the body of man or other animals." The definition of "new animal drug" in section 201(v) of the FD&C Act includes any drug intended for use in animals that is not generally recognized as safe and effective for use under the conditions prescribed, recommended, or suggested in the drug's labeling, or that is so recognized but has not been used to a material extent or for a material time.

Generally under the FD&C Act, a new animal drug is "deemed unsafe" under section 512(a)(1) unless FDA has approved a new animal drug application (NADA) for its intended use, unless the drug is only for investigational use and conforms to specified exemptions for such use under an Investigational New Animal Drug (INAD) exemption (21 U.S.C. 360b(a)(1), (a)(3)), or unless

the drug is used in conformance with regulations promulgated under sections 512(a)(4) or (5) of the FD&C Act (21 U.S.C. 360b(a)(4) or (5)). An unsafe new animal drug is "adulterated" under section 501(a)(5) of the FD&C Act.

For purposes of this guidance, "altered genomic DNA" refers to the portion of an animal's genome that has been intentionally altered. Unless otherwise excluded, e.g., certain mosquito-related products[9], the altered genomic DNA in an animal is a drug within the meaning of section 201(g) of the FD&C Act because such altered DNA is an article intended to affect the structure or function of the body of the animal, and, in some cases, intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in the animal.[10] Altered genomic DNA may result from random or targeted DNA sequence changes including nucleotide insertions, substitutions, or deletions, or other technologies that introduce specific changes to the genome of the animal. Non-heritable altered genomic DNA that is intended to affect the structure or function of the resulting animal or to cure, mitigate, or treat a disease in the animal also meets the drug definition. As noted previously, this guidance primarily addresses heritable genomic alterations.

A specific DNA alteration is an article that meets the definition of a new animal drug at each site in the genome where the alteration (insertion, substitution or deletion) occurs. The specific alteration sequence and the site at which the alteration is located can affect both the health of the animals in the lineage and the level and control of expression of the altered sequence, which influences its effectiveness in that lineage.[11] Therefore, in general, each specific genomic alteration is considered to be a separate new animal drug subject to new animal drug approval requirements. If a sponsor wishes to introduce multiple genomic alterations resulting in one final animal lineage, we recommend that the sponsor contact the agency to discuss regulatory options and the kinds of scientific questions that would have to be addressed in an application. During

[9] In Draft Guidance for Industry #236, "Regulation of Mosquito-Related Products," FDA has proposed to clarify that the phrase "articles (other than food) intended to affect the structure or any function of the body of man or other animals" does not include articles intended to prevent, destroy, repel, or mitigate mosquitoes for population control purposes. Instead, such products are pesticides regulated by the Environmental Protection Agency (EPA) (http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM533600.pdf)

[10] FDA does not intend to regulate altered genomic DNA that meets the definition of a veterinary biologic and is regulated by the Animal and Plant Health Inspection Service (APHIS) of the United States Department of Agriculture (USDA). 21 CFR 510.4.

[11] Because animals with intentionally altered genomes being used for commercial purposes are likely to be descendants of the initially altered animal, rather than the initially altered animal itself, the NADA safety and effectiveness evaluations should be focused on a generation as close to those animals to be used for commercial purposes as possible. Sponsors will need to demonstrate that following approval and use in commerce, the altered genotype and/or phenotype are stably maintained in a representative sample of animals. 21 CFR 514.1(b)(5).

the investigational phase, one INAD file may be established for multiple genomic alterations, and the file may contain information on investigational animals that contain different numbers or types of intentional genomic alterations, including those occurring at different locations of the genome, prior to selecting the lineage of animals with intentionally altered genomes intended for commercialization.

Each new animal drug approval covers all animals containing the same genomic alteration(s) (the regulated article or new animal drug) derived from the same alteration event(s). Animals containing the genomic alteration as a result of breeding between an intentionally altered animal and its non-intentionally altered counterpart animal are covered by the new animal drug approval.

B. Enforcement Discretion for INAD or NADA Requirements for Certain Animals With Intentionally Altered Genomic DNA

Although, unless otherwise excluded,[12] animals with intentionally altered genomes are subject to premarket approval requirements, in certain circumstances, based on the risk(s) they pose, we intend to exercise enforcement discretion with regard to INAD and NADA requirements for certain of these animals (that is, in specified circumstances, we do not intend to enforce the INAD and NADA requirements, including those described in this guidance). For example, FDA has not and does not intend to enforce INAD and NADA requirements for: (1) animals of nonfood-producing species whose genomes have been intentionally altered that are regulated by other government agencies or entities, such as insects whose genomes have been intentionally altered that are under APHIS oversight; and (2) animals of nonfood-producing species whose genomes have been intentionally altered that are raised and used in contained and controlled conditions such as laboratory animals with intentionally altered genomes used in research institutions. Although we generally intend to exercise enforcement discretion with regard to INAD and NADA requirements for such animals, we retain the discretion to take enforcement action if we learn of safety concerns associated with them.

Based on evaluation of risk factors, we may exercise enforcement discretion over INAD and NADA requirements for additional kinds or uses of nonfood-producing species of such animals, as we did after reviewing information about *Zebra danio* aquarium fish genetically engineered to

[12] See footnote 9 regarding mosquito-related products.

fluoresce in the dark (GloFish) (http://www.fda.gov/animalveterinary/developmentapprovalprocess/geneticengineering/geneticallyengineeredanimals/ucm413959.htm) and *Int'l Ctr. for Tech. Assessment v. Thompso*n, 421 F. Supp. 2d 1 (D.D.C. 2006)). We may also modify our approach with respect to INAD and NADA requirements for other kinds or uses of animals based on our evaluation of risk factors.

When FDA reviews and approves an INAD or NADA, it complies with the requirements of the National Environmental Policy Act (NEPA), including a review of environmental risks, if any, where required. When FDA exercises its enforcement discretion over the INAD or NADA requirements, no NEPA review would take place. As a result, the potential for environmental risks are among the factors we intend to consider in determining whether to exercise enforcement discretion.

Among the issues we intend to consider when determining whether to exercise enforcement discretion are whether:

- There is anything about the article itself that poses a human, animal, or environmental risk. For example, does the altered genomic DNA contain sequences that can cause human or animal disease either intrinsically or by recombination?

- For environmental releases, does the animal with intentionally altered genomic DNA pose any more of an environmental risk than its counterpart?

- There are concerns over the disposition of animals with intentionally altered genomic DNA that could pose human, animal, or environmental risks.

- There are any other safety questions that have not been adequately addressed by the sponsor.

You may contact CVM for further information on whether some form of enforcement discretion might be warranted for the intentionally altered genomic DNA in your animal. Although we may decide to exercise enforcement discretion with respect to regulatory requirements for certain animals with intentionally altered genomic DNA after reviewing information about potential risks, this decision may be reevaluated if we become aware of any changes in the animals' risk profiles. Such reevaluation could lead us to conclude that the intentionally altered genomic

DNA in these animals should be subject to FDA enforcement action until a full NADA has been approved.

III. Investigational Use of Animals With Intentionally Altered Genomic DNA

As noted earlier, under the FD&C Act, in general a new animal drug is "deemed unsafe" unless the FDA has approved an application for that particular use (21 USC 360b), unless it is for investigational use and is subject to an exemption from the approval requirement that conforms to FDA regulations or unless it is used consistent with regulations promulgated under sections 512(a)(4) and (5) of the FD&C Act. 21 USC 360b(a)(3), (4), (5), (j).

FDA regulations concerning investigational use of new animal drugs are codified at section 511.1 in Title 21 of the Code of Federal Regulations (21 CFR 511.1). These regulations cover shipments in interstate commerce of new animal drugs for tests *in vitro* and in laboratory research animals (21 CFR 511.1(a)) and for clinical investigation in animals (21 CFR 511.1(b)). The INAD requirements in 21 CFR 511.1(b) apply to investigational animals whose genomes have been intentionally altered. Further, the development of such animals constitutes clinical investigation because it involves studying the effectiveness of the drug in the target species and the effects of the intentionally altered genomic DNA, including those of its expression product(s), if any, on the animal containing it.

In general, the INAD regulations specify labeling and record-keeping requirements, animal disposition, and conditions under which food[13] from animals used for clinical investigations under section 511.1(b) can be introduced into the food supply. Section 511.1(b) also requires that prior to shipping a new animal drug for clinical tests, a sponsor must submit a Notice of Claimed Investigational Exemption for a New Animal Drug (INAD Notice) containing specified information.

We strongly recommend that you contact CVM early in the development process to determine what information should be submitted to CVM and the appropriate file type to utilize. Certain types of early information can be submitted without the establishment of an INAD file and FDA would consider such information to be confidential. You should note that establishment of an INAD file will result in an annual sponsor user fee unless you are eligible for a waiver. See

[13] The term "food" includes food for humans and animals.

Draft Revised Guidance for Industry #170, "Animal Drug User Fees and Fee Waivers and Reductions," http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM052494.pdf. CVM will work with you to determine the appropriate timeframe to open an INAD file, how best to develop the data and information that will be needed for an NADA, and how to provide such data and information to CVM for evaluation and comment. We recommend that the early information you provide to CVM include how you intend to develop the animal whose genome has been intentionally altered including the species of animal to be under study, the altered gene(s) or region of the genome, and the intention of the genomic alteration, including any gene product(s) that may be produced.

In most cases, you will need to submit an INAD Notice prior to shipping any animals with intentionally altered genomic DNA. Also, if you wish to introduce any food derived from investigational animals into the food supply, you must get prior FDA authorization to do so through the INAD process. 21 CFR 511.1(b)(5). We recommend that prior to making a request for such authorization, you schedule a teleconference or in-person meeting with us to determine which classes of investigational animals may be suitable for consideration for food use.

We encourage you to contact CVM if you have questions about submitting a request to establish an INAD file. Once we have established an INAD file, you will receive a letter assigning a unique INAD number to that file. This unique identifier (which we refer to as a file number) should be used for all subsequent communications with us regarding that INAD file. As previously stated, an INAD file can encompass animals derived from multiple alteration events, even though an NADA would generally only cover animals derived from a single alteration event.

We recommend that you schedule a meeting with us (either in-person or via teleconference) before an INAD file has been established or immediately thereafter. In that meeting, you can acquaint us with the nature of the animal under development and the intended use. We can then provide you with more specific information on the kinds of regulatory responsibilities you have under an INAD, and the nature of the regulatory decisions we can make during the investigational phase of research, including the following:

A. Shipping and Labeling Investigational Animals and Their Products

During the investigational phase of the development of a lineage of animals with intentionally altered genomic DNA, the animals may need to be moved from the initial laboratory or barn to other locations within the sponsor's facilities, or to other investigators at the same facilities or off-site. If the investigational animals or products derived from them are shipped to other investigators, it is important to ensure that those individuals/entities receiving the investigational animals or their products use them only for research purposes. All shipments must bear labeling that clearly identifies that edible products derived from investigational animals are not to be used for food without prior authorization from FDA. 21 CFR 511.1(b)(1)-(5). We recommend that you contact us to determine the appropriate labeling for the particular investigational animal or its products.

B. Animal Disposition

A primary goal during the investigational phase of development of the animal with an intentionally altered genome is to ensure that edible products from these investigational animals do not enter the food supply without prior FDA authorization. Edible products include, but are not limited to milk, honey, eggs, muscle tissue, as well as other tissues such as liver, kidney, skin, and fat. We encourage you to provide a disposition plan for all classes of investigational animals and animal products. We recommend that all surplus investigational animals and their biological products be disposed of by incineration, burial, or composting, and that appropriate records be kept of animal identification and disposition. In some special cases, alternative disposition may be appropriate provided that our safety concerns are met (see Section III.C). 21 CFR 511.1 (b)(5).

C. Investigational Food Use Authorizations

If you wish to introduce investigational animals or animal products into the food supply, you must request an Investigational Food Use Authorization (21 CFR 511.1(b)(5)). For those animals subject to slaughter inspection by the USDA Food Safety and Inspection Service (FSIS), we will inform FSIS if our safety concerns are met and we grant you an Investigational Food Use Authorization.

FSIS has oversight of meat, poultry, fish of the Order Siluriformes, and egg products, and tests for animal drug residues above tolerance levels (maximum allowable amounts). FDA and FSIS have enjoyed longstanding open communications during the drug approval process, and are discussing how to adapt and improve these existing procedures to fully accommodate the needs of both agencies in addressing animals with intentionally altered genomes intended to go into the food supply.

We recommend that prior to making a food-use authorization request, you schedule a teleconference or in-person meeting with us to determine which classes of investigational animals may be suitable for consideration for food use and the nature and extent of data you will need to provide for us to make that determination.

D. Environmental Considerations

Actions on INADs are considered major federal actions under the NEPA, and as such may require preparation of an environmental assessment (EA) and a finding of no significant impact (FONSI) (21 CFR 511.1(b)(10), 21 CFR 25.15) or an environmental impact statement (EIS) (21 CFR 25.22).

Through the preparation of an EA/FONSI or EIS, FDA will examine the potential for environmental impacts, including the potential for inadvertent release or escape of the animal with an intentionally altered genome and/or its products into the environment, and whether certain measures may mitigate any potential significant impacts that would adversely affect the human environment. Additionally, sponsors may be subject to applicable environmental requirements with respect to runoff from animal production facilities and land receiving animal waste under the Clean Water Act. 33 U.S.C. 1251 et. seq. and other statutes.

In order to determine the nature and extent of the potential for environmental risks that your investigational animals may pose, we recommend that you contact us early in the development of your animals with intentionally altered genomes so that we can determine the scope of this environmental assessment. These early discussions can help to focus your environmental assessment under the NADA component as well.

Categorical exclusion from the requirement to prepare an EA may be possible under 21 CFR 25.33(e) for investigational studies on certain animals, if you can provide sufficient information for us to conclude that extraordinary circumstances will not exist (21 CFR 25.21). This should

include sufficient information on the animals whose genomes have been intentionally altered and their containment to allow us to conclude that use and disposal of any investigational animals or their products would not have a significant impact on the human environment. We recommend that you contact us early to discuss whether your INAD may be eligible for a categorical exclusion under 21 CFR 25.33(e), or whether extraordinary circumstances may exist that would require an EA/FONSI or EIS.

IV. FDA Approval of Animals With Intentionally Altered Genomic DNA

A. Overview

Other than for investigational uses, section 512(a)(1) of the FD&C Act (21 U.S.C. 360b(a)(1)) requires that a new animal drug be the subject of an approved NADA based on a demonstration that it is safe and effective for its intended use.

When submitting an NADA, you should include the results of any investigations you conducted under an INAD. We will evaluate the NADA to determine whether you have demonstrated that the new animal drug is safe and effective for its intended use. To demonstrate effectiveness of an article intended to express an extractable protein (e.g., for use as a human biological product), generally you would simply have to show that the expression product is in fact expressed in the animal. To demonstrate effectiveness of an article intended to alter a characteristic of the resulting animal, in general you would have to show that the animal whose genomic DNA had been intentionally altered had the claimed altered characteristic (e.g., that its rate of growth was as claimed or that it was indeed resistant to a disease).

The agency is interested in increasing the transparency of its deliberations and actions. In particular, we intend to seek input from experts and the public where there is significant public interest in an issue, and FDA believes the public may have relevant data or information to contribute.

Additionally, as is the case for all NADAs, after completion of an NADA, the agency will post a summary of the information in the NADA file, including information used to assess safety (to the animal and for food consumption, if appropriate) and in support of the claims made by the sponsor. 21 CFR 514.11(e).

B. New Animal Drug Application Requirements

Section 512(b)(1) of the FD&C Act describes the information that must be submitted to FDA as part of an NADA. These statutory requirements are further explained and expanded upon in the regulations for new animal drug applications, 21 CFR 514.1.

The application of some of the statutory and regulatory requirements for new animal drug applications to animals with intentionally altered genomic DNA may not be obvious. For example, it may not be obvious how the requirement to provide a full list of the articles used as components of a drug as described in 512(b)(1)(B) of the FD&C Act and 21 CFR 514.1(b)(4) of the NADA regulations applies to such animals. Therefore, this section of the guidance document provides a brief summary of the NADA requirements in 21 CFR 514.1 and describes how these requirements may be addressed for applications submitted for animals with intentionally altered genomic DNA. Section IV.C describes our recommendations for how to present this information in the structure of an NADA submission to meet these regulatory requirements and the statutory requirements of safety and effectiveness.

1. Identification (21 CFR 514.1(b)(1))

   Section 514.1(b)(1) requires that certain identifying information be provided including the nature of the application (i.e., original or supplemental application), the name and address of the applicant, date of application, and the trade and/or chemical name of the new animal drug.

   The information that should be provided to satisfy this requirement for an application for a lineage of animals with an intentionally altered genome is similar to that provided for a conventional new animal drug. In the case of such an application, the "trade and/or chemical name of the new animal drug" should be described by identifying the animal, its ploidy and zygosity, the name and intended function of the altered genomic DNA, and the number and characterization of the site(s) of alteration[14], including unintended (e.g., off-target) alterations, as well as the intended use of the resulting lineage of animals. For a more

[14] The term "site of alteration" in this document refers to the genomic location in the animal with the altered genomic DNA either chromosomally integrated or maintained as an extrachromosomal element. In general, we are most interested in characterizations that are performed in animals close to commercialization.

complete description of how we recommend you present this information in the NADA submission, please see Section IV.C., Steps 1, 2, and 3.

We consider this component to be critical to the structure and content of an NADA submission and so encourage you to consult with us on this topic as early as possible in the development of these animals, for example, as an early part of the INAD process.

2. Table of Contents and Summary (21 CFR 514.1(b)(2))

Section 514.1(b)(2) requires that an NADA include a table of contents which identifies the data and other material submitted, and a well-organized summary of information that (1) describes the chemistry of the new animal drug, and (2) describes the clinical purpose and provides a summary of laboratory and clinical studies.

For more information on how we recommend you present this information in the NADA submission, please see Section IV.C., Steps 1, 2, and 3.

3. Labeling **(**21 CFR 514.1(b)(3))

Section 514.1(b)(3) requires that an NADA include three copies of each piece of labeling to be used for the new animal drug.[15]

In the context of animals with intentionally altered genomic DNA, this includes labels and other written, printed information (i.e., labeling) that will accompany the animals. Labeling should include a summary description of the article, the animal into which the article is introduced (e.g., common name/breed/line; genus and species), the name of the resulting animal lineage, and the intended use of the animals containing the article. Where the labeling for an animal whose genome has been intentionally altered contains animal care or safety information (e.g., husbandry or containment), we recommend that the labeling accompany the animal throughout all stages of its lifecycle. We recommend that you contact CVM for further information regarding the required labeling for such animals.

[15] This discussion pertains to new animal drug labeling requirements, not labeling requirements for food derived from animals whose genomes have been intentionally altered.

4. Components and Composition **(**21 CFR 514.1(b)(4))

Section 514.1(b)(4) requires that an NADA include (1) a list of all articles used as components of the drug product; (2) a statement of composition of the drug product; and (3) a complete description of the fermentation of antibiotic drug substances.

For animals whose genomes have been intentionally altered, (3) would not be relevant. The information described in (1) and (2) should encompass the molecular characterization of the article. It should enable us to determine whether the article contains any potentially mobilizable DNA sequences, and whether sequences are present that encode pathogens, toxicants, allergens, or substances likely to dysregulate the growth control of cells, tissues, or organs, except by explicit design. We would expect that such information would describe the source, identity, purity, and functionality of the introduced article. For a more complete description of how we recommend you present this information in the NADA submission, please see Section IV.C., Steps 2 and 3.

5. Manufacturing Methods, Facilities, and Controls (21 CFR 514.1(b)(5))

Section 514.1(b)(5) requires that an NADA include a detailed description of the methods used in and the facilities and controls used for the manufacturing, processing, and packing of the new animal drug.

For animals with intentionally altered genomes, this information should encompass:

- the method by which the alteration was introduced into the initial animal, including whether the initial animal whose genome was intentionally altered was chimeric;

- the breeding strategy used to produce the lineage progenitor. (A lineage progenitor is the animal whose genome has been intentionally altered from which subsequent animals used for commercial purposes are derived); and

- full characterization of the site of intentional alteration, any unintended alterations (e.g., off-target alterations, unanticipated insertions, substitutions, or deletions) and the alterations persisting once the genome has been stabilized in animals contributing to the lineage of animals to be commercialized, including the number and orientation of any

introduced DNA sequences, if applicable. In particular, we recommend that you evaluate whether there are any unintended interruptions of a coding or regulatory region.

Information submitted to satisfy the requirements for finished product analytical controls and a stability program should include information demonstrating the durability of the genotype and phenotype—that is, whether the article is stably inherited, and the phenotype is consistent and predictable. This should include developing a sampling plan.

For genotypic durability, we recommend that you use the results of studies demonstrating that the altered genomic DNA is stably inherited. For the phenotypic durability portion of the plan, we recommend that you submit data on the consistency of the expressed trait (based on the intended use) over multiple generations. We recommend that, where feasible, you gather data on inheritance from at least two generations, preferably more, and recommend that at least two of the sampling points be from non-contiguous generations (e.g., F_1 and F_3).

Your plan should include a method of identity with sufficient discrimination to determine (1) whether a given animal contains the altered genomic DNA, and (2) whether the altered genomic DNA has significantly changed from that which was evaluated in the NADA (i.e., a detection method for your animal and regulated article). For a more complete description of how we recommend you present this information in the NADA submission, please see Section IV.C., Steps 2, 3, and 5. We recommend that you consult with us on developing these plans.

6. Samples **(**21 CFR 514.1(b)(6))

Section 514.1(b)(6) requires that samples of the new animal drug and articles used as components and information concerning them be submitted to CVM if requested.

This requirement applies to NADAs for animals whose genomes have been intentionally altered as it does to conventional new animal drug applications. Sponsors are encouraged to contact CVM to determine what samples (such as a genomic sample containing the article) should be provided.

If FDA establishes a tolerance for the new animal drug, FDA will notify FSIS and provide it with a summary of the information and evaluation upon which it based the tolerance, and a method of analysis to be used to enforce the tolerance. FDA and FSIS are discussing how to

adapt and improve existing communication procedures so that they will fully accommodate the needs of both agencies in addressing animals whose genomes have been intentionally altered and that are intended to go into the food supply.

7. Analytical Methods for Residues **(**21 CFR 514.1(b)(7))

Section 514.1(b)(7) requires that an NADA include method(s) and data to enable determination of residues of the new animal drug in food-producing animals, except when data or other adequate information establish that it is not reasonable to expect the new animal drug to become a component of food at concentrations considered unsafe.

The information that should be provided to satisfy this requirement for an application for animals whose genomes have been intentionally altered includes a method of detection that can be used to identify the altered genomic DNA in the resulting animals.

8. Evidence to Establish Safety and Effectiveness **(**21 CFR 514.1(b)(8))

Section 514.1(b)(8) requires that an NADA include data and information to permit evaluation of the safety and effectiveness of the new animal drug product for the use as suggested in the proposed labeling. Section 21 CFR 514.1(b)(8)(iv) also requires that sponsors supply all information relevant to safety and effectiveness for a new animal drug, favorable and unfavorable.

Information relevant to the (1) target animal safety component of the NADA is described further in Step 4 of Section IV.C.; (2) food safety component of the NADA is addressed further in Step 6 of Section IV.C.; and (3) establishing effectiveness is described further in Step 7 of Section C.

We recommend that you contact the Center for help in determining the most efficient manner to submit all the above relevant information.

9. Veterinary Feed Directive **(**21 CFR 514.1(b)(9))

Section 514.1(b)(9) requires that in the case of NADAs for Veterinary Feed Directive (VFD) drugs the application must include three copies of the VFD in the format described in 21 CFR 558.6(a)(4).

This requirement is not applicable to NADAs for animals whose genomes have been intentionally altered.

10. Supplemental Applications **(**21 CFR 514.1(b)(10))

Section 514.1(b)(10) requires that if an NADA is a supplemental application, such application must include full information on each proposed change concerning any statement made in the previously approved application.

This requirement applies to NADAs for animals whose genomes have been intentionally altered as it does to conventional new animal drug applications. Sponsors seeking supplemental applications for such animals should contact CVM to determine how to prepare such an application.

11. Applicant's Commitment **(**21 CFR 514.1(b)(11))

Section 514.1(b)(11) requires that an NADA include a commitment by the applicant that any labeling and advertising for the new animal drug is consistent with the conditions stated in the labeling which is part of the application.

This requirement applies to NADAs for animals whose genomes have been intentionally altered as it does to conventional new animal drug applications. Sponsors should refer to 21 CFR 514.1(b)(11) for a complete description of the conditions of this commitment.

12. Additional Commitments **(**21 CFR 514.1(b)(12))

Section 21 CFR 514.1(b)(12) requirements that are relevant to an NADA for animals whose genomes have been intentionally altered include commitments by the applicants that

i) the methods, facilities and controls described in section 514.1(b)(5) conform to the current good manufacturing practice (GMP) regulations in 21 CFR 211, and

ii) any nonclinical laboratory studies included in the application are conducted in compliance with good laboratory practice (GLP) regulations (21 CFR 58), or, if not conducted in compliance with such regulations, a brief statement of the reason for the noncompliance.

The requirement to comply with GLP regulations, including a statement regarding compliance or noncompliance, applies to NADAs for animals whose genomes have been intentionally altered as it does to conventional new animal drug applications.

13. Environmental Assessment **(**21 CFR 514.1(b)(14))

Section 514.1(b)(14) requires that an NADA include either a claim for categorical exclusion or an environmental assessment (EA). An EA must be prepared for each agency action except when the action is categorically excluded by 21 CFR 25.30 – 34 and no extraordinary circumstances exist. 21 CFR 25.21. The EA is a public document that provides sufficient information to allow FDA to either prepare an environmental impact statement (EIS) or issue a finding of no significant impact (FONSI). The specific information required for an EA is outlined in 21 CFR 25.40. This requirement applies to NADAs for animals with intentionally altered genomes as it does to conventional new animal drug applications.

An EA that demonstrates the animals whose genomes have been intentionally altered will not significantly affect the quality of the human environment leads to a finding of no significant impact (FONSI). We recommend that the EA focus on environmental issues and potential impacts related to the use and disposal of the animals and their final products, if relevant. The appropriate scope and content of the EA may vary widely depending on the animal product, claim, and conditions of use. Therefore, we recommend that you contact and work closely with us on these issues before proceeding with preparation of the EA, which is described in more detail in Step 6 of Section C.

14. Assembling and Binding the Application **(**21 CFR 514.1(b)(15))

Section 514.1(b)(15) describes certain administrative requirements for submitting an NADA to FDA. These requirements apply to NADAs pertaining to animals whose genomes have been intentionally altered as they do to conventional new animal drug applications. We recommend that you contact CVM for further information on assembling your NADA.

C. Recommended Process for Completing Pre-approval Assessments for Animals Whose Genomes Have Been Intentionally Altered

To facilitate the evaluation of animals whose genomes have been intentionally altered under the existing regulatory framework for new animal drugs, we have developed the following approach for submitting data for an NADA. It fulfills the regulatory requirements described in the preceding section and helps guide sponsors in developing their regulatory submission strategies.

This approach is cumulative and risk-based. Each component of the assessment forms the basis on which the next step is evaluated. The approach is risk-based because it examines both the *potential hazards* (that is, components that may cause an adverse outcome) identified at each step along the pathway and the *likelihood of harm* among the receptor populations (the animals whose genomes have been intentionally altered themselves as well as those individuals or populations exposed to these animals). It is also conducted on a case-by-case basis, because the potential hazards and risks are likely to be unique to each application.

We encourage you to consult with us as you develop data to satisfy the elements below, to ensure that the process is as efficient as possible and that the data and information you provide is in a format that will facilitate our ability to review it.

Step 1: Product Identification

Product identification (21 CFR 514.1(b)(1)), which many molecular biologists would refer to as product definition, forms the foundation for the evaluation process and drives subsequent data generation and review. It encompasses the specific lineage of animals whose genomes have been intentionally altered (that is, the altered genomic DNA as well as the animals containing it) and the purpose (i.e., intended use) of the altered genomic DNA that is the subject of the NADA. We believe that the concept of product identification is so important to the structure and content of the NADA submission that we encourage you to consult us on

this topic as early as possible in the development process, for example as an early part of the INAD process.

A product definition characterizes the animal whose genome has been intentionally altered. Therefore, as indicated in section IV.B.1, as appropriate to the submission, we recommend that the product identification include the following information:

- Ploidy;
- Zygosity;
- Description of the animal (e.g., common name/breed/line; genus and species);
- Characterization of the alteration of the genomic DNA (e.g., site(s) of alteration, nature of the alteration (deletion, substitution, addition, and if so, number of copies, etc., including the sponsor's name for the altered genomic DNA (e.g., gamma virus receptor nonsense mutation, inserted [new gene] e.g., the fatty acid desaturase n))
- Name of resulting animal line; and
- The intended use or claim being made for the lineage of animals whose genomes have been intentionally altered.

Step 2: Molecular Characterization of the Altered Genomic DNA

This step of the process serves to describe the components and composition of the article. (21 CFR 514.1(b)(4).) For this step, we recommend that you provide information for identifying and characterizing the altered genomic DNA that will be introduced into the progenitor of the animal to be marketed. This and the next step in the process are part of the hazard identification component of the safety review of the NADA. (21 CFR 514.1(b)(8)). Typically, the information should include, but not be limited to the following, as applicable to the particular type of altered genomic DNA (e.g., inserted DNA sequences; replaced DNA /nucleotide(s); or deletion of nucleotides or sequences):

- details of how the genomic alteration(s) was achieved;
- a description of the source(s) of the various functional components of the altered genomic DNA, as appropriate;
- the sequence of the altered genomic DNA, or of a sufficient number of nucleotides surrounding it such that the alteration can be uniquely identified (e.g., especially in the case of deletion alterations);
- the purpose of the alteration;

- the intended function(s) of the genomic alteration; and
- the purity of the preparation containing the materials used to effect the genomic alteration prior to introduction into recipient animals or cells.

In order to determine whether any risks exist that would make the product unsafe, we expect to evaluate whether the altered genomic DNA contains any potentially mobilizable DNA sequences, or whether sequences are present that encode pathogens, toxins (including allergens), or the addition or deletion of substances likely to dysregulate the growth control of cells, tissues, or organs, except by explicit design.

Step 3: Molecular Characterization of the Lineage of Animals Whose Genomes Have Been Intentionally Altered

This step continues the analysis of the intentionally altered genomic DNA and the location of the genomic alteration in the resulting animal, as well as the production of the animal(s) intended to be used in commerce and any potential hazards that may be introduced into those animals as part of their production. As such, this step addresses the identity and some manufacturing requirements of your NADA. 21 CFR 514.1(b)(1) and (b)(5). We recommend that you provide data and information describing the method by which you effected the alteration to the genomic DNA in the initial animal, including whether the initial animal was chimeric. In addition, we recommend that you describe the breeding strategy you used to produce the lineage progenitor (the animal that contains the final stabilized version of the initial event and from which the animals to be used for commercial purposes are derived). You should fully characterize the final stabilized altered genomic DNA in the animal.

Step 4: Phenotypic Characterization of Animals Whose Genomes Have Been Intentionally Altered

The previous steps of the review process have concentrated on establishing and characterizing the altered genomic DNA in the resulting animals. Information in this and the following steps helps establish whether the genomic alteration poses any risks to humans, risks to health of the animal, or risks to the environment.

With regard to health of the animals whose genomes have been intentionally altered, including the target animal safety requirements of 21 CFR 514.1(b)(8), we recommend that you submit data regarding whether the genomic alteration or its expression product(s) cause

any direct or indirect toxicity. In general, we recommend that you compile and submit data and information addressing the health of these animals, including veterinary and treatment records, growth rates, reproductive function, and behavior. In addition, we recommend that you submit data on the physiological status of the animals whose genomes have been intentionally altered, including clinical chemistry, hematology, histopathology, and post-mortem results. We recommend that you collect data from a generation of animals as close as possible to those intended for use in commerce.

Step 5: Genotypic and Phenotypic Durability Assessment

As in Step 3, this step also addresses some additional components of the manufacturing requirements codified in 21 CFR 514.1(b)(5). It is intended to provide information to ensure that the altered genomic DNA in the animal resulting from the specific alteration event and defining (identifying) the animal being evaluated is durable — that there is a reasonable expectation that the altered genomic DNA is stably inherited, and the phenotype is consistent and predictable. This would include developing a sampling plan.

For genotypic durability, we recommend that you use the results of studies demonstrating that the altered genomic DNA is stably inherited. For the phenotypic durability portion of the plan, we recommend that you submit data on the consistency of the expressed trait (based on the intended use) over multiple generations. We recommend that, where feasible, you gather data on inheritance from at least two generations, preferably more, and recommend that at least two of the sampling points be from non-contiguous generations (e.g., F_2 and F_4).

Your plan should include a method of identity with sufficient discrimination to determine (1) whether a given animal contains the altered genomic DNA, and (2) whether the altered genomic DNA has significantly changed from that which was evaluated to be safe and effective (i.e., a detection method for your genomic alteration in its final stabilized genomic location(s) in the animal whose genome has been intentionally altered). We recommend that you consult with us on developing these plans.

Step 6: Food Safety and Environmental Safety Assessments

Food Safety

This part of Step 6 addresses the food safety requirements in 21 CFR 514.1(b)(8). It focuses on the issue of whether food derived from animals whose genomes have been intentionally altered is safe for humans or animals consuming edible products from the animals.

The risk issues involved in determining food safety can be divided into two overall categories. The first addresses whether there is any direct toxicity, including allergenicity, via food consumption of the expression product of the article. The second category addresses potential indirect toxicity associated with both the article and its expressed product (e.g., whether location or expression of the article affects physiological processes in the resulting animal such that unintended food consumption hazards are created, or whether existing food consumption risks are increased). Potential adverse outcomes via the food exposure pathway should be identified by determining whether there are any biologically relevant changes (1) to the physiology of the animal (assessed partly in *Step 3: Phenotypic Characterization*), and (2) in the composition of edible tissues from the animals whose genomes have been intentionally altered that suggest reason for toxicological concern compared with the appropriate comparator.

In the end, if the expression product(s) is shown to be safe, and the composition of edible tissues from the animals whose genomes have been intentionally altered is shown to be as safe as those from animals of the same or comparable type that are commonly and safely consumed, then we expect to view this as evidence that food derived from the animals whose genomes have been intentionally altered is safe (i.e., there is a reasonable certainty of no harm from consumption of the food).

FDA participated in the Codex ad hoc Intergovernmental Task Force on Foods Derived from Biotechnology and its Working Group that developed the guideline for assessing food safety of foods from rDNA animals (Codex Alimentarius Commission: *Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Animals*; in ALINORM 08/31/34, Appendix II; (http://www.codexalimentarius.org/download/standards/11023/CXG_068e.pdf). The information needed to establish food safety for food from animals whose genomes have been

intentionally altered under an NADA is consistent with that described in the Codex Guideline.

Environmental Safety

This portion of Step 6 addresses the environmental component of your NADA. 21 CFR 514.1(b)(14). We expect that, at least until we have more experience, most applications for animals whose genomes have been intentionally altered would have to be evaluated to determine whether such an approval will individually or cumulatively result in significant environmental impacts (i.e., whether an extraordinary circumstance exists). 21 CFR 25.21. An EA that demonstrates the animals whose genomes have been intentionally altered do not significantly affect the quality of the human environment leads to a finding of no significant impact (FONSI).

We recommend you contact us early in the development of your animal so that we can focus the EA on the environmental issues and potential significant impacts related to the use and disposal of your animal and its final product, if relevant. The appropriate scope and content of the EA may vary widely depending on the animal product, claim, and conditions of use (e.g., aquatic vs. terrestrial animal species). Therefore, we recommend that you contact and work closely with us on these issues before proceeding with preparation of the EA.

Step 7: Effectiveness/Claim Validation

The previous steps of the review process primarily address identity and safety issues. This last step of pre-market review addresses effectiveness, i.e., whether you have validated your claims for the characteristics that the animals whose genomes have been intentionally altered are intended to exhibit. 21 CFR 514.1(b)(8). For example, in the case of animals whose genomes have been intentionally altered that are intended to resist disease, you should demonstrate that those animals are indeed resistant to that disease. In the case of animals whose genomes have been intentionally altered that are intended to produce a non-food product, you should demonstrate that those animals indeed produce the claimed product. If that product is, for example, a drug or component of a drug intended for use in humans, the safety and effectiveness of that drug would be evaluated separately by Center for Drug Evaluation and Research. We recommend that you work closely with us to determine the nature and extent of data to meet these requirements, and to coordinate with CDER, CDRH, CFSAN, or CBER as appropriate.

V. Post-Approval Responsibilities

Once an animal whose genome has been intentionally altered is approved, sponsors have on-going responsibilities including registration and drug listing, recordkeeping, filing supplements, and periodic reporting. (21 USC 360, 21 USC 356a, 21 CFR 514.80, 21 CFR 514.8). We recommend that you use the following general approach to fulfill these requirements, but that you work closely with us during the development of the animals in order to determine the specific data and information to submit.

A. Statutory Registration and Drug Listing Requirements

As part of the registration requirements under 21 USC 360, you are required to register your name and place of business, and identify any facility(ies) engaged in the production or testing of the animals whose genomes have been intentionally altered. See 21 CFR Part 207. As part of your listing responsibilities, you are required to list all regulated articles, 21 CFR 207.22(a)(1), which should be a list of all lines of animals whose genomes have been intentionally altered that you have produced.

B. Recordkeeping

You must establish and maintain indexed and complete files containing full records of all information relevant to the safety or effectiveness of animals whose genomes have been intentionally altered that has not been previously submitted as part of the NADA. 21 CFR 514.80(a)(1). This would generally consist of Adverse Event Reports or other data or information from domestic or foreign sources, such as published literature.

C. Annual Reports, Supplements, and Other Changes to an Approved Application

We recommend that information demonstrating genotypic and phenotypic durability be collected on an annual basis from a subset of marketed approved animals whose genomes have been intentionally altered. You should consult with us during the INAD process on the nature of the information to be collected, as it will be determined on a case-by-case basis. We recommend that you maintain current standard operating procedures (SOPs) for each test method employed, and that you maintain SOPs for other procedures used in the husbandry of these animals (e.g., those resulting in biological containment).

You must submit information on all changes that have been made, or that you propose to make to the animals whose genomes have been intentionally altered (21 CFR 514.8(b)). Depending on the risk(s) that could be introduced by that change, the nature and timing of the reporting may be different. Information on the types of changes and which type of reporting they require are found in 21 CFR 514.8. We recommend contacting us if you have any questions regarding determining the category in which your changes may fall.

D. Records and Reports Concerning Experience with Approved Products

You are required to submit reports of data, studies, and other information of experience with the animals whose genomes have been intentionally altered. 21 CFR 514.80(a)(2). These experience reports must be submitted to our Division of Surveillance every six (6) months for the first two years following approval, and annually thereafter. 21 CFR 514.80(a)(4).

We remind you that the labeling associated with animals whose genomes have been intentionally altered may only prescribe, recommend, or suggest use under the conditions approved in the labeling that was submitted as part of the approval. 21 USC 360b(a)(1). This labeling must use the same language and emphasis as in the approval, including descriptions of relevant hazards and precautions.

VI. Import Tolerances

Section 512(a)(6) of the FD&C Act enables FDA to establish a safe level of new animal drugs and drug residues in edible portions of animals (i.e., food) imported into the United States (an import tolerance) when those drugs have not been approved for use in the United States. Whether a sponsor seeks approval of an NADA for a lineage of animals whose genomes have been intentionally altered or establishment of an import tolerance for food from such animals, the food safety standard is essentially the same.[16] Information about import tolerances, which enable imports of such food from animals whose genomes have been intentionally altered and that have been developed outside the United States, is found in the sections of this guidance relevant to evaluating food safety and is consistent with the recommendations in the Codex

[16] To establish an import tolerance, FDA must review data showing that the tolerance is safe based on food safety criteria similar to those used for a full NADA approval.

Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Animals. We recommend that you consult with us on establishing an import tolerance.

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Proposed Rule Questions Under Consideration [1]

The National Bioengineered Food Disclosure Standard was enacted on July 29, 2016. AMS has two years to establish a national standard and the procedures necessary for implementation. Below are 30 questions considered by interested stakeholders. USDA will use this input in drafting a proposed rule. The period for input closed on August 25, 2017. There will also be an opportunity for interested parties to comment on the proposed rule during the rulemaking process.

Input related to the questions below should be sent to GMOlabeling@ams.usda.gov [2]

1. What terms should AMS consider interchangeable with 'bioengineering'? (Sec. 291(1))

Context: The disclosure standard would be a mechanism to inform consumers about their food. AMS is considering the advantages and disadvantages of allowing the use of other terms to provide for disclosure.

2. Which breeding techniques should AMS consider as conventional breeding? (Sec. 291(1)(B))

Context: AMS is considering what would be defined as modifications that could otherwise be obtained through conventional breeding because these modifications would be exempt from mandatory disclosure.

3. Which modifications should AMS consider to be found in nature? (Sec. 291(1)(B))

Context: AMS is considering what would be defined as modifications that could otherwise be found in nature because these modifications would be exempt from mandatory disclosure.

4. Will AMS require disclosure for food that contains highly refined products, such as oils or sugars derived from bioengineered crops? (Sec. 291(1)(A))

Context: Many processed foods may contain ingredients derived from bioengineered crops, such as highly refined oils or sugars that contain undetectable levels of bioengineered genetic material such that they are indistinguishable from their non-engineered counterparts. AMS is considering whether to require disclosure for foods containing those derived ingredients that may be undetectable as bioengineered.

5. Although the Law states that the definition of bioengineering shall not affect any other definition, program, rule, or regulation of the Federal government, could there be potential areas of confusion between the definition of bioengineering as used in the Law and other similar terms used by the Federal government? If so, what are the potential remedies that could be added to this regulation to alleviate any confusion between this definition and others by the Federal government? (Sec. 292(b))

Context: AMS recognizes that other Federal agencies have different terms to describe organisms created through recombinant DNA techniques. AMS is considering areas of potential overlap or confusion over terms, as well as potential language to add to this regulation to ensure the term bioengineering does not affect any other definition, program, rule, or regulation.

6. Meat, poultry, and egg products are only subject to a bioengineered disclosure if the most predominant ingredient, or the second most predominant ingredient if the first is broth, stock, water, or similar solution, is subject to the labeling requirements under the Federal Food, Drug, and Cosmetic Act. How will AMS determine the predominance of ingredients? (Sec. 292(c))

Context: AMS is considering how to evaluate predominance to determine how the Law will apply to multi-ingredient food products.

7. How should AMS craft language in the regulations acknowledging that the Law prohibits animal products from being considered bioengineered solely because the animal consumed feed products from, containing, or consisting of a bioengineered substance? (Sec. 293(b)(2)(A))

Context: AMS is considering regulatory language similar to the wording in the Law and if the Agency should provide clarity that food derived from any animal, including invertebrates such as crickets or bee products, would not require disclosure as a bioengineered food solely because their nutrition came from food with bioengineered ingredients.

8. What is the amount of a bioengineered substance present in a food that should make it be considered bioengineered? (Sec. 293(b)(2)(B))

Context: The Law authorizes the Secretary to determine the amount of a bioengineered substance present in food in order for the food to be disclosed as a bioengineered food. The amounts of a bioengineered substance that may be present in food in order for the food to be a bioengineered food might be determined in a variety of ways: if a bioengineered substance is near the top of the list of ingredients, by determining the percentage of bioengineered ingredients in a food product, or by listing any ingredient that was produced through bioengineering, among others. AMS is considering how to determine the amount of bioengineered food or ingredient needed for a product to require a bioengineered disclosure, as well as the advantages and disadvantages of various methods.

9. Should AMS consider more than one disclosure category? (Sec. 293(b)(2)(D))

Context: AMS is considering if it should develop various categories for disclosure and if it should differentiate between those products that a) are bioengineered, b) contain ingredients that are bioengineered, or c) contain ingredients derived from bioengineered crops or animals. Additionally, AMS is considering the creation of a set of disclosures for a category of bioengineered foods for those products that, due to changes in sourcing, include bioengineered ingredients for part of the year, and non-bioengineered ingredients for other parts of the year. AMS is considering the advantages and disadvantages, based on cost, clarity, and other factors, of using a single disclosure category or multiple disclosure categories.

10. What other factors or conditions should AMS consider under which a food is considered a bioengineered food? (Sec. 293(b)(2)(C))

Context: AMS must develop a process to help stakeholders determine whether a food is subject to bioengineered disclosure. AMS anticipates the process would include considering factors such as: whether a food contains a substance that has been modified using recombinant in vitro DNA techniques (Sec. 291(1)(A)), whether the modification could not be obtained through conventional

breeding or found in nature (Sec. 291(1)(B); Question 2 and 3), , and whether a food requires disclosure based on the predominance of ingredients (Sec. 292(c); Question 6), among others. The outcomes of these determination requests might be publically posted on a Web site. The process to implement Sec. 293(b)(2)(C) is not intended to be an investigation or enforcement process (see Questions 26-29); instead, the implementation would likely be framed for manufacturers or developers of bioengineered food or ingredients who have a question on whether their food is subject to disclosure. AMS is considering the factors to be considered, the way to inform the public about the outcome of the requests, and ideas regarding the process to be used to make the determination.

11. Could AMS consider whether a type of food is considered a bioengineered food under the determination process? (Sec. 293(b)(2)(C))

Context: AMS is considering if it could exclude certain food types such as medical food and dietary supplements, among others from requiring disclosure as bioengineered.

12. If a manufacturer chooses to use text to disclose a bioengineered food, what text should AMS require for a text disclosure? (Sec. 293(b)(2)(D))

Context: Currently, some food manufacturers use language compliant with the Consumer Protection Rule 121 from the State of Vermont to identify their food products as bioengineered ("Produced with Genetic Engineering," "Partially Produced with Genetic Engineering," or "May be Produced with Genetic Engineering"). AMS is considering whether to allow manufacturers to continue using these disclosures under the new national bioengineered disclosure standard and if their language is appropriate. Further, AMS is considering what phrases could be used as a text disclosure for bioengineered food that consumers would find informative, truthful, and not misleading.

AMS is also considering whether there should be one standard text disclosure language, or whether manufacturers should be allowed flexibility to choose from more than one acceptable phrase and where the bioengineered food disclosure should be placed on food packages.

13. If a manufacturer chooses to use a symbol to disclose a bioengineered food, what symbol should AMS require for disclosure? (Sec. 293(b)(2)(D))

Context: AMS needs to ensure that the symbol designed for the bioengineered disclosure is not disparaging toward bioengineering. As with the text disclosure, AMS must develop criteria for placement of the symbol to ensure consumers can readily locate the symbol, the symbol is scalable for different sized packages, and the symbol is a meaningful representation of bioengineered foods. AMS is considering what the symbol should look like and guidance on its use.

14. If a manufacturer chooses to use an electronic or digital link to disclose a bioengineered food, what requirements should AMS implement for an electronic or digital link disclosure? (Sec. 293(b)(2)(D))

Context: See Questions 23-25.

15. Should AMS specify in the regulations the type of electronic or digital disclosure manufacturers, e.g. QR code, can use to disclose bioengineered food? What steps should AMS take if an electronic or digital disclosure method becomes obsolete? (Sec. 293(b)(2)(D))

Context: AMS recognizes that disclosure technologies may quickly surpass regulations. AMS is considering what terms will ensure the regulations keep pace with technological changes and how AMS can notify stakeholders about changes in technology as they occur. AMS is also considering

what the most appropriate electronic or digital disclosure technologies are currently and how to deal with obsolete technologies.

16. What kind of text, symbol, or electronic or digital disclosure should AMS require for bioengineered food that is not purchased from a grocery store shelf, such as food for sale in bulk (such as fresh produce in a bin or fresh seafood at a fish counter), in a vending machine, or online? (Sec. 293(b)(2)(D))

Context: In some situations, disclosures may not be easily located when such products are on display for sale. AMS is considering disclosure practices for these and other non-conventional purchasing or packaging scenarios.

17. The Law offers special provisions for disclosure on very small or small packages. How should AMS define very small or small packages? (Sec. 293(b)(2)(E))

Context: AMS is considering if it should mirror FDA's treatment of very small and small packages for nutrition labeling.

a. In 21 CFR 101.9(j)(13)(i)(B), FDA defines small packages as those with less than 12 square inches in total surface area available to bear labeling.

b. FDA also has allowances for packages that have less than 40 square inches of total surface are available to bear labeling.

18. What are the reasonable disclosure options AMS should provide for food contained in very small or small packages? (Sec. 293 (b)(2)(E))

Context: AMS is considering the disclosure standards for very small or small packages. FDA regulates nutrition labeling on very small or small packages differently. For example:

a. Could disclosure requirements for very small packages be met by providing an address or phone number where consumers could obtain the information?

b. Could disclosure requirements for small packages be met by providing abbreviated text disclosure or a Web site address where consumers could obtain disclosure information?

19. How should AMS define small food manufacturers? (Sec. 293(b)(2)(F))

Context: AMS is considering using regulatory language similar to that of other Federal government agencies that already define small businesses. For example:

a. FSIS considers small businesses to be those with 500 or fewer employees and that produces 100,000 pounds or less of annual production of a single product, including single forms of meat such as sausage, bulk, patties, links, consumer product, etc., when determining exemptions from nutrition facts labeling (9 CFR 317.400 (a)(1)(ii)).

b. FDA has several small business definitions with respect to food labeling rules, such as: i) retailers with total annual gross sales of $500,000 or less, 21 CFR 101.9(j)(1) and (18); ii) food and dietary retailers with annual gross sales of foods or dietary supplement products of $50,000 or less, 21 CFR 101.9(j)(1) and 101.36(h)(1); and iii) businesses that employ fewer than 100 full-time workers that produce a product that sells fewer than 100,000 units throughout the United States in a 12-month period, 21 CFR 101.9(j)(18) and 101.36(h)(2).

AMS is considering the advantages or disadvantages of these definitions of small food manufacturers for the bioengineered food disclosure regulations.

20. For disclosures by small food manufacturers, what is the appropriate language indicating that a phone number provides access to additional information? (Sec. 293(b)(2)(F)(ii)(I))

Context: AMS is considering using language in Sec. 293(d)(1)(B) of the Law.

21. The Law excludes restaurants and similar retail food establishments from disclosure requirements. How should AMS define similar retail food establishment to exclude these establishments from the requirements of the regulation? (Sec. 293(b)(2)(G)(i))

Context: AMS is considering how to treat establishments that sell food ready for human consumption, such as institutional food service, delicatessens, or catering businesses. In its regulations for Nutrition Labeling of Standard Menu Items in Restaurants and Similar Retail Food Establishments (21 CFR 101.11), FDA defines restaurant or similar retail food establishment and restaurant-type food

For FSIS, the Federal Meat Inspection Act (FMIA) provides for the mandatory inspection of commercial meat and meat products. The FMIA and implementing regulations do, however, provide exemptions from the continuous inspection provisions for retail operations and restaurants (9 CFR 303.1(d)(2)).

NOP also defines retail food establishment in its regulations (7 CFR 205.2).

AMS is using this information as it considers definitions for restaurants and similar retail establishments, with the understanding that these definitions will be used to determine what types of retail establishments are excluded from the requirements of the Law.

22. How should AMS define very small food manufacturers to exclude these manufacturers from the requirements of the regulation? (Sec. 293(b)(2)(G)(ii))

Context: See Question 19. AMS could use definitions similar to how other Federal agencies define very small businesses, and is considering definitions to distinguish small food manufacturers (Question 19) and very small food manufacturers, with understanding that very small food manufacturers would be excluded from the requirements of the Law.

23. Is there other equivalent on-package language that AMS should consider to accompany an electronic or digital disclosure besides “Scan here for more food information”? (Sec. 293(d)(1)(A))

Context: The word ‘scan’ may or may not be relevant for each type of electronic or digital disclosure in the present or in the future. AMS is considering if it should issue guidance to identify equivalent language as technology changes and what that equivalent language would be.

24. How should AMS ensure that bioengineered food information is located in a consistent and conspicuous manner when consumers use an electronic or digital disclosure? (Sec. 293(d)(2))

Context: AMS is considering requiring the same information associated with the text disclosure as the requirement language for an electronic or digital disclosure (See Question 12). Further, AMS is trying to determine how various disclosure options affect the amount and type of information available to consumers. AMS is also determining if there should be requirements or guidance on what size text would ensure the information is conspicuous to ensure the food information is located in a consistent and conspicuous manner when electronic or digital disclosure is accessed.

25. How should AMS ensure that an electronic or digital disclosure can be easily and effectively scanned or read by a device? (Sec. 293(d)(5))

Context: AMS is aware that electronic or digital disclosures need to be effective, that requirements will vary for each specific type of electronic or digital disclosure, and that the technology for electronic or digital disclosure may change faster than AMS will be able to update its regulations. AMS is determining how to address these issues given the variety of electronic or digital disclosures currently available in the marketplace, along with the specifications for these disclosures to be used effectively in a retail setting.

26. What types of records should AMS require to be maintained to establish compliance with the regulations? (Sec. 293(g)(2))

Context: Each person or entity subject to the mandatory disclosure requirement would be required to maintain and make available to the Secretary records that establish compliance with the Law. Typically, record keeping requirements include those for the records required to be kept, the place of maintenance of such records, the record retention period, and what it means for AMS to have adequate access to and inspection of such records.

Under current FSIS regulations, records must be maintained at a place where business is conducted, except that if business is conducted at multiple places of business, then records may be maintained at a headquarters office. When the business is not in operation, records should be kept in accordance with good commercial practices. For FSIS, records are required to be maintained for a 2-year period. The maintenance time for FDA records vary from 6 months through up to 2 years.

AMS is considering what recordkeeping requirements for persons subject to the Law would be most appropriate.

27. How should AMS obtain information related to potential non-compliance with these regulations? Is there information USDA should request prior to conducting an examination of non-compliance? (Sec. 293(g))

Context: AMS is considering what tools could be used to identify potential non-compliance and enforce compliance with the regulations. AMS is considering the types of information needed to verify compliance with the Law and the most optimal way to obtain such information.

28. What are the rules of practice for a hearing? (Sec. 293(g)(3)(B))

Context: AMS is considering the appropriate procedures for audits and other compliance actions, including opportunities for hearing. AMS is considering this aspect for the rules of practice and other options regarding a prospective hearing and internal adjudication process.

29. How should AMS make public the summary of any examination, audit, or similar activity? (Sec. 293(g)(3)(C))

Context: AMS is considering if the results and findings of any examination, audit, or similar activity should be posted after the notice and opportunity for a hearing described under Sec. 293(g)(3)(B). AMS is also considering how it should make summaries of the examination, audit, or similar activity public.

30. What should the requirements for imports into the United States of products covered by the Law/regulation be? (Sec. 294(a))

Context: AMS is considering how the disclosure requirements should be applied to imported products.

Rules & Regulations:
GMO Labeling & Disclosure [3]

Source URL: http://www.ams.usda.gov/rules-regulations/gmo-questions

Links
[1] http://www.ams.usda.gov/rules-regulations/gmo-questions
[2] mailto:GMOlabeling@ams.usda.gov
[3] http://www.ams.usda.gov/rules-regulations-terms/gmo-labeling-disclosure

III. Paperwork Reduction Act of 1995

This draft guidance refers to previously approved collections of information found in FDA regulations. These collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520). The collections of information have been approved under OMB Control Nos. 0910–0032, 0910–0045, 0910–0117, and 0910–0284.

IV. Electronic Access

Persons with access to the Internet may obtain the draft guidance at either *http://www.fda.gov/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/default.htm* or *http://www.regulations.gov.*

Dated: January 11, 2017.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2017–00839 Filed 1–18–17; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2016–N–0001]

Psychopharmacologic Drugs Advisory Committee; Cancellation

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The meeting of the Psychopharmacologic Drugs Advisory Committee scheduled for February 16, 2017, is cancelled. This meeting was announced in the **Federal Register** of December 27, 2016 (81 FR 95147). The meeting is no longer needed.

FOR FURTHER INFORMATION CONTACT: Kalyani Bhatt, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 31, Rm. 2417, Silver Spring, MD 20993–0002, 301–796–9001, FAX: 301–847–8533, email: *PDAC@fda.hhs.gov,* or FDA Advisory Committee Information Line, 1–800–741–8138 (301–443–0572 in the Washington, DC area), and follow the prompts to the desired center or product area. Please call the Information Line for up-to-date information on this meeting.

Dated: January 11, 2017.

Janice M. Soreth,

Associate Commissioner for Special Medical Programs.

[FR Doc. 2017–01170 Filed 1–18–17; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2016–N–4389]

Genome Editing in New Plant Varieties Used for Foods; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notification; establishment of docket; request for comments.

SUMMARY: The Food and Drug Administration (FDA or we) is announcing the establishment of a docket to receive comments on the use of genome editing techniques to produce new plant varieties that are used for human or animal food. We invite comment on specific questions contained in this document related to foods derived from such genome edited plant varieties. FDA is taking this action to help inform our thinking about foods derived from new plant varieties produced using genome editing techniques.

DATES: Submit either electronic or written comments by April 19, 2017.

ADDRESSES: You may submit comments as follows:

Electronic Submissions

Submit electronic comments in the following way:

- *Federal eRulemaking Portal: https://www.regulations.gov.* Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to *https://www.regulations.gov* will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on *https://www.regulations.gov.*
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see ''Written/Paper Submissions'' and ''Instructions'').

Written/Paper Submissions

Submit written/paper submissions as follows:

- *Mail/Hand delivery/Courier (for written/paper submissions):* Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Division of Dockets Management, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in ''Instructions.''

Instructions: All submissions received must include the Docket No. FDA–2016–N–4389 for ''Genome Editing in New Plant Varieties Used For Foods; Request for Comments.'' Received comments will be placed in the docket and, except for those submitted as ''Confidential Submissions,'' publicly viewable at *https://www.regulations.gov* or at the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

- Confidential Submissions—To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states ''THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.'' We will review this copy, including the claimed confidential information, in our consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on *https://www.regulations.gov.* Submit both copies to the Division of Dockets Management. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as ''confidential.'' Any information marked as ''confidential'' will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: *http://www.fda.gov/regulatoryinformation/dockets/default.htm.*

Docket: For access to the docket to read background documents or the electronic and written/paper comments

received, go to *https://www.regulations.gov* and insert the docket number, found in brackets in the heading of this document, into the ''Search'' box and follow the prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: *Regarding human food issues:* Jason Dietz, Center for Food Safety and Applied Nutrition (HFS–205), Food and Drug Administration, 5001 Campus Dr., College Park, MD 20740, 240–402–2282. *Regarding animal food issues:* Kathleen Jones, Center for Veterinary Medicine (HFV–220), Food and Drug Administration, 7519 Standish Pl., Rockville, MD 20855, 240–402–5938.

SUPPLEMENTARY INFORMATION:

I. Background

Use of Genome Editing Techniques To Produce New Plant Varieties Used for Human or Animal Food

Recently, new technologies have emerged that are intended to alter the genomes of various organisms, including plants. FDA is aware that these technologies make it easier for plant developers to produce new plant varieties with targeted genetic modifications. Using deoxyribonucleic acid (DNA) sequence information from a plant, plant breeders can make targeted changes to a plant's DNA sequence to alter expression of traits in the plant. These new methods include processes using targeted nucleases (clustered regularly interspersed short palindromic repeat associated nucleases, zinc-finger nucleases, meganucleases, and transcription activator-like effector nucleases or targeted oligonucleotides (oligonucleotide-directed mutagenesis) intended to modify a plant's DNA sequence by insertion, deletion, or substitution of nucleotides at a specific site in a plant's genome. The process of producing these targeted DNA sequence alterations is often referred to as ''genome editing.''

In the *National Strategy for Modernizing the Regulatory System for Biotechnology Products* (the *Strategy;* released by the White House Office of Science and Technology Policy on September 16, 2016),[1] FDA noted its intent to clarify its policy for the regulation of products derived from genome editing techniques, including, as appropriate, identifying and/or updating relevant existing guidance documents. Consistent with this commitment in the *Strategy* document, FDA is opening this docket to inform its thinking on foods derived from plants produced using genome editing techniques. FDA also looks forward to receiving the results from the study being conducted by the National Academies of Sciences, Engineering, and Medicine entitled ''*Future Biotechnology Products and Opportunities to Enhance Capabilities of the Biotechnology Regulatory System*'' commissioned under the Update to the Coordinated Framework for Regulation of Biotechnology, available at *http://nas-sites.org/biotech/.* As we consider this issue, we intend for our actions to be guided by the principles for the regulation of biotechnology products articulated in the 2017 Update to the Coordinated Framework (*https://www.whitehouse.gov/sites/default/files/microsites/ostp/2017_coordinated_framework_update.pdf*) and the goals and objectives of the July 2015 EOP memorandum (*https://www.whitehouse.gov/sites/default/files/microsites/ostp/modernizing_the_reg_system_for_biotech_products_memo_final.pdf*).

Producers of foods from plant varieties developed using genome editing techniques, like all food producers, have an obligation under the Federal Food, Drug, and Cosmetic Act (the FD&C Act) to ensure that the foods they offer consumers are safe and in compliance with applicable legal requirements (57 FR 22984 at 22985), available at *http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/Biotechnology/ucm096095.htm.* The FD&C Act gives FDA broad authority to initiate legal action against a food that is adulterated or misbranded within the meaning of the statute (id.). In 1992, FDA issued a statement of policy (57 FR 22984) that discussed scientific issues and provided guidance relevant to the safety assessment of foods derived from new plant varieties derived by traditional methods, tissue culture methods, and recombinant DNA methods (57 FR 22984 at 22991). The guidance provided in the 1992 policy has helped to ensure that developers of new plant varieties make market entry decisions consistent with the FD&C Act. FDA also explained that we have long regarded it to be a prudent practice for producers of foods using new technologies to work cooperatively with us to ensure that the new products are safe and comply with applicable legal requirements (57 FR 22984 at 22991). Over the past 20 years, developers have routinely consulted FDA about the safety and legality of foods from new genetically engineered plant varieties prior to marketing. These consultations have relied on the objective characteristics of foods to consider their safety and legality prior to marketing. This process has worked well and has helped developers ensure that all safety and other legal issues are satisfactorily addressed prior to market entry of foods derived from these new varieties. FDA intends to continue offering consultations for developers of new plant varieties, including those produced using genome editing, in order to help developers ensure that applicable safety and legal questions are resolved prior to market. In addition to the information we anticipate gathering from developers in the course of consultations, we recognize that developers, researchers, and other stakeholders may have valuable factual information and data about foods derived from new plant varieties produced using genome editing, which can help inform FDA's thinking for these specific products. Therefore, we invite comment in this notice.

II. Additional Issues for Consideration and Invitation for Comment: Genome Editing in Plants

To help inform our thinking on foods derived from new plant varieties produced using genome editing, we invite comment on the following questions:

1. In what ways are the food safety risks associated with human and animal foods from genome edited plants the same as or different from those associated with other plant development methods (*e.g.,* hybridization, chemical or radiation-induced mutagenesis and non-targeted genetic modifications using in vitro recombinant DNA technologies)? Please provide data and/or information to support your view.

- To what extent is the scientific knowledge of and experience with current new plant varieties (such as those developed with in vitro recombinant DNA technologies that have gone through the voluntary consultation process) relevant to the safety assessment and regulatory status of food from new plant varieties produced using genome editing? Is there additional scientific knowledge that would be relevant specifically to the safety assessment and regulatory status of new plant varieties produced using genome editing? Please provide data and/or information to support your view.

[1] *https://www.whitehouse.gov/sites/default/files/microsites/ostp/biotech_national_strategy_final.pdf.*

2. Are there categories of genome edited plant varieties for which there are scientific bases to conclude that foods from such categories are unlikely to present food safety risks different from or greater than those for traditional plant breeding? Similarly, are there categories of genome edited plant varieties for which the regulatory status of the food derived from such plant varieties can be said to be no different from that of traditionally-bred plants? If there are such categories, is there a basis upon which to determine that there would be no reason to include them in any voluntary premarket consultation process? If so, please describe the characteristics of such categories (including, for example, information about the types of phenotypes and modifications (insertions, deletions or substitutions) achieved through genome editing) and provide data and/or information for why plant varieties in these categories are unlikely to present food safety risks or regulatory status questions. Regulatory status questions may include, for example, whether food from the new plant variety contains an unapproved food or color additive such that premarket review and approval is required (see sections 409 and 721 of the FD&C Act). As another example, if food from the new plant variety has a different nutritional profile from food from traditionally-bred plants, then certain labeling may be required to disclose a material change in the food.

a. If such categories exist, how do plant developers ensure the safety of foods from new plant varieties in these categories? For example, how are safety assessments of foods from these varieties accomplished, and what data and information are or should be considered in such assessments?

b. If certain categories of genome edited plants do not raise questions of safety or regulatory status, should there nevertheless be a mechanism separate from the voluntary premarket consultation process through which plant developers may voluntarily notify FDA about their intent to market a food derived from a genome edited new plant variety that falls within these categories? If so, what process should plant developers use to notify FDA? What kind of information should be included in such a notification to FDA?

c. Given that genome editing techniques can give rise to a broad range of plant modifications, from simple gene deletions to totally novel genes, and that some such modifications can be achieved through traditional breeding, please discuss the basis upon which to determine that there would or would not be a reason to include, in any voluntary premarket consultation process, foods from genome edited crops with modifications that could have been achieved through traditional breeding.

3. Are there categories of genome edited plant varieties for which there are scientific bases to conclude that foods from these categories are more likely than traditionally-bred plants to present food safety risks? If so, please describe the characteristics of these categories (including, for example, information about the types of phenotypes and modifications (insertions, deletions or substitutions) achieved through genome editing) and provide data and/or information to support why plant varieties in these categories are more likely to present food safety risks than traditionally-bred plants.

4. What steps can we take to help small firms, including those who may be considering using genome editing to produce new plant varieties for use in human or animal food, to engage with FDA about any questions related to food safety or the regulatory status of foods from their new plant varieties? Please provide supporting data and other information to support your comments and responses to this question.

Dated: January 11, 2017.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2017–00840 Filed 1–18–17; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2017–N–0084]

Agency Information Collection Activities; Proposed Collection; Comment Request; Adverse Event Program for Medical Devices (Medical Product Safety Network)

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing an opportunity for public comment on the proposed collection of certain information by the Agency. Under the Paperwork Reduction Act of 1995 (the PRA), Federal Agencies are required to publish notice in the **Federal Register** concerning each proposed collection of information, including each proposed extension of an existing collection of information, and to allow 60 days for public comment in response to the notice. This notice solicits comments on the Adverse Event Program for Medical Devices (Medical Product Safety Network (MedSun)).

DATES: Submit either electronic or written comments on the collection of information by March 20, 2017.

ADDRESSES: You may submit comments as follows:

Electronic Submissions

Submit electronic comments in the following way:

- *Federal eRulemaking Portal: http://www.regulations.gov.* Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to *http://www.regulations.gov* will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on *http://www.regulations.gov.*
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see ''Written/Paper Submissions'' and ''Instructions'').

Written/Paper Submissions

Submit written/paper submissions as follows:

- *Mail/Hand delivery/Courier (for written/paper submissions):* Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Division of Dockets Management, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in ''Instructions.''

Instructions: All submissions received must include the Docket No. FDA–2017–N–0084 for ''Adverse Event Program for Medical Devices (Medical Product Safety Network (MedSun)).'' Received comments will be placed in the docket and, except for those submitted as ''Confidential Submissions,'' publicly viewable at

DEPARTMENT OF AGRICULTURE

Animal and Plant Health Inspection Service

7 CFR Part 340

[Docket No. APHIS–2015–0057]

RIN 0579–AE15

Importation, Interstate Movement, and Environmental Release of Certain Genetically Engineered Organisms

AGENCY: Animal and Plant Health Inspection Service, USDA.

ACTION: Proposed rule.

SUMMARY: APHIS is proposing to revise its regulations regarding the importation, interstate movement, and environmental release of certain genetically engineered organisms in order to update the regulations in response to advances in genetic engineering and understanding of the plant pest and noxious weed risk posed by genetically engineered (GE) organisms, thereby reducing burden for regulated entities whose organisms pose no plant pest or noxious weed risks. This would be the first comprehensive revision of the regulations since they were established in 1987.

DATES: We will consider all comments that we receive on or before May 19, 2017.

ADDRESSES: You may submit comments by either of the following methods:

- *Federal eRulemaking Portal:* Go to *http://www.regulations.gov/#!docketDetail;D=APHIS-2015-0057.*
- *Postal Mail/Commercial Delivery:* Send your comment to Docket No. APHIS–2015–0057, Regulatory Analysis and Development, PPD, APHIS, Station 3A–03.8, 4700 River Road Unit 118, Riverdale, MD 20737–1238.

Supporting documents and any comments we receive on this docket may be viewed at *http://www.regulations.gov/#!docketDetail;D=APHIS-2015-0057* or in our reading room, which is located in room 1141 of the USDA South Building, 14th Street and Independence Avenue SW., Washington, DC. Normal reading room hours are 8 a.m. to 4:30 p.m., Monday through Friday, except holidays. To be sure someone is there to help you, please call (202) 799–7039 before coming.

FOR FURTHER INFORMATION CONTACT: Dr. Sidney Abel, Assistant Deputy Administrator, Biotechnology Regulatory Services, APHIS, 4700 River Road, Unit 147, Riverdale, MD 20737–1238; (301) 851–3896.

SUPPLEMENTARY INFORMATION:

Background

Overview of the Current Regulations

The Animal and Plant Health Inspection Service (APHIS) of the United States Department of Agriculture (USDA) administers regulations in 7 CFR part 340, ''Introduction of Organisms and Products Altered or Produced Through Genetic Engineering Which are Plant Pests or Which There is Reason to Believe are Plant Pests'' (referred to below as the regulations). The current regulations govern the introduction (importation, interstate movement, or release into the environment) of certain genetically engineered (GE) organisms that are considered ''regulated articles.''

Under the current regulations, a GE organism is considered to be a regulated article if the donor organism, recipient organism, vector, or vector agent [1] is a plant pest or if the Administrator has reason to believe the GE organism is a plant pest. A *plant pest* is defined in § 340.1 as ''Any living stage (including active and dormant forms) of insects, mites, nematodes, slugs, snails, protozoa, or other invertebrate animals, bacteria, fungi, other parasitic plants or reproductive parts thereof; viruses; or any organisms similar to or allied with any of the foregoing; or any infectious agents or substances, which can directly or indirectly injure or cause disease or damage in or to any plants or parts thereof, or any processed, manufactured, or other products of plants.'' If a GE organism is a regulated article, in order for the organism to be imported into the United States, to be moved in interstate commerce, or to be released into the environment through a confined release (collectively referred to in the regulations as an ''introduction''), a permit must be issued or the movement or environmental release must occur under a notification procedure. The organism must also be moved in a container that meets certain regulatory requirements, and the container must be marked in accordance with the regulations.

The regulations also provide a process to petition APHIS to determine that a GE organism is nonregulated. A determination of nonregulated status means that the regulated article is no longer subject to the regulations in 7 CFR part 340 and, therefore, there is no longer any authority for APHIS to require a permit or notification for the importation, interstate movement, or environmental release of the regulated article pursuant to 7 CFR part 340.

[1] These terms are defined in § 340.1 of the regulations.

Agency Actions Following Promulgation of the Current Regulations

APHIS first issued these regulations in 1987 under the authority of the Federal Plant Pest Act of 1957 (FPPA) and the Plant Quarantine Act of 1912 (PQA), two acts that were subsumed into the Plant Protection Act (PPA, 7 U.S.C. 7701 *et seq.*) in 2000, along with other provisions. Since 1987, APHIS has amended the regulations six times, in 1988, 1990, 1993, 1994, 1997, and 2005, to institute exemptions from permitting for certain microorganisms and *Arabidopsis,* to institute the notification, petition, and extension procedures referenced above, and to exclude plants engineered to produce industrial compounds from the notification process.

Although, as discussed above, the current regulations have various functions, their primary function to date has been as a means for APHIS to authorize the importation, interstate movement, and introduction of certain GE organisms via the permit and notification procedures referred to above. Permits and notifications are collectively known as ''authorizations.'' To date, APHIS has issued more than 18,000 authorizations for the environmental release of GE organisms in multiple sites, primarily for research and development of improved crop varieties for agriculture. Additionally, APHIS has issued more than 12,000 authorizations for the importation of GE organisms, and nearly 12,000 authorizations for the interstate movement of GE organisms. APHIS has, to date, denied slightly more than 1,500 requests for permits or notifications, many of which were denied because APHIS ultimately decided the requests lacked sufficient information on which to base an Agency decision.

For authorizations under notification, the regulations require the environmental release to meet performance-based standards set forth in the regulations. These include, among other things, that, when the regulated article is a plant and is to be used for environmental release, it must be planted in such a way that it is not inadvertently mixed with non-regulated plant material that is not part of the environmental release. In addition, the environmental release must be conducted such that the regulated article will not persist in the environment, and no offspring can be produced that could persist in the environment. This latter requirement is accomplished through various measures such as required minimum isolation distances from sexually compatible

plants, effective removal or devitalization of viable plant materials, and monitoring of release sites after completion of the tests and removal of any ''volunteer'' plants that are found. APHIS conducts inspections of authorized facilities or environmental release sites to evaluate compliance with the regulations.

The interstate movement, importation, or environmental release of regulated articles may be authorized under permit if developers follow the permit conditions specified by the Administrator to be necessary for each activity to prevent the dissemination and establishment of the GE organism. Such conditions include, but are not limited to, maintenance of the regulated article's identity through labeling, retention of records related to the article's specified use, segregation of the regulated article from other organisms, inspection of a site or facility where regulated articles are to undergo environmental release or will be contained after their interstate movement or importation, and the maintenance and disposal of the regulated article and all packing material, shipping containers, and any other material accompanying the regulated article to prevent the dissemination and establishment of plant pests. If a permit holder has been found out of compliance with any of the permit conditions, the permit may be canceled, and if so, further movement or environmental release of GE organisms under that permit will be prohibited.

In addition to issuing permits and authorizing notifications, APHIS has responded to petitions requesting nonregulated status under these regulations. Under this petition procedure, which is described in § 340.6, a petitioner must present detailed information and scientific data regarding the regulated article indicating why the article should not be regulated. To date, APHIS has granted 124 determinations of nonregulated status, of 159 submitted for APHIS review, and all of these determinations have been for GE plants (more information about these is posted at *https://www.aphis.usda.gov/biotechnology/petitions_table_pending.shtml*). Many of these plants are grown for agricultural production in the United States. APHIS determinations of nonregulated status apply to the GE plant(s) as well as their progeny, meaning the deregulated GE plant can be used in plant breeding programs and in agriculture without further oversight from APHIS.

Basis for the Proposed Rule

Advances in APHIS' Understanding of Genetically Engineered Organisms

While the current regulations have been effective in ensuring the safe importation, interstate movement, and environmental release of GE organisms developed using genetic engineering during the past 29 years, advances in genetic engineering have occurred since they were promulgated and new challenges have emerged. Additionally, APHIS has now accumulated nearly three decades of experience in evaluating GE organisms for plant pest risk. The Agency's evaluations to date have provided evidence that most genetic engineering techniques, even those that use a plant pest as a vector, vector agent, or donor, do not result in a GE organism that presents a plant pest risk. This is discussed at greater length later in this document, under the section titled ''*General Restrictions and Scope (§ 340.0).*'' Additionally, genetic engineering techniques, such as genome editing and synthetic genomics, have been developed that do not employ plant pests as donor organisms, recipient organisms, vectors, or vector agents; such techniques could be used to produce GE organisms with plant pest risks without falling within the scope of *regulated article.*

Need To Evaluate GE Plants for Noxious Weed Risks

Advances in genetic engineering have also made the need to evaluate GE plants for noxious weed risk more pressing. When APHIS issued the current regulations under the authority of the FPPA and PQA, APHIS' authority to regulate noxious weeds was the Federal Noxious Weed Act of 1974 (7 U.S.C. 2801, FNWA). That act defined *noxious weed* as ''Any living stage (including but not limited to, seeds and reproductive parts) of any parasitic or other plant of a kind, or subdivision of a kind, which is of foreign origin, is new to or not widely prevalent in the United States, and can directly or indirectly injure crops, other useful plants, livestock, or poultry or other interests of agriculture, including irrigation, or navigation or the fish or wildlife resources of the United States or the public health.'' Because APHIS' noxious weed authority was limited at the time to plants that were of foreign origin and new to or not widely prevalent in the United States, and most GE plants at the time were modified crops that were developed in the United States and were widely prevalent, in their unmodified form, within the United States, APHIS had no basis that would allow it to evaluate most GE plants for noxious weed risk.

In 1994, Congress amended the FNWA to allow APHIS to issue permits for the interstate movement of noxious weeds. This amendment, however, did not revise the definition of *noxious weed* in the Act.

In 2000, the PPA was issued; In addition to subsuming the FPPA and PQA, it also replaced the FNWA, and provided a new definition of noxious weed: ''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.'' The PPA also provided explicit authority to issue regulations listing noxious weeds that are prohibited or restricted from entering the United States or that are subject to restrictions on interstate movement within the United States, and provided persons with the right to petition APHIS to add or remove noxious weeds from this list.

This revised noxious weed authority led APHIS in 2010 to revise the noxious weed regulations, found in 7 CFR part 360, to reflect the provisions of the PPA. It also led APHIS to revise the manner in which APHIS evaluates plants for noxious weed risk to determine whether to list them in part 360. Under the revised approach that APHIS uses for part 360, the first two considerations in determining whether a plant is a noxious weed are: (1) Identifying what direct injury or damage (physical harm) the plant causes; and (2) identifying what indirect damage the plant may cause to interests of agriculture, irrigation, navigation, the natural resources of the United States, the public health, or the environment. APHIS then evaluates how likely the plant is to become established in areas within the United States in which it was not known to exist, in the absence of Federal regulation; for example, if it can only become established in tropical climates, Federal regulation is not necessary to prevent its establishment in temperate and subarctic climates. APHIS' final consideration is whether placing the plant under Federal regulation will affect the likelihood of introduction or dissemination of the plant. In general, APHIS lists a plant as a Federal noxious weed if APHIS determines the plant to be invasive and to have significant negative impacts, if introduced or disseminated within the United States, and if APHIS determines that Federal regulation could reduce the likelihood of such introduction or

dissemination. If APHIS determines that Federal regulation of a GE plant—pursuant to the authorities granted in the PPA—is incapable of mitigating identified noxious weed risks, the plant would not be regulated.

This approach means that there are certain plants that APHIS has determined to be weeds, but not to be Federal noxious weeds. This distinction between a weed and a Federal noxious weed warrants emphasis. ''Weeds,'' in the broadest sense of the term, could include any plant growing where and/or when it is unwanted; even plants that are desirable in some settings could be considered weeds in others. The plants that APHIS evaluates for inclusion on the Federal noxious weed list are, in general, a particular type of weed: An invasive, usually non-native plant that impacted natural and/or agronomic ecosystems, often with significant negative consequences. Of the problematic weeds APHIS evaluates, only a fraction [2] are determined to be ones for which Federal regulatory controls to prevent their introduction or dissemination are justified; these plant taxa are added to the list of Federal noxious weeds in part 360. Part 360 currently lists 111 aquatic, terrestrial, or parasitic plant taxa as Federal noxious weeds. Many weeds in the United States are not regulated as Federal noxious weeds because they have reached the extent of their ecological range and regulation (*i.e.,* controls on movement) would be costly and provide little if any benefit.

The regulations in part 360, while effective, continue to have a significant restriction that limits their applicability to GE organisms: They are predicated on a determination by APHIS that a taxon is a Federal noxious weed. This determination is easier for plants that have not been genetically engineered, because there are usually many reference points that are available and pertinent to this determination, including international experience with the weed, scientific literature regarding the plant's biology, published studies, and other data.

For GE plants, there is usually a great deal of data and experience with the non-GE organism. In most cases these non-GE organisms are highly domesticated and cultivated widely within the United States, and there is an extensive body of scientific literature regarding their biology. However, when a GE trait is introduced into the plant, there may in certain instances be little data or previous experience available for APHIS to rely on in evaluating the properties of the resulting GE plant. Instead, in order to determine whether the GE plant could function as a noxious weed, APHIS would have to rely on its own independent evaluation of the plant itself, based on information provided by the plant's developers.

Historically, there has not been a significant need for such a noxious weed evaluation of GE plants. Most of the GE plants that APHIS regulated in the past, such as varieties of corn and soybeans modified with common agronomic traits, do not qualify as ''noxious weeds.'' This is because most GE plants to date have been agricultural crops, and most agricultural crops are not biologically weeds prior to modification. Indeed, in order to domesticate a plant for crop production, farmers often had to deliberately eliminate weedy traits, such as seed shattering, thorns, and seed dormancy, from the plant using traditional breeding techniques. Moreover, the phenotypic traits that have historically been introduced into crops through genetic engineering do not confer weediness. Because the plants have not been weeds prior to genetic engineering, and genetic engineering has not introduced weediness, evaluating the plant solely for plant pest risk has not been problematic.

Additionally, the means by which most GE plants to date have been genetically engineered has brought them under APHIS' regulatory authority. To date, most GE plants have been engineered using a plant pest as either the donor or vector of genetic material. Because of this use of a plant pest as a donor, vector agent, or vector, the resulting GE organisms fall within the scope of *regulated articles.*

However, in recent years, there has been an increasing diversity of both agronomic and non-agronomic traits engineered in plants. There has also been an increased use of plants in genetic engineering that, in their unmodified state, are known to possess weedy traits. This is especially true of plants used in the production of biofuel. For example, switchgrass (*Panicum virgatum*), which has long been used in the production of ethanol biofuel, has growth patterns in an unmodified state that are characteristic of a weed, and, recently, has been genetically engineered for increased ethanol production. Accordingly, since such plants are somewhat weedy in their unmodified state, and genetic engineering can, in certain instances, enhance the weediness traits that are already present in a plant in its unmodified state, there is a correspondingly higher risk that such a plant may be genetically engineered into a noxious weed.

Moreover, APHIS' current regulatory structure, which entails evaluating such plants solely for plant pest risk, is not sufficient to properly identify all risks that these plants present to other plants and plant products. Indeed, under the current structure, such plants may entirely escape regulation. While, in the past, GE plants have almost always used a plant pest to vector genetic material, as we mentioned previously in this document, in recent years, GE techniques have arisen that do not use plant pests as donor organisms or vectors. Moreover, if plants are genetically engineered without the use of a plant pest as a vector or donor, this would require APHIS to consider the plant itself to be a plant pest in order to designate it as a regulated article. However, under the PPA's definition of *plant pest,* a plant must be parasitic in order to be considered a plant pest. With limited exceptions, such as mistletoe, dodder, and striga, few plants are known to be parasitic. Thus, APHIS considers it both appropriate and necessary to begin to evaluate GE plants for noxious weed risk.

While APHIS discusses the nature of this proposed evaluation later in this document, it is important to delineate, in broad terms, how the Agency would consider a GE plant to be a noxious weed under the proposed regulations. For purposes of the regulations in part 340, APHIS would begin by evaluating whether the plant, in its unmodified state, has weedy characteristics, that is, a plant biologically capable of causing notable physical injury or damage. This would serve as the baseline against which to evaluate the genotype of the GE plant. In evaluating the GE plant, APHIS would assess the likelihood that the modifications made to the genome of the plant alter its ability to cause notable physical harm or injury.

For GE plants that APHIS determines to be weedy prior to genetic modification, APHIS would endeavor to determine whether the plant's weediness has been enhanced to an extent that it has been engineered into a noxious weed. For GE plants that APHIS determines not to possess weedy traits prior to modification, APHIS would endeavor to determine whether weediness had been introduced into the organism through genetic engineering. Finally, in the event that a Federal noxious weed is genetically engineered (something that has not occurred to date), APHIS would endeavor to determine whether the GE plant is still

[2] Since 2011, 1700 weeds have been evaluated. Only 24 have been deemed to meet the criteria for inclusion on the list of Federal noxious weeds.

a noxious weed and warrants continued regulation.

If APHIS determines that the GE plant is a noxious weed, it would endeavor to gauge the direct or indirect injury or damage it could cause to crops, livestock, poultry, or other interests of agriculture, irrigation, navigation, the natural resources of the United States, the public health, or the environment. APHIS would make the results of this evaluation publicly available and share both the evaluation and the information on which it is based with the Environmental Protection Agency (EPA) and the U.S. Food and Drug Administration (FDA), as warranted.

Maintaining communication with EPA and FDA as we evaluate GE plants for noxious weed risks is consistent with APHIS' role in the Coordinated Federal Framework for Regulation of Biotechnology (Coordinated Framework).[3] Since 1986, the U.S. government has regulated GE organisms consistent with the regulatory framework described in the Coordinated Framework. The Coordinated Framework, published by the Office of Science and Technology Policy, describes the comprehensive Federal regulatory policy for ensuring the safety of biotechnology research and products, and explains how Federal agencies use existing Federal statutes in a manner to ensure public health and environmental safety while maintaining regulatory flexibility to avoid impeding the growth of the biotechnology industry. The Coordinated Framework explains the regulatory roles and authorities for the three major agencies involved in exercising oversight and/or review of GE organisms: APHIS, EPA, and FDA.

The Coordinated Framework provides as a guiding principle that, ''[i]n order to ensure that limited Federal oversight resources are applied where they will accomplish the greatest net beneficial protection of public health and the environment, oversight will be exercised only where the risk posed by the introduction is unreasonable.'' APHIS considers this proposed rule to be entirely consistent with this principle: It will no longer consider GE organisms to be regulated articles solely because of the donor, vector, or vector agent used in genetic engineering, thereby focusing APHIS resources on those GE organisms that may present a plant pest and/or noxious weed risk. However, it is worth noting, as the Coordinated Framework itself does, that a ''mosaic'' of statutes have, to date, provided Agencies with authority to exercise oversight of GE organisms. APHIS acknowledges that the Agencies functioning within the Coordinated Framework oversee different aspects of risk and that, accordingly, other Federal Agencies may continue to exercise oversight over GE crops that APHIS no longer views as plant pests or noxious weeds. To that end, APHIS acknowledges that the proposed revisions to 7 CFR part 340 could have direct or indirect impacts on the manner in which FDA and EPA exercise their roles within the Coordinated Framework. To the extent that the public health impacts are due to changes in APHIS regulatory oversight, APHIS discusses them within this document. Economic impacts, in contrast, are discussed in the economic analysis prepared for this rule, while potential environmental impacts are discussed in the draft programmatic environmental impact statement prepared for the rule.

[3] To view the framework, go to *https://www.aphis.usda.gov/brs/fedregister/coordinated_framework.pdf*.

OIG Audits and 2008 Farm Bill

Audits conducted by USDA's Office of Inspector General (OIG) are another basis for this rule. In 2005, OIG conducted an audit of APHIS' regulatory program for GE organisms. OIG found that the use of performance-based standards in APHIS' notification process allowed for a broad spectrum of methods to meet the standards, particularly regarding how the release would be contained to its test field, but Agency practices did not require responsible persons to provide written protocols detailing the exact methods that person would use to meet the standards. OIG suggested that APHIS revise the regulations to minimize the risk of inadvertent dissemination of regulated articles from a test field. Specific recommendations were to require GPS coordinates of all test field sites; to require scientific protocols or study designs from applicants prior to authorizing a field test of a GE organism; and to seek legislative authority to require applicants to provide proof of financial responsibility in the event of an unauthorized release, as APHIS considered necessary.

OIG also suggested that APHIS develop risk-based criteria for conducting inspections and exercising oversight of field tests for the release of GE organisms, and suggested that APHIS provide more explicit guidance regarding how to terminate a field test and document this termination.

In 2015, OIG issued another audit, urging APHIS to implement the recommendations from the 2005 audit that APHIS had not yet implemented.

Finally, in 2008, The Food, Conservation, and Energy Act of 2008 (Farm Bill) was promulgated. Section 10204 of the Farm Bill requires the Secretary of Agriculture to take action on each issue identified in the APHIS document entitled ''Lessons Learned and Revisions under Consideration for APHIS' Biotechnology Framework,'' [4] and, where appropriate, promulgate regulations. Like the 2005 OIG audit, this APHIS document suggested the need for greater regulatory oversight of field tests of regulated articles.

On October 9, 2008, APHIS published a proposal [4] in the **Federal Register** (73 FR 60007–60048, Docket No. APHIS–2008–0023) to amend the regulations to address advances in genetic engineering, to make explicit our evaluation of GE organisms for noxious weed potential, and to respond to the recommendations of the 2005 OIG audit and the provisions of the Farm Bill.

APHIS sought public comment on the proposal from October 9, 2008, to June 29, 2009. APHIS received more than 88,300 comments during the comment period. These were received in 5,580 submissions that included unique comments, form letters, and signatories to petitions. Many commenters expressed concerns regarding the lack of details surrounding a proposed risk-based system that would determine which organisms would fall under APHIS oversight, as well as concerns about a proposed multi-tiered permit system. Commenters also expressed concern about what they perceived to be a significant expansion of Agency regulatory authority.

Based on the breadth and nature of the comments received, APHIS published a notice in the **Federal Register** on March 4, 2015, withdrawing the proposal to allow APHIS to begin a fresh stakeholder engagement process aimed at exploring a variety of regulatory approaches.

Based on the feedback received following the withdrawal of the proposed rule, as well as to reflect provisions of The Food, Conservation, and Energy Act of 2008 (Farm Bill) and recommendations received from the 2005 and 2015 OIG audits, APHIS is proposing to update its regulations in 7 CFR part 340. APHIS is proposing to evaluate GE organisms for noxious weed potential using a different approach

[4] *https://www.aphis.usda.gov/biotechnology/downloads/supportingdocs/LessonsLearned10-2007.pdf*.

[4] To view the 2008 proposed rule, the subsequent withdrawal, all supporting documents, and comments APHIS received, go to *http://www.regulations.gov/#!docketDetail;D=APHIS-2008-0023*.

from that of the 2008 proposed rule, and proposing a new risk analysis process to determine which organisms would require a permit. As previously proposed in 2008, APHIS is also proposing to eliminate the notification process in favor of permitting. APHIS is committed to working with stakeholders to ensure a smooth transition from the current regulatory process to the proposed regulatory process. We request comment on suggestions for ways to smooth the transition period, avoiding disruption in the market, while continuing to ensure that APHIS meets its statutory requirements.

Regulation of GE Biological Control Agents

Additionally, under the new approach, APHIS would regulate a GE organism that is intended for use as a biological control (biocontrol) agent if APHIS determines that it is a plant pest or noxious weed, with a limited exception. Biocontrol involves the reduction of plant pest and weed populations through the use of natural enemies such as parasitoids, predators, pathogens, antagonists, or competitors to suppress plant pest and weed populations.

The exception would be for GE vertebrate biocontrol agents. Although such organisms could fall within the scope of the PPA's definition of *plant pest,* particularly if they are herbivores, it is long-standing APHIS policy not to regulate vertebrates as plant pests. This policy is discussed later in this document.

Regulation of Plants That Produce Plant-Made Industrials and Pharmaceuticals

APHIS recognizes that certain plants are genetically engineered in order to produce pharmaceutical and industrial compounds, also known as plant-made pharmaceuticals and industrials (PMPIs).

When plants are genetically engineered in such a manner, the plants and the pharmaceutical and/or industrial products they produce may fall within the purview of multiple regulatory Agencies: APHIS, EPA, and/or FDA.

Under the current regulations in 7 CFR part 340, APHIS requires permits, as opposed to Notifications, for the environmental release of all GE plants that meet the definition of a regulated article and produce PMPIs. APHIS exercises oversight of all outdoor plantings of these regulated PMPI-producing plants. This oversight includes establishment of appropriate environmental release conditions, inspections, and monitoring. Products obtained from PMPI-producing plants may be regulated by FDA (authority over pharmaceuticals) or EPA (chemical substances as defined by the Toxic Substances Control Act (TSCA)), depending on their intended use. To date, producers of PMPI-producing plants, or products derived from such plants, have not intended for such plants or plant products to be used for human or animal food. However, if such a plant or plant product is used for human or animal food, the food would be subject to applicable statutory and regulatory requirements under the Federal Food, Drug, and Cosmetic Act.

To date, PMPI-producing GE plants regulated by APHIS have been genetically engineered using a plant pest as the donor, vector, or vector agent, and thus fall under the scope of regulated article in the current regulations in 7 CFR part 340. However, under the provisions of this proposed rule, as discussed at greater length later in this document, a GE plant that is developed using a plant pest as a vector, vector agent, or donor of genetic materials would not necessarily be a regulated organism. Rather, the GE plant would be a regulated organism if it had a plant/trait combination that the Agency has not yet evaluated for plant pest and/or noxious weed risk, if it has received DNA from a taxon that contains plant pests and the DNA from the donor organism is sufficient to produce an infectious entity capable of causing plant disease or encodes a compound known to be pathogenesis-related that is expected to cause plant disease symptoms, or if it was evaluated and found to represent plant pest or noxious weed risks. Additionally, APHIS' evaluations of GE plants for plant pest or noxious weed risk would generally not require data from outdoor plantings.

Even if the plant represents a new plant/trait combination not previously reviewed, there is a likelihood that most, if not all, GE PMPI-producing plants that are currently under APHIS permits could be determined not regulated under the provisions of the proposed regulations after a regulatory status evaluation because they do not represent risks as a plant pest or noxious weed. Thus, such plants could be grown outdoors without the need for permits and without APHIS oversight.

Federal oversight of outdoor plantings of PMPI-producing plants, however, could be necessary to prevent unlawful entry into the food supply of material from such plants. Establishing growing and handling conditions to confine such plants, and inspecting to ensure such conditions are followed, may enable corrective actions before material from the plants is inadvertently released and causes public health or economic impacts. One of the reasons APHIS' oversight of such crops has been an important part of the coordinated framework for oversight of GE plants is that companies are not necessarily required to notify FDA or EPA when the company plants PMPI-producing plants. For example, for PMPI-producing plants whose products fall under FDA authority, FDA has no regulations governing planting of such crops. For crops genetically engineered to produce pharmaceuticals, companies only have to come to FDA when they have reached the point that they are ready to begin clinical trials with the pharmaceutical derived from the plant. This could be years after they first started growing the pharmaceutical-producing plant in the field.

Under TSCA, EPA has requirements for new chemical substances, including industrial compounds produced in genetically engineered plants. However, given existing APHIS oversight, EPA does not currently have an oversight program nor regulations for genetically engineered plants with industrial compounds.

A gap in Federal oversight of PMPI producing-plants could result in the intentional or inadvertent introduction into the human or animal food supply of unevaluated pharmaceutical or industrial PMPI products, even when the principal purpose of the plants is not for human or animal food use. For example, a company could self-determine that the PMPI produced by the plant was generally recognized as safe (GRAS), and therefore conclude it had no legal obligation to keep surplus PMPI-producing plants out of the human or animal food supply, to keep such PMPI-producing plants from spreading pollen to plants grown for human and animal food purposes, or even to notify any Federal agency that they were planting such crops. In addition to potential food safety risks posed by such plants should they enter the food supply, a gap in Federal oversight could generate concerns from the general public regarding the safety and wholesomeness of the human or animal food supply, which could adversely impact agricultural interests.

APHIS has identified several options that have the potential for adequate Federal oversight of outdoor plantings of plants engineered to produce PMPIs. Under one option, a statute would be enacted, or existing statutory authority amended, to grant one or more Federal agencies explicit authority to provide oversight of outdoor plantings of all GE

PMPI-producing plants and to evaluate GE PMPI-producing plants for all possible risks, beyond plant pest and noxious weed risks. For industrial-producing plants subject to EPA's jurisdiction, a second option is for EPA to develop a program to regulate industrial-producing plants and issue regulations if warranted. Under a third option, APHIS would enter into a memorandum of understanding (MOU) and services agreement with the appropriate Federal Agencies to provide personnel and other resources to assist those Agencies in their oversight of outdoor plantings of PMPI-producing GE plants, recognizing that Federal agencies may not have authority to require notification and/or oversight of the outdoor planting of some of these plants. Under a fourth option, those Federal Agencies would supply their own personnel and resources to exercise oversight of outdoor plantings of PMPI-producing GE plants, recognizing that Federal agencies may not have authority to require notification and/or oversight of the outdoor planting of some of these plants.

APHIS recognizes that there are challenges associated with each of these options. For example, the first option would require legislation to be enacted, which is not within the purview of the Executive Branch of the Federal government. Additionally, all options could require Federal Agencies to incur the costs associated with setting up new regulatory programs. The second option would require time for EPA to stand up a genetically engineered industrial-producing plant oversight program for plants subject to EPA jurisdiction. The third option, in turn, would require policies, procedures, and guidance regarding APHIS' interaction with other Federal Agencies to be developed prior to implementation. To that end, it is important to note that APHIS does not prefer any of these options over the other, nor does the Agency consider the options listed above necessarily to be exhaustive. Rather, we put them forward to indicate that the Agency is aware of the implications of this rule with regard to PMPIs, and to request specific public comment regarding the best manner to address this issue.

Plant-Incorporated Protectant Small-Scale Field Testing

Certain plants are genetically engineered to produce plant-incorporated protectants (PIPs), meaning that they produce pesticides. PIPs fall under the regulatory oversight of EPA. However, currently only APHIS exercises regulatory oversight of PIP plantings on 10 acres or less of land. Under the proposed rule, APHIS would only require permits for PIPs planted on 10 acres or less if they present a plant pest or noxious weed risk or have not yet been evaluated by APHIS for such risk. Under the current regulations in 7 CFR part 340, APHIS requires permits or notifications for the environmental release of all GE plants that meet the definition of a regulated article and produce PIPs. APHIS exercises oversight of all outdoor plantings of these regulated PIP-producing plants. This oversight includes establishment of appropriate environmental release conditions, inspections, and monitoring.

To date, PIP-producing GE plants regulated by APHIS have been genetically engineered using a plant pest as the donor, vector, or vector agent, and thus fall under the scope of regulated article in the current regulations in 7 CFR part 340. However, under the provisions of this proposed rule, as discussed at greater length later in this document, a GE plant that is developed using a plant pest as a vector, vector agent, or donor of genetic materials would not necessarily be a regulated organism. Rather, the GE plant would be a regulated organism if it had a plant/trait combination that the Agency has not yet evaluated for plant pest and/or noxious weed risk, or if it has received DNA from a taxon that contains plant pests and the DNA from the donor organism is sufficient to produce an infectious entity capable of causing plant disease or that encodes a compound known to be pathogenesis-related that is expected to cause plant disease symptoms. Additionally, APHIS' evaluations of GE plants for plant pest or noxious weed risk would generally not require data from outdoor plantings.

Even if the plant represents a new plant/trait combination not previously reviewed, there is a likelihood that many GE PIP-producing plants that are currently regulated under APHIS permits or notifications could be determined not regulated under the provisions of the proposed regulations after a regulatory status evaluation because they do not represent risks as a plant pest or noxious weed. Thus, such plants could be grown outdoors without the need for an APHIS permit and without undergoing APHIS oversight.

APHIS understands that this proposal would shift Federal oversight of small-scale (10 acres or less) outdoor plantings of PIPs to EPA. EPA may decide to require experimental use permits (EUP) for all, some, or none of such PIPs, and may conduct inspections of all, some, or none of those PIPs under permit. EPA would need to develop a program to oversee small-scale testing of PIPs and issue regulations if warranted. APHIS is fully committed to coordinating with EPA in this matter in order to give EPA sufficient time to stand up such a program. APHIS understands that an MOU and services agreement may be necessary to provide personnel and other resources to assist EPA during the interim period while EPA implements its own program of oversight for the oversight of outdoor planting of PIPs 10 acres or less.

APHIS recognizes that there are challenges associated with such a transition that would also require EPA to incur the costs associated with setting up a revised regulatory program. Further, such a transition would require policies, procedures, and guidance regarding APHIS' interaction with EPA. APHIS does not consider the approach listed above necessarily to be exhaustive. Rather, APHIS puts it forward to indicate that the Agency is aware of the implications of this rule with regard to small-scale testing of PIPs and to request specific public comment regarding the best manner to address this issue.

Herbicide Resistant GE Crops and Herbicides—Synchronous Decisions With EPA

Certain plants are genetically engineered to make them resistant to herbicides. EPA registers the herbicide products used on herbicide resistant crops, but does not regulate herbicide-resistant crops themselves. APHIS has evaluated and deregulate many GE herbicide resistant plants. To date, the herbicide-resistant GE plants regulated by APHIS have been genetically engineered using a plant pest as the donor, vector, or vector agent, and thus fall under the scope of regulated article in the current regulations in 7 CFR part 340. However, under the provisions of this proposed rule, as discussed at greater length later in this document, a GE plant that is developed using a plant pest as a vector, vector agent, or donor of genetic materials would not necessarily be a regulated organism. Rather, the GE plant would be a regulated organism if it had a plant/trait combination that the Agency has not yet evaluated for plant pest and/or noxious weed risk, or if it has received DNA from a taxon that contains plant pests and the DNA from the donor organism is sufficient to produce an infectious entity capable of causing plant disease or that encodes a compound known to be pathogenesis-related that is expected to cause plant disease symptoms, or has been evaluated by APHIS in accordance with and determined to pose a risk as

a plant pest or noxious weed. Additionally, APHIS' evaluations of GE plants for plant pest or noxious weed risk would generally not require data from outdoor plantings.

Even if the plant represents a new plant/trait combination not previously reviewed, there is a likelihood that many GE herbicide-resistant plants that are currently regulated under APHIS permits or notifications could be determined not regulated under the provisions of the proposed regulations after a regulatory status evaluation because they do not represent risks as a plant pest or noxious weed. Thus, such plants could be grown outdoors without the need for permits and without APHIS oversight.

Commenters to the proposed update to the Coordinated Framework on the Regulation of Biotechnology published on September 22, 2016 (81 FR 65414–65415), expressed the need for coordination between USDA and EPA regarding the timing of deregulation/determination of nonregulated status of herbicide-resistant crops and the registration of herbicides. APHIS recognizes that the asynchronous timing of the deregulation of herbicide-resistant plants and the associated herbicide registration has led to situations where a developer could sell the herbicide-resistant plant/seed without waiting for the associated herbicide registration. In such a situation, farmers may be tempted to illegally use an unregistered herbicide on a crop.

In light of the challenges associated with the asynchronous regulatory actions on the part of APHIS and EPA, APHIS will work with EPA to explore possible solutions to better coordinate the commercial availability of seed for herbicide resistant crops concomitant with the registration of herbicides intended to be used on those crops. Furthermore, APHIS intends to limit the scope of its decisions to be on an individual/specific herbicide resistant crop basis (*e.g.,* glyphosate resistant cotton) so that the EPA and APHIS are making decisions on the same specific herbicide resistant crop/herbicide combinations. This coordination presents challenges because once APHIS determines a GE organism does not represent a risk as a plant pest or noxious weed, APHIS cannot continue to regulate the GE organism or delay announcing the regulatory status determination. When APHIS receives a request for regulatory status determination of an herbicide resistant crop, it is likely to be three or more years before a developer is ready to undergo registration review at EPA. If APHIS determines that the herbicide resistant plant is not a risk as a plant pest or noxious weed, APHIS does not have the authority in the PPA to require permits with regulatory controls for the movement and outdoor planting of that herbicide tolerant plant during those subsequent years. Nor is it within APHIS authority for APHIS to withhold making a regulatory status evaluation decision for several years and requiring permits for field testing during that time. The issue has not been the illegal use of pesticide during the field testing of herbicide resistant crops by developers but instead is the illegal use of pesticide by farmers on seed that has been deregulated by APHIS and is commercially available before the commercial availability of the herbicide designed for those crops. One option to address this coordination would be to enact a new statute or amend an existing statute to make it illegal to sell seeds for herbicide resistant crops before the registrations were completed for use on those crops. Another option might involve a voluntary agreement by seed developers to withhold selling seed of herbicide-resistant crops until EPA registrations are completed for the herbicide products designed for those crops. In cases where APHIS makes a decision deregulating an herbicide-resistant crop or determines under § 340.4 that an herbicide-resistant crop is unlikely to pose a risk as a plant pest and/or noxious weed and will no longer be a regulated organism and no herbicide product has been registered by EPA for use on that herbicide-resistant crop, APHIS would indicate on the APHIS Regulatory Status List Web site and Web sites associated with deregulation decisions that no herbicide product is registered bv EPA for use on this herbicide-resistant crop and it is illegal to use any herbicide product on these crops unless registered by EPA for such use. Additionally, APHIS would include language in deregulation decision letters sent to the developer and **Federal Register** notices associated with § 340.4 final determinations indicating it is illegal to use herbicides on these crops until the herbicide product is registered by EPA for use on the herbicide-resistant crop. This decision letter and all other information regarding APHIS's decisions would also be made available to the public on the APHIS Web site.

APHIS does not consider the approaches listed above necessarily to be exhaustive and recognizes that one of the options listed would require legislation to be enacted, which is not within the purview of the Executive Branch of the Federal government. However, APHIS puts them forward to indicate that the Agency is aware that asynchronous timing of the deregulation of herbicide-resistant plants and the associated herbicide registrations can lead to significant problems, and to request specific public comment regarding the best manner to address this issue.

An Overview of Our Proposed Regulatory Structure

Before discussing the specifics of these proposed revisions, APHIS wishes to provide an overview of how the Agency generally envisions the various sections of the proposed rule interacting, from the perspective of a developer of a GE organism. This overview assumes that the organism falls within the scope of our proposed definition of *GE organism,* and is a regulated organism under proposed § 340.0.

Until such time as the developer wishes to import the organism, move it interstate, or release it into the environment, no action would be required of the developer. However, if the developer believes that it possesses sufficient information to demonstrate that the organism presents no plant pest or noxious weed risk, and wished to release it into the environment, it would have to submit this information to APHIS and request that APHIS conduct an evaluation of such risk. The process for submitting such a request, as well as the possibilities for how APHIS would act on that request, is set forth in proposed § 340.4.

If APHIS evaluates the GE organism in accordance with § 340.4 and determines that it is unlikely to pose a risk as a plant pest and/or noxious weed, it would no longer be a regulated organism and may be imported, moved interstate, or released into the environment without further restriction under the proposed regulations. APHIS would maintain a list of such organisms on a Web site. If new information is obtained which indicates that a previously deregulated GE organism may present a plant pest and/or noxious weed risk, APHIS may reevaluate the GE organism and reconsider its regulatory decision.

If the organism is still a regulated organism following such an evaluation, with one, limited exception (the interstate movement of GE *Arabidopsis thaliana* under certain conditions, which APHIS discusses later in this document) the developer would need to obtain a permit for its importation, interstate movement, or environmental

release. APHIS' proposed permitting process is set forth in § 340.3.

If APHIS issues a permit to the developer for the importation, interstate movement, or release into the environment of the organism, the developer would have to comply with permitting conditions regarding such importation, interstate movement, or release into the environment. The developer would also have to comply with container and shipment requirements that pertain to the movement of regulated organisms. These requirements would also be set forth in § 340.3.

The developer would also have to retain certain records regarding permitted activities. These are set forth in proposed § 340.5. Failure to retain such records, or comply with other regulatory requirements or permitting conditions, could result in enforcement activities. These would also be set forth in § 340.5.

If, in the course of interacting with APHIS, the developer had to provide the Agency with confidential business information (CBI), the developer could denote such CBI in accordance with § 340.6.

Finally, § 340.7 would provide the developer with information regarding APHIS policy related to costs and charges incident to compliance with the regulations.

This is, again, a general overview of the proposed regulations. As such, it does not attempt to capture every nuance of the proposed regulations, nor does it apply to every scenario that may occur under those regulations.

What follows is a more in-depth discussion of the provisions of the rule.

What Constitutes a Genetically Engineered Organism Under the Proposed Regulations

While APHIS discusses most of its proposed definitions later in this document, the Agency considers it necessary, at the outset of discussion of the provisions of the proposed rule, to discuss two of its proposed definitions, for the terms *genetic engineering* and *genetically engineered (GE) organism.* This is because the proposed regulations would not apply to organisms that are created using techniques that APHIS does not consider to constitute *genetic engineering* or that fall outside the scope of *GE organism.* Such organisms, which would not be regulated by APHIS under 7 CFR part 340, would not be expected to come to APHIS for evaluation. However, if such organisms are submitted to APHIS, APHIS would evaluate them for plant pest and/or noxious weed risk and provide guidance on their regulatory status.

By *genetic engineering,* APHIS would mean techniques that use recombinant or synthetic nucleic acids with the intent to create or alter a genome. APHIS considers synthetic nucleic acids to be nucleic acid molecules that are chemically or by other means synthesized or amplified, including those that are chemically or otherwise modified but can base pair with naturally occurring nucleic acid molecules.

APHIS would exclude from the definition of *genetic engineering* traditional breeding techniques (including, but not limited to, marker-assisted breeding, as well as tissue culture and protoplast, cell, or embryo fusion) or chemical or radiation-based mutagenesis. APHIS would do so because the Agency has never considered such techniques to constitute genetic engineering. Accordingly, organisms created through such techniques are currently excluded from regulation under 7 CFR part 340, and would continue to be so excluded.

For the purposes of proposed 7 CFR part 340, APHIS would define *GE organism* as an organism developed using genetic engineering. Thus, if an organism is created using techniques that do not fall within the scope of *genetic engineering,* the organism itself would not fall within the scope of *GE organism.* APHIS would also exclude, from its definition of *GE organism,* certain organisms that are created using techniques that fall within the scope of *genetic engineering,* but that could otherwise have been produced using traditional breeding techniques or chemical or radiation-based mutagenesis. Such organisms are essentially identical, despite the method of creation, because while there may be small genetic differences, those differences are not phenotypically observable and these types of changes occur naturally in all organisms. APHIS would also exclude ''null segregants,'' that is, the progeny of a GE organism where the only genetic modification was the insertion of donor nucleic acid into the recipient's genome, but the donor nucleic acid is not passed to the recipient organism's progeny and the donor nucleic acid has not altered the DNA sequence of the progeny. Specifically, for purposes of the revised regulations, an organism would not be considered a *GE organism* if:

- The genetic modification to the organism is solely a deletion of any size or a single base pair substitution which could otherwise be obtained through the use of chemical- or radiation-based mutagenesis.[5]
- The genetic modification to the organism is solely introducing only naturally occurring nucleic acid sequences from a sexually compatible relative that could otherwise cross with the recipient organism and produce viable progeny through traditional breeding (including, but not limited to, marker-assisted breeding, as well as tissue culture and protoplast, cell, or embryo fusion).
- The organism is a ''null segregant.''

APHIS would exclude the first two types of organisms from the definition of *GE organism* for three reasons. First, as mentioned above, it would do so because the organisms could otherwise have been produced from practices that APHIS is proposing to exclude from the definition of *genetic engineering.* Genetic engineering is often used instead of traditional breeding practices, including chemical or radiation-based mutagenesis, in order to expedite development of an organism with a desired genotype and/or phenotype.

Examples from the realm of GE plants illustrate these practices. Chemical and radiation-based mutagenesis creates thousands of mutations in a single organism, and most of the plant breeders' subsequent efforts involve eliminating unwanted mutations by repeated crosses and selection, each of which can take months to years to complete. Conversely, using genetic engineering, single base pair substitutions, as well as deletions of differing sizes, can be precisely administered very quickly, avoiding this lengthy process of eliminating unwanted mutations. The resulting organism, however, remains identical to one that could otherwise have been developed using chemical or radiation-based mutagenesis.

Similarly, traditional breeding techniques may require many generations of crossing to introduce a naturally occurring trait. For example, it can take decades to introduce a disease-resistant trait to apples through traditional breeding techniques. However, genetic engineering can introduce the same trait in a fraction of the time while maintaining all other cultivar characteristics of the apple.

The second reason for the exclusions is that GE plants as a class, which constitute the vast preponderance of GE organisms to date, pose no greater plant pest or noxious weed risk than their

[5] A single base pair substitution is the most common type of substitution induced by chemical mutagenesis or natural variation and, therefore, most similar to the type of genetic variation that is possible through conventional breeding.

counterparts developed through traditional breeding techniques or chemical or radiation-based mutagenesis. Moreover, it is both impracticable and unnecessary to regulate plants created through traditional breeding techniques or chemical or radiation-based mutagenesis for plant pest or noxious weed risk.

This is not to say that plants with undesirable phenotypes have never been bred through traditional breeding, or chemical or radiation-based mutagenesis never result it mutations that are undesirable. Indeed, as mentioned above, chemical and radiation-based mutagenesis tend to create thousands of mutations in an organism, most of which are undesirable.

However, traditional breeding techniques, in the form of deliberate selection and breeding of those plants with desirable phenotypes, have been used since the advent of sedentary agriculture, and nearly every domesticated crop has, at one point, been subject to traditional breeding techniques. Chemical and radiation-based mutagenesis, in turn, have been used for nearly a century in the development of thousands of commodities, including such commercial commodities as ruby red grapefruit and many commercial varieties of wheat and rice. If APHIS were to regulate organisms developed through traditional breeding techniques or chemical or radiation-based mutagenesis, that would entail the regulation, at least provisionally, of almost every commercially available human or animal food crop. This is impracticable.

Such regulations would also fail to take into consideration the usual purpose of applying traditional breeding techniques or chemical or radiation-based mutagenesis to a plant: To introduce desirable phenotypic traits into the organism or remove phenotypically undesirable traits from the organism. Additionally, it would fail to take into adequate consideration that phenotypic traits that could increase the plant pest or noxious weed risk posed by a plant tend to also adversely impact its vitality, uniformity, or commercial viability. For example, a mutation caused by chemical or radiation-based mutagenesis could render a plant more susceptible to certain viroids or pathogens and able to transfer this increased susceptibility to sexually compatible relatives, and thus increase the plant pest risk associated with the plant. However, it would also directly adversely affect the plant's vitality. For these reasons, farmers and developers have long bred out unwanted phenotypic traits that arise as the result of traditional breeding techniques and/or chemical or radiation-based mutagenesis, and planted and/or commercialized the most phenotypically desirable plant produced using such techniques.

In this regard, it is important to note that genetic engineering is used to create this phenotypically desirable organism, rather than the other products created through traditional breeding techniques, including chemical or radiation-based mutagenesis. In 1987, the Council of the National Academy of Sciences concluded that there is no evidence of a unique risk inherent in the use of recombinant DNA techniques or the movement of genes between unrelated organisms. This means that risks associated with the introduction of recombinant DNA engineered organisms are the same as those associated with non-genetically engineered organisms and organisms modified by other methods and that the assessment of such risks should be based on the nature of the organism and the environment into which it is introduced rather than the methods by which it was produced. Furthermore, this same conclusion is a basis of the Coordinated Framework that regulation should be based on the risks of the organism and not the process used to create it. Accordingly, because the plant pest and noxious weed risk posed by the plant is equivalent, regardless of whether it was created through genetic engineering or traditional breeding (including chemical or radiation-based mutagenesis), and such risk is likely to be low because of the purpose of applying traditional breeding techniques, including chemical or radiation-based mutagenesis to a plant,, APHIS is proposing to exclude GE plants that could have otherwise been developed through traditional breeding techniques, including chemical or radiation-based mutagenesis, from the definition of ''genetically engineered organism'' and hence from regulation under the revised 7 CFR part 340.

This same exclusion would apply to non-plant organisms. Non-plant organisms, which fall under the scope of the regulations as defined in § 340.0, are either plant pests, or organisms which have received genetic material sufficient to produce an infectious entity capable of causing plant disease or that encodes a compound known to be pathogenesis-related that is expected to cause plant disease symptoms. Organisms of the latter type would not qualify for the exclusion, as receipt of genetic material capable of conferring the new properties could not be achieved through traditional breeding techniques, including chemical or radiation-based mutagenesis. However, it can be envisioned that plant pests might be altered in such a way that the exclusion would apply. In these cases, since the resulting plant pest would not be defined as a genetically engineered organism under 7 CFR part 340, they would be regulated, if needed, under APHIS's plant pest regulations in7 CFR part 330. This is appropriate since these organisms are biologically analogous to non-GE plant pests with mutations. It is important to note that, to date, we have not encountered GE organisms of this type and that the GE plant pests that we do have experience with (*e.g.,* pink bollworm expressing marker genes, citrus tristeza virus expressing antimicrobial compounds) would still be regulated under 7 CFR part 340 since this exclusion would not apply. The two APHIS program areas responsible for regulating under 7 CFR parts 330 and 340 are coordinating to ensure that together they are prepared to regulate any type of plant pest as needed.

However, APHIS has prepared a proposed rule that would remove this exception. In its place, all plant pests would require permits issued pursuant to part 330, unless the importation, interstate movement, or environmental release of the organism is explicitly authorized in other APHIS regulations in 7 CFR. Under APHIS' proposed revision to the regulations in part 340, the importation, interstate movement, or environmental release of GE organisms that could have otherwise been developed through traditional breeding techniques or chemical or radiation-based mutagenesis would not be explicitly authorized; rather, such organisms would be exempted from the regulations in part 340, with no reference to the conditions for movement or environmental release of such organisms. Accordingly, GE organisms that could have otherwise been created through traditional breeding techniques, including chemical or irradiation-based mutagenesis, and could pose a potential plant pest risk, would now be subject to 7 CFR part 330.

This touches on several important caveats with regard to the first two proposed exemptions from the definition of *genetically engineered organism.* The first is that the exemptions pertain only to 7 CFR part 340. As noted above, an organism may be exempted from regulation under 7 CFR part 340, and yet still subject to other APHIS regulations. The second

caveat is that the proposed exemptions are based on APHIS' statutory authority under the PPA. They should therefore be taken as a statement of one Agency's regulatory policy, rather than scientific findings regarding all possible risks posed by such organisms. Accordingly, for organisms that APHIS determines to present negligible plant pest or noxious weed risk, FDA and EPA may anticipate more substantial human or animal food adulterant or pesticide risks, and therefore not reduce their oversight of the same organisms.

The third caveat is that APHIS is not claiming that additions, deletions, and substitutions to an organism's genome are inherently risk-free. Indeed, as discussed later in this document, the addition into an organism's genome of a sequence that encodes an infectious entity capable of causing plant disease or encodes a compound known to be pathogenesis-related that is expected to cause plant disease symptoms introduces plant pest risk into that organism, and would be one of APHIS' criteria for regulating the organism under the proposed regulations. Rather, APHIS considers such additions, deletions, or substitutions to present an acceptable plant pest and/or noxious weed risk when they are used to create an organism that could otherwise have been created through traditional breeding techniques and/or chemical or radiation-based mutagenesis; in other words, it is the product, rather than the techniques used to derive the product, that APHIS considers to present an acceptable level of risk. The Agency considers this to be consistent with the principles set forth in the Coordinated Framework.

The third proposed exclusion is for progeny of GE organisms where the only genetic modification was the insertion of donor nucleic acid into the recipient's genome, but the inserted donor nucleic acid is not passed to the recipient organism's progeny and has not altered the DNA sequence of the recipient organism's progeny. Such progeny are often referred to as null segregants. Traits can sometimes be introduced by genetic engineering into breeding lines to simplify breeding without altering the DNA sequence of progeny; the traits can be eliminated with a simple cross and are no longer present in the final organism. An example of use of such techniques to facilitate traditional breeding would be the introduction of certain genes into trees solely to reduce the time to flowering, thereby speeding up a tree-breeding program. In this example, the progeny do not contain the early flowering gene and their DNA sequence has not been altered by the early flowering gene. Because the DNA of the progeny is no different from the DNA of the recipient organism prior to the use of genetic engineering, APHIS does not consider the progeny to be GE organisms for purposes of the proposed regulations.

APHIS requests specific comment on its definition of genetically engineered organism, specifically the appropriateness of the proposed exemptions, and whether commenters can identify any scenarios in which they would exempt from APHIS regulation an organism that presents a plant pest and/or noxious weed risk. APHIS also requests specific comment on whether any other types of organisms should be excluded from the definition of *genetically engineered organism.* Finally, APHIS is interested in whether the terms ''traditional breeding techniques'' and ''chemical or radiation-based mutagenesis'' should be defined, and whether the exclusions themselves are sufficiently delineated.

APHIS wishes to point out that its proposed definition for *genetically engineered organism* is limited to the regulations in 7 CFR part 340 and may not reflect the definition of *genetically engineered organism* that is in use by other Federal Agencies. Differences in definitions are, in part, attributable to the differences in the agencies' statutory and regulatory authorities. Under the Coordinated Framework for the Regulation of Biotechnology, we intend to work cooperatively with other relevant agencies that may also be considering their policies or approaches related to genome editing applications within their jurisdictions.

General Restrictions and Scope (§ 340.0)

Section 340.0 would set forth general restrictions regarding the movement and environmental release of GE organisms, as well as the scope of the revised regulations in part 340.

Paragraph (a) of § 340.0 would provide that no person may move any regulated GE organisms except in accordance with part 340. Movement of regulated organisms that is not in accordance with the part could present a risk of introducing or disseminating plant pests and noxious weeds within the United States.

Paragraph (b) of § 340.0 would specify the types of GE organisms APHIS would consider to be regulated organisms under the revised regulations.

Under our proposed regulations, a GE organism would be a regulated organism if:

- Prior to genetic engineering, the GE organism belonged to any taxon listed in accordance with § 340.2 and met the definition of *plant pest* in § 340.1. (As § 340.2 currently does, proposed § 340.2, which APHIS discusses below, would specify that certain taxa are plant pests or are known to contain plant pests. Section 340.1 would contain definitions of terms used in the proposed regulations.)
- The GE organism has received DNA from any taxon listed in accordance with § 340.2, the DNA from the donor organism is sufficient to produce an infectious entity capable of causing plant disease or encodes a compound known to be pathogenesis-related that is expected to cause plant disease symptoms, and the GE organism has not been evaluated by APHIS for plant pest risk in accordance with § 340.4.
- The GE organism is a plant that has a plant and trait combination that has not been evaluated by APHIS for plant pest and noxious weed risk in accordance with § 340.4 [5]; or
- The GE organism is any of the foregoing that has been evaluated by APHIS in accordance with § 340.4 and determined to pose a risk as a plant pest or noxious weed, or is a GE organism that has otherwise been determined by the Administrator to pose a risk as a plant pest or noxious weed.

The proposed criteria differ from the current criteria in several respects. First, the current criteria consider a GE organism to be a regulated article if the donor, vector, or vector agent is a plant pest. This reflects the concern in 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 into an organism, the resulting GE organism could also be a plant pest.

Based on APHIS' experience evaluating field trial data from thousands of permits that authorize environmental release of regulated organisms, as well as more than 150 petitions for nonregulated status, this has not proven to be the case. Although a plant pest may contribute or vector genes to a GE organism, this has not been shown in APHIS' evaluation of data to cause that GE organism, particularly if it is a plant, to become a plant pest. Indeed, experience has shown that the use of genes from donor organisms which are plant pests, as well as the use of vectors which are from plant pests, has not resulted in plant pest risks of any sort in recipient organisms.

[5] As APHIS discusses below, APHIS would maintain a list of plant and trait combinations that APHIS has evaluated for plant pest and noxious weed risk online if this rule is finalized.

Rather, the most common use of plant pest components in genetic engineering involve either the use of a disarmed version of the plant pathogenic bacterium *Agrobacterium tumefaciens* to vector genes into a plant or use of genetic material from plant pest donors which function as regulatory sequences in the plant. Use of *Agrobacterium tumefaciens* as a vector of genetic material does not leave viable bacteria behind in the recipient organism and does not cause disease. Likewise, regulatory sequences such as the 35S promoter from Cauliflower Mosaic Virus and the nopaline synthase (nos) terminator from *A. tumefaciens* are themselves unable to be expressed and do not confer plant pest traits. Rather, they facilitate the expression of other genes in the GE organism. The use of plant pests in these ways either as donors of 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.

It is conceivable that a donor organism that is a plant pest could result in a GE organism that is itself a plant pest if (1) the DNA sequence that is encoded in the organism is able in itself to be expressed phenotypically or confers plant pest traits, or (2) if the inserted DNA enables the organism to produce pathogenesis-related compounds, that is, compounds that are typically produced by pathogens and involved in producing disease symptoms. Examples of such compounds would include plant degrading enzymes, plant growth regulators, phytotoxins, or compounds that can clog plant vascular systems. In either instance, APHIS would not expect phenotypic expression of plant disease unless large portions of a genome from a plant pest were introduced to a recipient organism, a practice that APHIS considers unlikely for developers to use based on their practices to date.

Likewise, based on APHIS' evaluation of field trial data to date, there is no evidence that the use of plant pests as vectors or vector agents in the production of GE organisms results in a GE organism that is itself a plant pest.

Accordingly, APHIS would regulate GE organisms that have received DNA from a taxon containing a plant pest only if the DNA from the donor organism is sufficient to produce an infectious entity or encodes a pathogenesis-related compound that is expected to cause plant disease symptoms. By ''sufficient to produce an infectious entity,'' APHIS means that the DNA sequence that is encoded in the organism is able in itself to be expressed phenotypically or confers traits that meets the definition of *plant pest.* In such instances, APHIS considers it appropriate and prudent to regulate the GE organism until such time as APHIS evaluates the risk it poses as a plant pest in accordance with proposed § 340.4, and thereafter to regulate it only if APHIS determine it to pose a risk as a plant pest.

Additionally, APHIS would no longer regulate a GE organism solely because its vector or vector agent is a plant pest. APHIS adopted this approach in 1987 because the use of plant pest vectors in recombinant DNA technologies was, at the time, a relatively recent development, and there was a corresponding need to exercise precaution in regulating such use until the plant pest risk associated with the practice was further evaluated. In twenty-nine years of regulating GE organisms because of the use a plant pest as a vector or vector agent, APHIS has no evidence that using genetic material from plant pests as vectors or vector agents for other genetic material results in a GE organism that is itself a plant pest. Accordingly, this proposed rule would change APHIS' approach, and GE organisms that were created using a plant pest as a vector or vector agent would no longer be regulated solely because of the use of such a vector or vector agent. Instead, the organisms would be regulated if they themselves presented a known or unevaluated plant pest risk. This is in keeping with the overarching aim of this proposed rule, which is to regulate the products of genetic engineering, rather than the methods by which those products are developed.

A second difference from the current criteria is that, for reasons discussed previously in this document, APHIS is proposing that APHIS may regulate a GE plant under 7 CFR part 340 if APHIS determines that it is a noxious weed.

Our proposed criteria would also attempt to clarify a current category of regulated articles, GE plants that are regulated because the Administrator has reason to believe they are a plant pest. When the current regulations were issued, APHIS had less experience regulating GE organisms, and there was corresponding uncertainty regarding the degree to which subjecting a plant to genetic engineering, without the use of a plant pest as a donor, vector, or vector agent, would cause the plant to become a plant pest. This category was intended to allow APHIS to consider such plants to be regulated articles, until APHIS had sufficient information to classify it either definitively as a plant pest, or to determine that it presented no plant pest risk. The category was especially useful when a GE plant was developed using novel genetic engineering techniques.

In the 29 years since the current regulations were issued, APHIS' evaluation of petitions for nonregulated status for more than 150 GE plants has provided a basis to help the Agency delineate the plant and trait combinations that cause a GE organism to act as a plant pest from the combinations that pose no plant pest risk.

Accordingly, APHIS now considers there to be two instances in which a GE plant should be a regulated organism. The first instance is when APHIS has reached a determination that the plant and trait combination associated with the GE plant causes it to act as a plant pest or noxious weed. APHIS is making a draft list of such combinations available along with this proposed rule, as well as a list of combinations that APHIS has determined to present no plant pest or noxious weed risk,[6] and APHIS invites public comment on these draft lists. For purposes of this proposed rule, the lists would be maintained at the following Web site: *http://www.aphis.usda.gov/biotechnology/2016-340-proposed-rule.* If the rule is finalized, APHIS would develop a different URL that would contain the lists, as well as all other information regarding this rule, and that would indicate that the rule had been finalized.

The second instance in which APHIS would consider it necessary to regulate a GE plant is when APHIS is presented with a GE plant with a novel plant and trait combination, and has not yet evaluated this plant and trait combination for its plant pest and noxious weed risk.

On a related matter, APHIS acknowledges that a novel GE organism could be developed that does not fall into any of the Agency's other categories of regulated organisms, but that APHIS determines poses a risk as a plant pest or noxious weed. APHIS's last criteria for regulated organisms would allow APHIS to regulate such an organism.

[6] APHIS encourages stakeholders to review these lists and submit specific public comment regarding the listed plant/trait combinations. In particular, while the vast majority of listed plant/trait combinations correspond to specific organisms that have been granted nonregulated status under the current regulations, the list would not be event-specific. This means that if a crop-trait combination has nonregulated status on the list, all specific events that have that crop-trait combination would be nonregulated. Practically speaking, this means that the list would grant nonregulated status to almost all GE corn and soybean that developers have brought to APHIS to date.

Taxa That Are or Contain Plant Pests (§ 340.2)

As stated previously, § 340.2 contains a list of taxa that are considered to be plant pests. That list has not been amended since it was established in 1987.

To improve regulatory flexibility and help ensure the list remains current, APHIS is proposing to remove the list of taxa from § 340.2 and place it on the Internet at *http://www.aphis.usda.gov/biotechnology/2016-340-proposed-rule.* APHIS would advise the public of changes to the list through notices published in the **Federal Register**. These notices would request public comment.

APHIS is not proposing any changes to the listed taxa at this time, however.

Per the definition of ''plant pest'' in the PPA, any organism belonging to any taxon contained within any listed genus or taxon is only considered to be a plant pest if the organism ''can directly or indirectly injure, or cause disease, or damage in any plants or parts thereof, or any processed, manufactured, or other products of plants.'' Thus a particular unlisted species within a listed genus would be deemed a plant pest if the scientific evidence indicates that the organism is a cause of direct or indirect injury, disease, or damage to any plants, plant parts, or products of plants.

Section 7711 of the PPA generally requires permits for the importation or interstate movement of plant pests, but allows the Secretary to create ''exceptions'' to this general permitting requirement when the Secretary deems that a permit is not necessary. That is, these regulated activities are allowed, under certain conditions, without seeking prior authorization via permit. The current APHIS regulations refer to these PPA exceptions as ''exemptions.'' Paragraph (b) of current § 340.2 contains a list of exemptions from the requirement for a permit for the interstate movement of certain GE strains of the microorganisms *Escherichia coli, Saccharomyces cerevisiae,* and *Bacillus subtilis,* and the plant *Arabidopsis thaliana.* One of the conditions for this exemption for the listed microorganisms is that the cloned material does not include the complete infectious genome of a known plant pest.

Because, under § 340.0, APHIS must have determined that a GE microorganism is a plant pest in order for it to be a regulated organism, the GE microorganism strains mentioned above, which APHIS has evaluated and determined to present no plant pest risk, would not be regulated organisms. Thus APHIS would not need to retain specific permitting exemptions for them in § 340.2.

APHIS would also retain the exemption from interstate movement permits for GE organism *A. thaliana* due to its historically exempted status. The exemption would be contained in § 340.3.

APHIS would propose changes to the list through publication of a **Federal Register** notice. The notice would state why APHIS has determined it necessary to add or remove a taxon from the list, and would request public comment.

APHIS would review the comments received and publish its final decision in the **Federal Register**.

The PPA also allows for a person to petition the Secretary to add or remove a plant pest from the regulations. Currently, § 340.5 contains provisions for petitioning the Administrator to amend the list of organisms in § 340.2 by either adding or deleting any genus, species, or subspecies. The list of requirements for petitioning the Administrator include formatting and submission procedures that are currently contained in § 340.5(b).

However, these procedures have not been updated since 1994. While most of the procedures are still accurate, some of them have changed. For example, the requirements do not consider the potential for electronic submission of a petition via email. They also provide an obsolete address for postal submissions. Therefore, APHIS is proposing to remove the specific requirements related to formatting and submission procedures for petitions from the regulations. The procedures would instead be located on the Internet at *http://www.aphis.usda.gov/biotechnology/2016-340-proposed-rule.* APHIS is also proposing to revise the submission procedure to allow petitions to be submitted via email, and to update the address for postal submissions.

These changes would update the submission procedure, and allow for greater flexibility in revising procedures, if, for example, the address for submissions changes in the future.

Please note that, regarding the formatting procedures, APHIS is proposing to retain a requirement that the petition not contain trade secrets or CBI. APHIS often needs CBI for permit applications, particularly for those that request the release of a GE organism into the environment, in order to determine the appropriate permitting conditions, and APHIS may need CBI as part of a regulatory status evaluation in accordance with proposed § 340.4 in order to assess the plant pest and/or noxious weed risk associated with the organism submitted for evaluation. However, a determination that a taxon is or contains a plant pest will be based on a review of scientific literature, and thus, CBI is not germane to our determination.

Following the receipt of a petition to amend the list of organisms in § 340.2, APHIS would publish a notice announcing the availability of the petition in the **Federal Register** and solicit public comment on the petition for 60 days. Following the close of the comment period, the Administrator would announce his or her decision to either approve the petition in whole or in part or deny the petition in a subsequent **Federal Register** notice.

Finally, APHIS is proposing to add an appeals process in the event that the Administrator denies a request to amend the list of taxa that are described in § 340.2. Any person whose petition has been denied would be able to appeal the decision in writing to the Administrator within 30 days after receiving the written notification of the denial. The appeal would have to state all of the facts and reasons upon which the person relies to assert that the petition was wrongfully denied. The Administrator would then grant or deny the appeal, in writing, stating the reasons for the decision as promptly as circumstances allow.

Notification

The current regulations in § 340.3 provide criteria for a notification procedure whereby certain GE plants may be authorized for importation, interstate movement, or environmental release in lieu of a permit. As mentioned previously in this document, rather than using customized requirements, like the permitting conditions used for the permitting procedure, the notification procedure uses performance-based standards that are described in the regulations themselves. The use of the performance-based standards that do not vary from one notification to the next facilitates rapid administrative turnaround on notifications. However, in some ways, the term ''notification'' has been misleading to the public, since sending a notification does not mean automatic authorization by APHIS.

Rather, currently, APHIS reviews notifications to verify that the GE plants meet the eligibility criteria and also evaluates whether the proposed importation, interstate movement, or environmental release can be done in a manner that meets the performance-based standards described in the regulation. In many ways, these APHIS evaluations for notifications are very

similar to those done for permit applications, but the notification procedure relies on applicants agreeing to meet the performance-based standards described in the regulations rather than submitting an application for APHIS review describing the specific measures they will employ for the activity (as is the case for permits). With permits, but not with notifications, APHIS can accept the proposed measures or add to them, and the result is a set of binding customized permit conditions.

Because the notification procedure uses only the performance-based standards in the regulations, it is more administratively streamlined, but the general nature of the standards has made it difficult for APHIS inspectors to determine if a notification holder is in compliance with the standards. This, in turn, can also make enforcement more difficult.

For example, under the current regulations, one of the performance-based standards for notifications relevant to controlled outdoor uses states that: ''The field trial must be conducted such that (1) the regulated article will not persist in the environment, and (2) no offspring can be produced that could persist in the environment.'' Conversely, conditions which APHIS places on permits are more specific, and do not rely as much on subjective determinations by APHIS personnel. A specific permit condition that could be used to address just part of the performance-based standard described above might read: ''After final harvest of the plants covered under this environmental release permit, the site will be monitored every 4 weeks for the emergence of volunteer seedlings for 1 year, and any emerging volunteer plants will be devitalized before they produce pollen. Records of the monitoring and management of volunteers must be maintained by the permit holder and made available to APHIS upon request.''

The use of performance-based standards under the notification procedure has some benefits, such as providing the responsible person with flexibility in how the standard is met, *e.g.,* allowing for appropriate changes in protocols used during the growing season. However, there are some disadvantages in not specifically enumerating the specific measures that constitute compliance with the regulations. The permitting procedure avoids this disadvantage, because the permit conditions specify which actions need to be taken by the responsible person to be in compliance.

Because of this, APHIS has determined that it would have more risk-appropriate oversight, better regulatory enforcement, and improved transparency if all regulated movements are authorized under the permitting procedure. Therefore, APHIS is proposing to remove current notification provisions from the regulations and require that all authorizations for movement be conducted under permit.

As mentioned earlier in this document, the use of the permitting procedure in lieu of notifications is also necessary for APHIS to address some of the recommendations arising from the OIG audits and the provisions of the 2008 Farm Bill. Both the OIG audit and the Farm Bill expressed concern with the use of performance-based standards to regulate field tests of regulated organisms, and recommended that APHIS amend the regulations to exercise greater oversight and enforcement of such field tests and to require more extensive reporting and record retention regarding such tests. These requirements can be added to a permit as permitting conditions, but do not lend themselves to performance-based standards. Some permit conditions, however, are, and have always been, performance-based. APHIS acknowledges that there is more than one way to manage risks and works with the permit applicant to find a mutually acceptable way to do so. In some instances, permit conditions may allow for the flexibility inherent in performance standards, while ensuring a specific requirement is addressed, something not possible with the notification procedure.

In short, if APHIS were to retain the notification procedure, in order to be responsive to the risk factors that may be associated with certain field trials, but not others, to make it easier to assess compliance, and to be responsive to both the OIG audits and the 2008 Farm Bill, APHIS would need to significantly revise the procedure to substantially reduce its reliance on performance-based standards. However, doing so would eliminate the primary benefit of the current notification procedure, which is that it is more administratively streamlined than the permitting procedure. Indeed, a revised procedure which took into consideration all risk factors that may be associated with specific field trials would be both complex and exhaustive. For these reasons, APHIS is proposing to do away with the notification procedure, rather than revise it.

Permits (§ 340.3)

The permitting procedure found in § 340.4 of the current regulations describes types of permits, information required for permit applications, standard permit conditions, and administrative information (*e.g.,* time frames, appeal procedure, etc.). Permits include specific conditions that must be followed by the permit holder. Standard permit conditions, or ''general conditions,'' are listed in the current regulations and APHIS can supplement these with additional conditions as necessary. The current regulations specify the amount of time that APHIS is allotted for review of complete permit applications: 60 days for permits for importation and interstate movement; 120 days for controlled outdoor use. The current regulations also outline requirements for protecting CBI when submitting a permit application.

APHIS proposes to reorganize the regulations to improve the clarity of the permit application and evaluation procedures. In addition, APHIS is proposing changes to the regulations to reflect certain provisions of the 2008 Farm Bill. As APHIS mentioned previously in this document, section 10204 of Title X of the Farm Bill requires the Secretary of Agriculture to take action on each issue identified in the document entitled ''Lessons Learned and Revisions under Consideration for APHIS' Biotechnology Framework'' and, where appropriate, promulgate regulations.

APHIS is proposing certain regulatory changes concerning permit application information requirements, permit conditions, records, and reports that address many of the considerations outlined in the ''Lessons Learned and Revisions under Consideration for APHIS' Biotechnology Framework.'' The permitting procedure would continue to identify and obtain information relevant to evaluating the risks associated with a proposed movement, and determine and document whether, and under what conditions, the activity should be allowed.

Paragraph (a)(1) of proposed § 340.3 would provide that, except as provided in paragraph (a)(2) of the section, APHIS must have evaluated a regulated organism in accordance with § 340.4 before APHIS will issue a permit for its importation, interstate movement, or release into the environment. As mentioned previously in this document, § 340.4 would contain our process for evaluating regulated organisms for plant pest or noxious weed risk. In order to draft permitting conditions that are commensurate with the risk a GE organism poses as a plant pest or noxious weed, it is necessary for APHIS to have evaluated this risk.

If this rule is finalized, when it is fully implemented, APHIS believes that such

evaluations will take a matter of months. Additionally, such evaluations could often result in a determination that the organism poses no risk as a plant pest and/or noxious weed, and thus is not subject to the regulations. For these reasons, APHIS envision that, if this rule is finalized, most developers would wait for APHIS to issue a final determination of regulatory status, in accordance with § 340.4, before submitting a permit application to import the regulated organism, move it interstate, or release it into the environment.

However, APHIS also envisions that there could be instances in which there would be an immediate need to import a regulated organism or move it interstate, even though APHIS has not yet evaluated the risk it poses as a plant pest and/or noxious weed. This could occur when, for example, a developer consolidates research laboratories. To allow for such instances, proposed paragraph (a)(2) of § 340.3 would provide that APHIS may issue a permit pursuant to the section for the importation or interstate movement of a regulated organism that has not been evaluated in accordance with § 340.4. For the purposes of permitting conditions, APHIS would assume that the regulated organism presents a risk as a plant pest and/or noxious weed. If the regulatory status of the organism is evaluated in accordance with § 340.4 during the duration of the permit, APHIS could amend the permit, or, if the organism is determined to pose no risk as a plant pest and/or noxious weed, terminate the permit and communicate this termination to the permittee.

While APHIS could foresee the need for the Agency to issue such permits, APHIS does wish the public to be aware of some of the issues that it has identified with doing so. First, because APHIS would not have evaluated the organism for plant pest and/or noxious weed risk, the Agency would need to presume a high degree of such risk. Accordingly, permitting conditions could be significantly more stringent for such unevaluated organisms than they would be for the same organisms, following evaluation in accordance with § 340.4. Second, unlike organisms evaluated in accordance with § 340.4 prior to permitting, determining nonregulated status for such organisms would not be a category of action that is exempt under APHIS' regulations implementing the National Environmental Policy Act (43 U.S.C. 4321 *et seq.*).

For these reasons, APHIS requests specific public comment regarding whether paragraph (a)(2) of § 340.3 is necessary, or addresses a scenario that is unlikely to occur under the proposed regulations. APHIS also requests public comment regarding whether there are any instances in which there would be an immediate need to issue a permit for the environmental release of a regulated organism that had not yet been evaluated in accordance with § 340.4.

Paragraph (a)(3) of § 340.3 would state that, except as provided in paragraph (c) of § 340.3, a permit must be issued by APHIS for the importation, interstate movement, or release into the environment of all regulated organisms. Paragraph (c) would provide exemptions from interstate permitting requirements for GE *A. thaliana.*

Paragraph (b) of proposed § 340.3 would outline how to submit a permit application. Applicants would have to submit a permit application through a method listed at the Web address contained in the regulations; for purposes of this proposed rule, that address is *http://www.aphis.usda.gov/biotechnology/2016-340-proposed-rule.* That Web site specifies that permit applications must be submitted using APHIS' current electronic permitting system, ePermits, or the paper-based APHIS form 2000.

APHIS is proposing to list the methods for submitting a permit application on the Internet, rather than in the regulations, in order to make it easier to ensure they remain up-to-date. For example, APHIS is currently developing a new electronic permitting system to replace ePermits.

APHIS is also proposing to remove the specific requirements for what should be included in a permit application from the regulations. Instead, they would be listed on an APHIS Web site; for purposes of the proposed rule, that Web site is *http://www.aphis.usda.gov/biotechnology/2016-340-proposed-rule.*

That Web site would first list general application requirements for all permit applications, and then break out additional requirements for specific permit applications. General information requirements that all types of permit applications would have to provide include the name, title, and contact information of the responsible person and agent, if possible; the country and locality where regulated organism was collected, developed, manufactured, reared, cultivated or cultured; the intended activity (*i.e.,* importation, interstate movement, or release into the environment) for the regulated organism; and information regarding how the regulated organism was developed using genetic engineering.

For interstate movement or importation, the permit application would also have to contain the origin and destination of the regulated organism, including information on the addresses and contact details of the sender and recipient, if different from the responsible person; the method of shipment, and means of ensuring the security of the shipment against unauthorized release of the regulated article, to be used in the importation or interstate movement; and the manner in which packaging material, shipping containers, and any other material accompanying the regulated organism will be disposed to prevent the unauthorized release of the regulated article.

Permit applications for release into the environment would have to address the spread, persistence risk, and potential harm of the regulated organism in the environment, including but not limited to a description of how the phenotype of the regulated organism differs from the phenotype of the recipient organism, particularly with respect to potential interactions with, and its likelihood of spread and/or persistence in, the environment; and the location and size of all proposed environmental release sites, including area, geographic coordinates, addresses, land use history of the site and adjacent areas, and name and contact information of a person at each environmental release site, if different from the responsible person. In the even that additional release sites are requested after the issuance of a permit, APHIS would continue the practice of evaluating and amending permits to add new release sites.

The categories of information listed above reflect the categories of information that APHIS considers necessary to be included in all permit applications, as well as additional basic information required for each permit type. APHIS has learned that there are certain areas that are not specified in the current regulations where APHIS routinely needs information from the applicant in order to ensure safety. These areas do not become apparent to applicants until they submit a permit application and APHIS subsequently follows up for additional information in order to assess the activities listed on each permit application for plant pest and/or noxious weed risk. This had led to two *de facto* lists of information requirements for permit applications: The list in the regulations themselves, and the list of information that APHIS routinely requires in order to decide

whether to grant a permit. By maintaining a single list of permit application requirements on the Internet, APHIS can ensure that the list is up-to-date and increase clarity regarding the information that the Agency needs.

The categories of information above also align with the recommendations of the 2005 and 2015 OIG audits, and the provisions of the 2008 Farm Bill. For example, the OIG recommendations have led to provisions that would enable APHIS to require geographic coordinates for the locations of environmental releases.

As mentioned previously, paragraph (c) of § 340.3 would continue to exempt *A. thaliana* from permitting requirements for interstate movement. This is based on that organism's historically exempt status, which has not resulted in the dissemination of plant pests within the United States. In the 1990 proposed rule (55 FR 28637–28638, Docket No. 90–052) in which APHIS proposed to grant such an exemption, the Agency stated its rationale for the exemption: *A. thaliana* has desirable phenotypic traits (including small size, short generation times, high seed set, and ease of growth) that lend themselves to use in scientific studies; *A. thaliana's* small genome size, lack of repetitive DNA, and ease of genetic modification using *Agrobacterium tumefaciens* make it especially useful for molecular genetic analysis; GE *A. thaliana* often needs to be moved interstate between laboratories and other containment facilities as part of scientific studies; and safeguards exist which can adequately mitigate the plant pest risk associated with such movement. This rationale still holds true.

APHIS contemplated a Web-based list of other regulated organisms that have been granted exemptions from permitting requirements for interstate movement. However, APHIS was not able to identify any organisms that would fall within the same category as *A. thaliana:* A taxon for which certain, but not all, types of movement have been evaluated and present no plant pest risk. That said, APHIS requests public comment regarding any taxa that may be similarly situated.

Paragraph (d) of § 340.3 would contain specifics regarding APHIS' review of permit applications. APHIS would review permit applications to determine completeness. If the application is incomplete, APHIS would notify the applicant in writing, and the applicant would be provided an opportunity to revise the application. APHIS is proposing to institute a time limit for receiving additional information in the event that a permit application is determined to be incomplete. If the applicant does not respond to a request for more information within 30 days of receipt of APHIS' request, APHIS would deem the permit application withdrawn and return it to the applicant. This time limit would help preclude the Agency from acting on a permit application when the responsible person no longer desires a permit, and would allow APHIS to focus its review of permit applications, while also affording applicants sufficient time to provide APHIS additional information in the event that they submit incomplete applications.

Once an application is complete, APHIS would review it to determine whether to approve or deny the permit application.

Paragraph (d)(2) of proposed § 340.3 would contain provisions regarding APHIS' assignment of permit conditions. If a permit application is approved, permit conditions would be assigned to each permit commensurate with the risk of the regulated organism and activity. General permit conditions, which APHIS is proposing to list in paragraph (e) of § 340.3, would be assigned to all permits. Additional or expanded permit conditions may also be assigned that are commensurate to the risk that the activities listed on the permit application present of disseminating the regulated organism, or other plant pests or noxious weeds. Examples of such additional requirements include, but are not limited to, specific requirements for reproductive, cultural, spatial, and temporal controls; monitoring; post-termination land use; site security or access restrictions; management practices such as training of personnel involved in the movement; and practices to prevent articles associated with the movement of a regulated organism from becoming contaminated with plant pests or noxious weeds.

Under paragraph (d)(3) of proposed § 340.3, all premises associated with the permit would be subject to inspection before and after permit issuance. APHIS would require that the responsible person provide APHIS inspectors access to inspect any relevant premises, facility, location, storage area, waypoint, materials, equipment, means of conveyance, and other articles related to the movement of organisms regulated under 7 CFR part 340. While this requirement is functionally the same as current inspection requirements, it clarifies what locations and articles may be subject to inspection. Failure to allow the inspection of premises prior to the issuance of a permit would be grounds for the denial of a permit application. Failure to allow an inspection after permit issuance would be grounds for revocation of the permit.

While the current regulations provide for review of permit applications by State regulatory officials, they do not include review by Tribal officials when a permit application is submitted for the importation into, interstate movement through, or release into the environment on Tribal lands of a regulated organism. To correct this oversight, APHIS proposes to state in proposed § 340.3(d)(4) that APHIS will include relevant Tribal officials when it provides copies of permit applications to State regulatory officials.

Under the current regulations, the permitting procedure does not include a formal acknowledgement from the applicant prior to permit issuance that they are aware of and consent to the permit conditions. APHIS considers such an acknowledgement to be necessary, however, in order to verify that applicants are aware of and willing to abide by the conditions. Accordingly, APHIS is proposing to add a requirement in § 340.3(d)(5) that, prior to permit issuance, applicants must agree, in writing and in a manner prescribed by the Administrator, that they are aware of, understand, and will comply with all permit conditions. If an applicant fails to comply with this provision, their application would be denied.

The use of permits and permit conditions gives APHIS and the responsible person an understanding as to what actions must be taken for the permit holder to comply with the regulations. However, in the current regulations, APHIS also provides a list of general permitting conditions that are assigned to all permits in order to provide as much transparency and predictability as possible about permit conditions. To that end, as APHIS mentioned above, APHIS would continue to maintain general conditions that APHIS would assign to all permits issued under the regulations within the regulations themselves. Paragraph (e) of § 340.3 would contain these general conditions. APHIS would require that:

- The regulated organism must be maintained and disposed of in a manner so as to prevent the unauthorized release of the regulated organism.
- The regulated organism must be kept separate from other organisms, except as specifically allowed in the permit.

• The regulated organism must be maintained only in areas and premises specified in the permit.

• The regulated organism's identity must be maintained at all times.

• In the event of an unauthorized release, the regulated organism must undergo the application of remedial measures determined by the Administrator to be necessary to prevent the spread of regulated organism, and the responsible person must contact APHIS as described in the permit within 24 hours of discovery, and subsequently supply a statement of facts in writing no later than 5 business days after discovery.

• The duration that a permit is valid will be listed on the permit itself. During that time, the responsible person must maintain records related to permitted activities of sufficient quality and completeness to demonstrate compliance with all permit conditions and requirements under the proposed regulations. The responsible person must submit reports and notices to APHIS at the times specified in the permit and containing the information specified within the permit. Inspectors must be allowed access, during regular business hours, to the place where the regulated organism is located and to any records relating to the movement of a regulated organism. APHIS access to records includes visual inspection and reproduction (photocopying, digital reproduction, etc.) of all records required to be maintained under the proposed regulations, as requested by APHIS.

• The responsible person must notify APHIS in writing if any permitted activity associated with environmental release will not be conducted.

• Within 28 days after the initiation of any permitted activity related to environmental release, the responsible person must report to APHIS in writing the actual release site coordinates and details of the release, such as how many acres planted, how many organisms released, etc., based on permit conditions, as well as every 28 days thereafter until all releases are completed.

• A person who has been issued a permit must submit to APHIS an environmental release report within 6 months after the termination of any release into the environment. The report must include the APHIS reference number, methods of observation, resulting data, and analysis regarding all deleterious effects on plants, non-target organisms, or the environment.

Most of the conditions listed above are drawn from the conditions found in the current regulations, although APHIS has added some additional details to clarify their meaning. For example, while the existing regulations provide that APHIS inspectors shall be allowed access to records related to the permit, they do not specify what ''access to records'' means. APHIS would clarify that this includes visual inspection and reproduction (photocopying, digital reproduction, etc.) of all records required to be maintained under the proposed regulations. APHIS believes that these additional details will better communicate with applicants what the general permitting conditions are, and will better support administration of the permitting program, including compliance and enforcement.

APHIS is also proposing to specify that regular reporting regarding any activities associated with environmental release of a regulated organism is a general permitting condition. As APHIS mentioned previously in this document, the 2005 and 2015 OIG audits suggested that APHIS exercise greater and more coordinated oversight over field tests of GE organisms. APHIS identified regular reporting regarding actual release site coordinates and details of the release as a key means of exercising such oversight. Adding this reporting requirement as a general permitting condition will ensure that it is communicated to all permittees.

Similarly, to respond to the recommendations of the 2005 and 2015 OIG audits, APHIS would add a requirement for Agency notification if any permitted activity associated with environmental release will not be conducted as a general permitting condition. This general condition would work in tandem with the reporting requirement mentioned above, and help APHIS resolve what could otherwise be considered inconsistencies between the permit conditions and the regular reports.

In addition, while the current general permitting conditions require a field test report following termination of a field test, in recent years, APHIS has required a more extensive report, an environmental release report, through permitting conditions. Our general permitting conditions would reflect this.

APHIS recognizes that these last three general permitting conditions pertain only to activities associated with environmental release of a regulated organism. APHIS also recognizes that it is possible that certain permit applications may not request to release the regulated organism into the environment. However, the permit issued would still contain these general conditions to communicate to the permittee APHIS' general requirements regarding environmental release of regulated organisms. This will ensure that all permitees are aware of those requirements, and is consistent with the recommendations of the OIG audits. The conditions would also prove useful, should the responsible person subsequently request amendments to the permit to authorize environmental release.

While the general permitting conditions that are currently in the regulations contain a condition that pertains to packing material used to transport the regulated organism, APHIS would not retain this as a general permitting condition. This is because it would be covered by shipping requirements that APHIS is proposing to add to the regulations in paragraph (i) of § 340.3.

Under the current regulations, the Administrator may deny or cancel a permit if the applicant has not complied with one or more of the conditions listed on the permit. The Administrator will confirm the reasons for the cancellation or denial in writing within 10 days, and the applicant may appeal the decision in writing within 10 days after receiving the written notification of cancelation or denial. The Administrator may then grant or deny the appeal, in writing, stating the reason for the decision as promptly as circumstances allow.

APHIS is proposing to elaborate on the circumstances under which a permit application may be denied in § 340.3(f)(1). Such circumstances would include when the Administrator concludes that, based on the application or additional information, the actions proposed under the permit may result in the unauthorized release of a regulated organism, or another plant pest or noxious weed; or when the Administrator determines that the responsible person or any agent of the responsible person has failed to comply at any time with any APHIS regulation or the conditions of any permit that has previously been issued in accordance with the regulations.

The first condition pertains to instances in which APHIS cannot reach a conclusion that the risk of dissemination of regulated organisms, plant pests, or noxious weeds will be adequately mitigated if APHIS issued a permit authorizing the actions requested on the permit application. This could occur when, for example, a responsible person does not formally acknowledge that he or she understands the permitting conditions.

The second condition would pertain to instances in which prior actions taken by the applicant or his or her

agents call into question their ability to abide by permitting conditions.

While the current regulations contain procedures for denying a permit application, they do not detail measures for APHIS to revoke a permit. Therefore, APHIS proposes to establish explicit procedures for the revocation of permits. Procedures for revoking a permit would be contained in § 340.3(f)(2). These procedures would state that a permit may be revoked if, following issuance of the permit, the Administrator receives information that would otherwise have provided grounds for APHIS to deny the permit application; if the Administrator determines that actions taken under the permit have resulted in the unauthorized release of a regulated organism, or another plant pest or noxious weed; or if the Administrator determines that the responsible person or any agent of the responsible person has failed to comply at any time with any APHIS regulation or the conditions of any permit issued.

Paragraph (g) would contain the current procedures for appealing the denial of a permit application or revocation of a permit.

APHIS is also proposing to clarify in § 340.3(h) of the regulations the procedure to be used when amendment of existing permit conditions is sought by the responsible person or required by APHIS. Such amendments may include the transfer of the permit to a new responsible person. Currently, the administrative practices that APHIS uses to amend permits have not been explicit in the regulations, and these additions would provide increased transparency and efficiency.

Under the current regulations, notifications for environmental releases and interstate movement are valid for 1 year. Interstate movement permits are only valid for 1 year from the date of issuance, and a new import permit must be obtained for each imported shipment. These permits are referred to as ''limited permits.'' The duration period for a permit issued solely for an environmental release is not currently specified.

APHIS has found that it often takes considerably longer than 1 year for activities authorized under a permit to be completed. For example, with a perennial plant such as a tree, it may take much longer than a year to gather relevant data about the plant for the purpose of determining risk. Additionally, monitoring activities may be required for several years after a field test is complete. In other cases, multiyear research projects may require multiple shipments of regulated organisms for analysis. APHIS is therefore proposing to eliminate the current limits in the regulations on the duration of permits for interstate movement and importation. APHIS also would continue not to specify a duration that an environmental release permit is valid in the regulations. The duration that a permit is valid would instead be specified on the permit itself, as a permitting condition. These changes should give APHIS the flexibility to issue these permits with suitable durations to meet individual circumstances.

Paragraph (i) of § 340.3 would contain shipping requirements for regulated organisms. These would specify that all shipments of regulated organisms must be secure shipments, which APHIS would define as shipments in a container or a means of conveyance of sufficient strength and integrity to withstand leakage of contents, shocks, pressure changes, and other conditions incident to ordinary handling in transportation.

Currently, § 340.8 contains container requirements for regulated organisms. These requirements are very prescriptive. While they do allow responsible persons to request variances from the requirements, this request process, by its nature, results in a case-by-case determination that other types of containers are acceptable for the transportation of regulated organisms. The current regulations also do not clearly reflect the performance-based standard that APHIS used to develop the requirements, which was that the container should be sufficient to prevent dissemination of a regulated organism during movement. Our proposed requirements would maintain this performance-based standard, while making this standard more explicit and the requirements less prescriptive, thus eliminating the need for a request process for variances.

APHIS would, however, retain a provision in the current regulations, currently a footnote to § 340.8, that specifies that all regulated organisms must be shipped in accordance with the regulations in 49 CFR part 178. Those regulations, which are administered by the Department of Transportation (DOT), provide packaging requirements for materials, including regulated organisms that DOT has designated as hazardous materials.

Paragraph (i) of § 340.3 would also specify that the container must be accompanied by a document that includes the names and contact details for the sender and the recipient. It would also specify that, following the completion of the shipment, all packing material, shipping containers, and any other material accompanying the regulated organism would have to be treated or disposed of in such a manner so as to prevent the unauthorized dissemination and establishment of regulated organisms. As mentioned above, this latter requirement is currently a general permitting condition, but could more accurately be described as a shipping requirement.

Finally, paragraph (i) would contain container marking and identity requirements for imported GE organisms. These requirements are currently found in § 340.7.

APHIS has occasionally received inquiries from stakeholders regarding whether a permit could authorize the commercial distribution of a regulated organism. Currently, most developers of GE organisms generally have not commercialized their products until after those products were granted a determination of nonregulated status. However, APHIS does not prohibit commercializing GE organisms that have not been granted a determination of nonregulated status. APHIS currently authorizes a small number of permits for such commercial production.

Under the proposed regulations, there may be some regulated organisms that an entity wishes to commercialize or grow on a large scale, under permit. As currently occurs, APHIS would evaluate these permit applications on a case-by-case basis, to determine whether permitting conditions can be developed that adequately address the risk associated with the permitted actions.

Courtesy Permits

The current regulations in § 340.4(h) provide APHIS with the ability to issue courtesy permits in order to facilitate the movement of GE organisms that are not subject to the regulations in 7 CFR part 340 but whose movement might otherwise be hindered because of their similarity to organisms or articles that are regulated by other APHIS programs. APHIS commits significant resources to the issuance of these courtesy permits for the movement of organisms that are not subject to the provisions of part 340.

Courtesy permits have been part of the regulations since their inception in 1987, and have been useful to inform shippers and State and Federal inspectors not yet fully familiar with requirements for GE organisms that the shipments in question were not regulated. However, their continued use has led to the widespread misunderstanding by some researchers that courtesy permits are actually required for the movement of certain organisms, or that issuance of a courtesy

permit removes the requirement for applicants to follow other applicable regulations, such as the plant pest regulations found in 7 CFR part 330. This confusion partially stems from the similarities between the application form for courtesy permits and those for other types of permits, as well as between the courtesy permit itself and other permits. Therefore, in an effort to alleviate confusion and to better focus and allocate APHIS resources, APHIS is proposing to remove the regulations concerning courtesy permits. It has been common APHIS practice to facilitate the importation of non-regulated articles through the use of letters indicating that no permit is required. APHIS would continue to work with researchers and relevant government regulatory officials to facilitate the transition.

Petitions for Nonregulated Status

The current regulations in § 340.6(a) provide that any person may submit a petition to APHIS seeking a determination that an article should not be regulated under 7 CFR part 340. Paragraphs (b) and (c) of § 340.6 describe the form that a petition for a determination of nonregulated status must take and the information that must be included in the petition. Those organisms which are granted nonregulated status are free of all requirements under 7 CFR part 340. This nonregulated status is different from that of certain organisms that meet the definition of regulated articles, but which are exempt from the requirement for a permit when moved interstate under the specific conditions specified in the regulations.

Published APHIS decisions made under the current regulations have used different ways to express the basic standard ''unlikely to pose a plant pest risk'' in determining whether to grant nonregulated status to a specific GE organism. In its determinations, APHIS has conveyed the basic standard of ''unlikely to pose a plant pest risk'' by concluding that the GE organism ''poses no more of a plant pest risk than its non-GE counterpart,'' ''will not pose a plant pest risk''; or that there is ''no plant pest risk,'' or ''no direct or indirect plant pest effects.'' Regardless of the phrases used in its determination of nonregulated status to date, APHIS has applied the same basic evaluation criteria to each determination to conclude that the GE organism is unlikely to pose a plant pest risk and therefore is not subject to the part 340 regulations. Those criteria include, among other things, conclusions on the potential of the GE organism to create pest or disease problems; the potential for nontarget effects that might affect organisms beneficial to agriculture; changes in agricultural practices that might exacerbate pest or disease problems; and potential of the GE organism to transmit the introduced trait to organisms with which it does not interbreed.

The current regulations also have a provision in § 340.6(e) to extend a determination of nonregulated status to a GE organism based on its similarity to an antecedent organism that has already been granted nonregulated status. This existing ''extension procedure'' was designed for APHIS to take into account the previous evaluation used to grant nonregulated status conducted by APHIS and thereby afford the potential for expedited evaluations of a petition for extension.

These provisions in the current regulations are necessary because of the manner in which *regulated article* is defined in the current regulations. As APHIS mentioned previously, the current regulations consider a GE organism to be a regulated article if the donor organism, recipient organism, vector, or vector agent is a plant pest. However, because of complexities in the science, and the changing nature of the technologies, questions can arise as to whether certain GE organisms meet the definition of *regulated article.* To address these questions, a process is necessary to allow parties to request that APHIS evaluate the GE organism for plant pest properties, and deregulate it if the Agency determines that it is not.

APHIS does not consider it necessary to retain this process in the regulations. As mentioned in our discussion of proposed § 340.0, APHIS would no longer regulate a GE organism solely because the donor organism, recipient organism, vector, or vector agent of the organism is a plant pest. Rather, for the GE organism to be regulated, APHIS would have to determine that it is a plant pest or noxious weed, or the GE organism would have to not yet be evaluated for plant pest and/or noxious weed risk. In other words, APHIS' focal point would change from the method by which the organism is genetically engineered, to the resulting GE organism itself, and the Agency would no longer assume that the use of a plant pest within the development of the GE organism necessarily and in every instance results in a GE organism with plant pest properties.

Based on the manner in which proposed § 340.0 is structured, APHIS envisions four types of inquiries from developers of GE organisms if this rule is finalized. The first would be from developers of organisms that are uncertain of the regulatory status of their organism, but that consider it to either be outside the scope of regulated organisms or similar to an organism that APHIS has already evaluated and assigned nonregulated status. The developers would present what they consider to be the regulatory status of the organism, as well as the information on which the developers rely to support this consideration. In such instances, APHIS would review the information [7] and communicate to the developer whether the regulatory status that they presented to APHIS was accurate. This is substantially similar to the structure of APHIS' current ''Am I regulated?'' program.[8] That being said, because there would be some changes to that program based on the provisions of this proposed rule, if it is finalized APHIS would make guidance available to aid developers in making such inquiries of APHIS.

The second type of inquiries that APHIS would expect to receive would come from developers of GE organisms that belonged to taxa that are listed in accordance with proposed § 340.2 prior to genetic engineering, or that have received DNA from such taxa during genetic engineering. The developers would provide information regarding the development of the GE organism, and would provide information regarding why they do, or not consider, the GE organism to be a plant pest, or to have received DNA sufficient to produce an infectious entity or encode a pathogenesis-related compound that is expected to cause plant disease symptoms. Such requests would have to be made in accordance with proposed § 340.4.

The third category of inquiries would come from developers of GE plants that APHIS has not yet evaluated for plant pest and noxious weed risk and developers of other GE organisms, such as GE insects and other invertebrates,

[7] In evaluating the similarity between two GE plants, APHIS considers whether the mechanisms of action of the introduced traits are functionally equivalent. For example, one mechanism of action for resistance in plants to the herbicide glyphosate relies on an inability of glyphosate molecules to bind and inactivate an enzyme called EPSPS, which is responsible for an essential step in a biochemical pathway for the synthesis of certain amino acids. If glyphosate cannot bind to the EPSPS enzyme, the plant is resistant to the herbicide. APHIS has granted nonregulated status to two very similar types of GE plants which differed in the donor organism for the EPSPS genes: One version of the gene was derived from corn (mEPSPS) and the other from a strain of Agrobacterium (CP4 EPSPS). However, in both cases the added gene encodes an EPSPS protein which does not bind to glyphosate. Accordingly, these two glyphosate resistance traits have mechanisms of action which are functionally equivalent.

[8] See *https://www.aphis.usda.gov/aphis/ourfocus/biotechnology/am-i-regulated.*

that were not plant pests prior to genetic engineering, but that APHIS has not yet evaluated for plant pest risk as GE organisms. These inquiries would request APHIS to evaluate the regulatory status of the GE organism. Such requests would also have to be made in accordance with proposed § 340.4.

The fourth category of inquiries would come from developers of GE organisms that APHIS has determined to be plant pests or noxious weeds, asking for a reevaluation of this determination. Such requests would have to be made in accordance with proposed § 340.4.

Regulatory Status Evaluation (§ 340.4)

Proposed § 340.4 would contain the process by which persons could request an initial evaluation or subsequent reevaluation of the regulatory status of a GE organism. The outcome of a regulatory status evaluation is a determination by the agency that a GE organism is a nonregulated organism or a regulated organism subject to permitting.

Requests for Evaluation or Reevaluation

Paragraph (a) of proposed § 340.4 would state that any person may submit a request to APHIS to have a GE organism's regulatory status evaluated, or to request the reevaluation of the regulatory status of a previously evaluated regulated organism. It would provide that the information that would have to be submitted with a regulatory status request in order for APHIS to evaluate the request is on the Internet, at *http://www.aphis.usda.gov/biotechnology/2016-340-proposed-rule.* Such information would include:

- A description of the recipient organism (including common name; genus, species, and any relevant subspecies information that would distinguish the organism; and, for microorganisms, the strain).
- The genotype of the GE organism, including a detailed description of the differences in genotype between the organism subject to the request and the non-GE organism. If genetic material is inserted into the genome, the method of transformation would also have to be described and the following provided for each gene:
  - For gene sequences, the name of the sequence, donor organism(s) or source, function of sequence, nucleic acid sequence, and publicly available sequence identification. If the genes have been modified, the nature of the modification and its purpose would have to be stated, and the request would have to identify and highlight the modifications by submitting an alignment of the modified sequence with the unmodified sequence. If the gene is not naturally occurring, the request would have to state whether the sequence is based on that of a specific organism, and, if so, identify the organism and gene it was based on.
  - For regulatory sequences, the function of each regulatory sequence as it relates to the gene sequence and the source of each regulatory sequence. Promoters (sites on DNA to which the enzyme RNA polymerase can bind to initiate the transcription of DNA into RNA) would have to be identified as constitutive, inducible, developmental, or tissue-specific. If inducible, the inducer would have to be described. If developmental, stages at which the promoter is active would have to be described. If tissue-specific, the tissues in which the promoter is active would have to be described. The strength of the promoter would also have to be described. Finally, for microorganisms, descriptions of mobile genetic elements would also have to be included.
  - If the genome is edited, the following would also have to be provided: The nature of the edit(s) and the gene(s) and function(s) being modified, as well as what pathways are expected to be affected; for multiple substituted base pairs, the number of substitutions; the original unmodified sequence aligned to the modified sequence; and if the edits were created using genetic material which was integrated into the chromosome, but later eliminated through segregation, techniques used to confirm absence of the genetic material.
- A detailed description of the intended phenotype(s) of the GE organism. This would include the purpose of the new phenotype and the mechanisms of action by which the intended phenotype is conferred; any new enzymes, other gene products, or expected changes in metabolism; if applicable, the protein accession number and the enzyme commission number; and the known and potential differences from the non-GE organism that would substantiate that the GE organism is unlikely to pose a greater noxious weed risk or plant pest risk than the non-GE organism from which it was derived.
- For plants, any information that exists on known or likely changes that may affect any of the following would have to be provided: Weediness and plant pest characteristics of the plant; competitive growth ability; reproduction, spread, and persistence; stress tolerance, including a consideration of abiotic stresses such as cold and drought tolerance and biotic stresses such as herbivory (consumption of the plant) or diseases; and any other weediness or plant pest characteristics identified of the plant or other plants with which the plant can interbreed.
- For non-plant, non-vertebrate organisms, any information that exists on known or likely differences to herbivory or virulence must be provided, including: Any observed or anticipated changes due to the genetic modification that might affect the ability of the organism to cause direct or indirect damage to plants; a description of any changes to known factors of pathogenesis and virulence factors such as polysaccharides (complex sugars consisting of multiple sugar molecules bonded together) and suppressors (genes that suppress expression of another gene); a consideration of changes that might affect geographic distributions, host range, means of dissemination, horizontal gene transfer, reproductive cycle, and persistence; and a description of any characteristics introduced to mitigate harm to plants.
- Any experimental data (including field tests) and publications that the developer believes might be relevant to APHIS's evaluation of the potential of the organism to affect plant health.

APHIS considers the categories of information specified above, which are drawn from our current conditions in § 340.7 for a petition for nonregulated status for a GE organism, to be sufficient for APHIS to evaluate a GE organism and determine its appropriate regulatory status. That being said, the Agency solicits public comment on the adequacy of the requested information in proposed 340.4(a), and whether additional or alternate requirements would be more appropriate. Specifically, APHIS is interested in instances that commenters identify in which the above information may be insufficient to reach a regulatory status determination.

To that end, APHIS wishes to highlight some of the differences between the above information and the information currently required for a request for deregulated status of a GE organism. With regard to the genotype of the GE organism, APHIS would add specific information requirements for gene sequences, regulatory sequences, and genome editing. The current regulations require the petitioner to supply a detailed description of the genotype of the GE organism, but do not specify that a description of the gene sequences, regulatory sequences, or genome editing of the organism is required. Operationally, however, APHIS considers this information to be necessary in order for the petitioner to provide a detailed description of the

genotype, and the revised regulations would reflect this operational need.

APHIS would also remove a current regulatory requirement that requires the petition to state the country and locality of the donor organism from which a GE organism has received genetic material in order for APHIS to evaluate the genotype of the GE organism. In the Agency's experience, this information has not proven germane to evaluating the genome of the GE organism, since it does not provide information regarding the modified genome of the GE organism, or the manner in which the genome was modified.

With regard to the phenotype of the GE organism, the proposed requirements would contain additional details that APHIS considers necessary in order to evaluate the plant pest risk of microorganisms, insects, and other invertebrates. For GE plants, it would also include information that APHIS needs in order to prepare a plant pest risk assessment and/or a weed risk assessment (WRA, discussed below).

APHIS is also proposing a significant departure from the current requirements for a petition for nonregulated status. The current requirements specify that a petition must contain field reports for all trials conducted under permit or notification procedures involving the regulated organism, including the APHIS reference number, methods of observation, resulting data, and analysis regarding all deleterious effects on plants, non-target organisms, or the environment.

Currently, most of the field data submitted by the regulated community to meet this requirement is to demonstrate that there have not been unintended deleterious effects on plants, non-target organisms, or the environment. To date, APHIS has authorized more than 100,000 field trials—a single permit or notification may authorize multiple trials—and APHIS has not received a report of plant pest or noxious weed issues. In addition, APHIS has not received any information in such reports indicating a potential for such effects. Rather, the Agency has discovered that the expressed phenotype of the regulated organism provides the most reliable indicator of the organism's potential for deleterious effects on plants and plant products. These observations are expected and are consistent with findings of several reports of the National Research Council.[9]

Accordingly, APHIS considers information from field tests to not always be necessary for a determination of regulatory status under the proposed regulations. The approach APHIS is proposing focuses primarily on evaluating the genetics and expressed phenotype of the regulated organism, and the likelihood that, based on these genetics and phenotype, the organism will act as a plant pest or noxious weed if it is released into the environment for the uses intended by the developer.

This would not preclude a developer from providing field test information, if he or she considered such information to be pertinent to our determination. For example, if a developer wished APHIS to reevaluate the status of an organism that the Agency had previously considered to be a regulated organism, field test information demonstrating a lack of adverse effects on plants and plant products could be provided in support of that request. Nor would the provisions preclude APHIS from asking for field test information if APHIS considers it necessary in order to conclude review of a particular request. However, field test information would not be a generally applicable requirement for requests for a regulatory status determination, and would only be requested rarely, and on an as-needed basis.

Risk Analyses in Response to Regulatory Status Requests

Paragraph (b) would outline the actions the Administrator would take in response to a regulatory status request. If the request is complete, APHIS would conduct a risk analysis that includes an evidence-based, standardized approach to analyzing plant pest and/or noxious weed risks associated with the GE organism.

Currently, when APHIS receives petitions for a determination of regulated status, APHIS conducts risk assessments. Historically, these assessments have focused on evaluating the plant pest risk of the regulated organism. However, in recent years, they have also included a weediness assessment when the regulated organism is a plant.

The proposed regulations would specify that, if APHIS receives a request to evaluate the regulatory status of a GE organism, the Agency will conduct a risk analysis. The analysis would include, *inter alia,* preparation of a plant pest risk assessment, a weed risk assessment, or both. APHIS would prepare a plant pest risk assessment (PPRA) for organisms that have received DNA from any taxon listed in accordance with § 340.2, if the DNA from the donor organisms are sufficient to produce an infectious entity capable of causing plant disease or encodes a compound known to be pathogenesis-related that is expected to cause plant disease symptoms, and the GE organisms have not been evaluated by APHIS for plant pest risk. APHIS would also prepare a PPRA for GE plants, if our initial evaluation of the plant suggested the plant may be parasitic. APHIS would also prepare a weed risk assessment for GE plants with plant and trait combinations that have not been evaluated by APHIS for noxious weed risk.

APHIS' weed risk analysis processes would use a WRA, a system developed by APHIS for the purpose of assessing noxious weed risk of GE organisms. Regulatory status decisions for GE plants would be informed based on a risk manager's evaluation and interpretation of the results of the WRA (and, for parasitic plants or plants that may otherwise fall within the scope of the definition of *plant pest,* the PPRA).

While this risk analysis would be informed by APHIS's risk assessment experience with GE organisms as well as APHIS' evaluation of other existing weed risk assessment systems that have been developed, since the WRA system for GE organisms is new, APHIS is making the WRA system publicly available along with this proposed rule. (To view the WRA system or guidance, go to *http://www.aphis.usda.gov/biotechnology/2016-340-proposed-rule.*) Similarly, APHIS will make WRAs available to the public to help make our risk management decisions as transparent as possible.

Notices of Request for Evaluation of Regulatory Status

Proposed paragraph (c) of § 340.4 would discuss our proposed notice-based process for making evaluation of regulatory status available to the public. APHIS would make both the request and the risk analysis available for public review through a notice published in the **Federal Register**. This first notice would request public comment, and would propose a regulatory status for the organism.

If no comments are received on the notice, or if the comments do not affect the conclusions of the risk analysis or the proposed regulatory status of the organism, APHIS would provide notification through the APHIS stakeholder registry at the end of the

[9] See: NRC (National Research Council). 1989. *Field Testing Genetically Modified Organisms: Framework for Decisions.* Washington, DC: National Academy Press. NRC (National Research Council). 2004. *Safety of Genetically Engineered Foods: Approaches to Assessing Unintended Health Effects.* Washington, DC: National Academies Press.

comment period announcing that the proposed regulatory status has been finalized.[10] APHIS would subsequently publish a notice in the **Federal Register** compiling these determinations.

Alternatively, if comments lead APHIS to change its proposed regulatory status for the organism, APHIS would publish a subsequent notice in the **Federal Register** characterizing these comments and announcing the new regulatory status.

Record Retention, Compliance and Enforcement (§ 340.5)

APHIS is proposing to consolidate all record retention, compliance, and enforcement requirements in 7 CFR part 340 into a new § 340.5. APHIS is also proposing to strengthen its program in order to manage compliance with the regulations more efficiently, to augment the approaches used to prevent or remediate potential risks to plant health, and to utilize appropriate enforcement strategies. These proposed regulatory changes also reflect certain provisions of the 2008 Farm Bill and align with recommendations of the 2005 and 2015 OIG audits.

The current regulations require a responsible person to retain records demonstrating that a regulated organism that was imported or moved interstate under a permit arrived at its intended destination for 1 year, but contain no record retention requirements related to environmental release of a regulated organism. While APHIS has frequently added this record retention requirement as a permitting condition, both the 2005 and 2015 OIG audits and the 2008 Farm Bill recommended that the Agency specify the retention requirement in the regulations themselves, recommendations that are corroborated by the Agency's own experience administering the regulations.

Therefore, APHIS is proposing that all records related to permit conditions, other than those demonstrating that a regulated organism that was imported or moved interstate arrived at its intended destination, be retained for 10 years following permit expiration, unless APHIS determines otherwise and documents an alternate record retention requirement. In the event of an investigation into the possible unauthorized environmental release of a regulated organism, or the escape of a regulated organism from a containment facility, a thorough record of activities taken under the permit is necessary in order for APHIS to assess compliance and determine whether enforcement actions are needed. When APHIS has investigated unauthorized environmental releases of regulated organisms, this has necessitated obtaining information from field trials that were conducted up to 10 years prior to the investigation. In instances in which the information was not available, this adversely impacted APHIS' ability to do an expeditious and thorough investigation.

APHIS is also proposing to extend the record retention requirement that demonstrates that a regulated organism that was imported or moved interstate arrived at its intended destination from 1 to 2 years. In the event that there is uncertainty regarding whether the organism arrived at this location, it may take APHIS more than 1 year to investigate the matter.

APHIS recognizes that, in practice, our proposed requirements would require most records associated with permitted activities to be retained 10 years, and that this is a significant duration to retain potentially a substantial number of records pertaining to permit activities. However, retaining documents for less than 10 years may impede an investigation into compliance infractions. The Agency requests specific public comment regarding whether a shorter duration is warranted for certain records pertaining to permit activities, and which activities these may be. Additionally, APHIS requests comment on any alternate means that stakeholders may identify for the Agency to obtain necessary information from developers in the event of an investigation of possible regulatory noncompliance.

The section would specify that responsible persons and their agents must comply with the proposed regulations. Failure to comply with the regulations could result in denial of a permit application or revocation of a permit, application of remedial measures in accordance with the PPA, or criminal or civil penalties.

Pursuant to sections 7714 and 7731 of the PPA, APHIS may seize, quarantine, treat, destroy, or apply other remedial measures to a regulated organism that is new to or not widely prevalent or distributed in the United States to prevent dissemination of the organism. APHIS typically issues an Emergency Action Notifications or administrative order to the owner of the regulated organism to specify these remedial measures.

If APHIS intends to issue a civil penalty, the Agency may enter into a stipulation prior to issuance of the complaint seeking the penalty. Our regulations regarding such stipulations are located in 7 CFR 380.10.

Finally, the section would specify that for purposes of enforcing the regulations, the act, omission, or failure of any agent for a responsible person may be deemed also to be the act, omission, or failure of the responsible person.

Container and Shipment Requirements

The regulations in current §§ 340.7 and 340.8 provide detailed requirements for identifying and securely shipping containers of regulated organisms. In the revised regulations, general requirements which apply to all shipments of regulated GE organisms under permit are now listed in paragraph (i) of § 340.3. Additional supplemental conditions will be used when permits are issued to add additional case-specific measures. These supplemental conditions will be listed on the permit itself as permitting conditions. This will allow the agency to take into account the widely varying types and quantities of GE organisms to be shipped and apply highly effective yet reasonable requirements.

Confidential Business Information (§ 340.6)

As mentioned previously, in the current regulations, there are guidelines for denoting information on a permit application or petition for a determination of nonregulated status as CBI in different sections of the regulations. In the proposed regulations, APHIS is proposing to consolidate these guidelines for protecting CBI into a single section, § 340.6. This change would support the overall administration of the program by consolidating all relevant requirements, thereby making it easier for interested persons to find the necessary information.

Definitions (§ 340.1)

APHIS proposes to retain certain definitions currently found in § 340.1 of the regulations, to change other definitions, to add some new definitions, and to remove definitions that no longer appear in the regulations.

APHIS is proposing to retain the following definitions from the current regulations, without change: *Administrator, Animal and Plant Health Inspection Service (APHIS), donor organism, environment, organism,* and *person.*

APHIS is proposing to change the definitions of the following terms from those in the current regulations:

As mentioned in the discussion of proposed § 340.0, the definition of

[10] To subscribe to the APHIS stakeholder registry, go to: *https://public.govdelivery.com/accounts/USDAAPHIS/subscriber/new.*

genetic engineering would read ''techniques that use recombinant or synthetic nucleic acids with the intent to create or alter a genome,'' and would exclude traditional breeding techniques (including, but not limited to, marker-assisted breeding and chemical or radiation-based mutagenesis, as well as tissue culture and protoplast, cell, or embryo fusion).

This would replace the current definition for *genetic engineering,* ''the genetic modification of organisms by recombinant DNA techniques.'' The regulations do not define ''recombinant DNA techniques,'' and the current definition could also be construed to exclude the use of synthetic DNA, in-vivo DNA manipulation, and genome editing. For the purposes of this rule, APHIS is proposing to consider genome editing to be within the definition of genetic engineering. APHIS is also proposing to exclude from the definition of *genetically engineered organism* GE organisms that could have been produced via traditional breeding.

APHIS recognizes that APHIS had previously suggested this proposed rule would use the term *biotechnology,* and would define *biotechnology* in the following manner: ''Laboratory-based techniques to create omodify a genome that result in a viable organism with intended altered phenotypes. Such techniques include, but are not limited to, deleting specific segments of the genome, adding segments to the genome, directed altering of the genome, creating additional genomes, or direct injection and cell fusion beyond the taxonomic family that overcomes natural physiological reproductive or recombination barriers. For the purposes of this part, this definition does not include traditional breeding, marker-assisted breeding, or chemical or radiation-based mutagenesis.''

A number of stakeholders understood the limitations associated with the current definition of *genetic engineering,* but questioned the need to abandon the term in favor of *biotechnology.* They pointed to APHIS' long-standing use of the term *genetic engineering,* and suggested that using a different term could lead to confusion among the regulated community and the general public.

Additionally, several stakeholders expressed concern regarding the proposed definition of *biotechnology.* They pointed out to APHIS that traditional breeding often uses laboratory-based techniques, such as tissue culture and embryo rescue, to create or modify a genome, and radiation-based mutagenesis, which modifies genomes, is often conducted in a laboratory. The stakeholders expressed concern that the definition could result in widespread confusion regarding which laboratory-based techniques to alter a genome are considered *biotechnology,* and which are not.

Stakeholders also encouraged APHIS to refer to other existing definitions used to define *biotechnology* or *genetic engineering.*

When APHIS issued the current regulations, the Agency relied on guidelines developed by the National Institutes of Health (NIH) regarding research on genetically engineered organisms to craft the definition of ''genetic engineering.'' Accordingly, in light of the above stakeholder concerns, APHIS revisited NIH guidelines regarding research on genetically engineered organisms. The definition that APHIS is proposing is based on NIH's ''Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules,'' which are located at *http://osp.od.nih.gov/sites/default/files/NIH_Guidelines.html.* The section in that document that pertains to research on plants that have been genetically engineered contextually delineates the scope of genetic engineering in a manner that is equivalent to the scope of our proposed definition.

Inspector would read ''Any individual authorized by the Administrator of APHIS or the Commissioner of Customs and Border Protection, Department of Homeland Security, to enforce the regulations in this part.'' The current definition predates the establishment of the Department of Homeland Security, as well as the transfer of certain inspection responsibilities for imported organisms from APHIS to Customs and Border Protection.

Interstate would read ''From one State into or through any other State or within the District of Columbia, Guam, the Virgin Islands of the United States, or any other territory or possession of the United States.'' This change aligns the definition of ''interstate'' in 7 CFR part 340 with the definition of ''interstate'' used in the PPA.

Move (moving, movement) would read ''To carry, enter, import, mail, ship, or transport; aid, abet, cause, or induce the carrying, entering, importing, mailing, shipping, or transporting; to offer to carry, enter, import, mail, ship, or transport; to receive to carry, enter, import, mail, ship, or transport; to release into the environment; or to allow any of the above activities to occur.'' This change aligns the definition of ''move'' in 7 CFR part 340 with the definition of ''move'' used in the PPA.

Permit would read ''A written authorization, including by electronic methods, by the Administrator to move regulated organisms and associated articles under conditions prescribed by the Administrator.''

This change generally aligns the definition of *permit* in 7 CFR part 340 with the definition of *permit* used in the PPA. However, whereas the definition in the PPA mentions that a permit may authorize the movement of plants, plant products, and biological control organisms, plant pests, noxious weeds, and associated articles, APHIS would specify that, for purposes of part 340, it pertains to the movement of regulated organisms and associated articles. This reflects the scope of the proposed regulations.

Additionally, while the PPA allows for the issuance of oral permits, APHIS would not. Oral permits do not provide adequate documentation that a responsible person was aware of and understood permitting conditions at the time the permit was issued.

Plant would read ''Any plant (including any plant part) for or capable of propagation, including a tree, a tissue culture, a plantlet culture, pollen, a shrub, a vine, a cutting, a graft, a scion, a bud, a bulb, a root, and a seed.'' This change is necessary because the current definition of ''plant'' used in the regulations precedes the issuance of the PPA, and is broader than that definition. Therefore, APHIS would align the definition with the definition in the PPA itself.

A result of this alignment would be that APHIS would no longer consider ''cellular components,'' such as ribosomes, to be plants. However, cellular components are not capable of propagating to cause plant pest or noxious weed risks.

Plant pest would read ''Any living stage of a protozoan, invertebrate nonhuman animal, parasitic plant, bacterium, fungus, virus or viroid, infectious agent or other pathogen, or any article similar to or allied with any of the foregoing, that can directly or indirectly injure, cause damage to, or cause disease in any plant or plant product.'' This change generally aligns the definition of ''plant pest'' in 7 CFR part 340 with the definition of ''plant pest'' used in the PPA. However, while the PPA gives APHIS authority to regulate any nonhuman animal as a plant pest, it is longstanding APHIS policy not to regulate vertebrate animals as plant pests. In the absence of such a policy, all herbivores and omnivores could be considered plant pests, and thus subject to regulation, an untenable position considering that this would

require APHIS to consider livestock, such as cows, sheep, and horses, to be plant pests.

Recipient organism would read ''The organism whose nucleic acid sequence will be altered through the use of genetic engineering.'' In contrast, the current definition is ''the organism which receives genetic material from a donor organism.'' This change from the former definition is intended to be more precise by distinguishing an organism with altered traits from the same organism prior to transformation.

Release into the environment (environmental release) would read ''The use of a regulated organism outside the physical constraints found in a contained facility.'' This change from the former definition removes the word ''regulated article,'' which APHIS proposes to replace with the term ''regulated organism.'' This change also removes examples of types of physical confinement and replaces them with the term ''contained facility,'' which APHIS is proposing to define. Finally, this term clarifies that ''release into the environment'' and ''environmental release'' are synonymous terms. This can be inferred from the current regulations, but is not explicit.

Responsible person would read ''The person who has control and will maintain control over a regulated organism during its movement and ensures compliance with all conditions contained in any applicable permit or exemption as well as other requirements in this part. A responsible person must be at least 18 years of age and be a legal resident of the United States.'' This change would remove the term ''introduction'' and replace it with the term ''movement.'' It would also replace the term ''GE organism'' with the term ''regulated organism'' and add that a responsible person must be ''at least 18 years of age.'' The first two changes are to reflect the nomenclature used in the proposed regulations. The last change is necessary because individuals under the age of 18 are minors.

State would read ''Any of the several States of the United States, the Commonwealth of the Northern Mariana Islands, the Commonwealth of Puerto Rico, the District of Columbia, the Virgin Islands of the United States, or other Territories or possessions of the United States.'' This change aligns the definition of ''State'' in 7 CFR part 340 with the definition of ''State'' used in the PPA.

State or Tribal regulatory official would read ''State or Tribal official with responsibilities for plant health, or any other duly designated State or Tribal official, in the State or on the Tribal lands where the importation, interstate movement, or environmental release is to take place.'' The change from the former definition is the acknowledgement of Tribal authority on Tribal lands.

APHIS proposes to add definitions of the following new terms:

Agent would read ''A person who is authorized to act on behalf of the responsible person to maintain control over a regulated organism during its movement and ensures compliance with all conditions contained in any applicable permit or exemption as well as other requirements in this part. Agents may be, but are not limited to, brokers, farmers, researchers, or site cooperators. An agent must be at least 18 years of age and be a legal resident of the United States.'' This proposed definition would clarify that the responsible person may designate another person to act on the responsible person's behalf, but that the person so designated must comply with all relevant regulations regarding the regulated organism as the responsible person must.

Contained facility would read ''A structure for the storage and/or propagation of living organisms designed with physical barriers capable of preventing the escape of the enclosed organisms. Examples could include laboratories, growth chambers, fermenters, and containment greenhouses.'' While the current regulations use the term contained facility, the term is not currently defined. APHIS proposes to add this definition to clarify what constitutes a *contained facility.*

Genetically engineered organism (GE organism) would read ''an organism developed using genetic engineering.'' As mentioned previously in this document, for purposes of the proposed regulations, APHIS would not consider an organism to be a *GE organism* if any of the following are the case:

- The genetic modification to the organism is solely a deletion of any size or a single base pair substitution which could otherwise be obtained through the use of chemical- or radiation-based mutagenesis.[4]
- The genetic modification to the organism is solely introducing only naturally occurring nucleic acid sequences from a sexually compatible relative that could otherwise cross with the recipient organism and produce viable progeny through traditional breeding (including, but not limited to, marker-assisted breeding, as well as tissue culture and protoplast, cell, or embryo fusion).
- The organism is a ''null segregant,'' that is, the progeny of a GE organism where the only genetic modification was the insertion of donor nucleic acid into the recipient's genome, but the donor nucleic acid is not passed to the recipient organism's progeny and the donor nucleic acid has not altered the DNA sequence of the progeny.

Import (importation) would read ''To move into, or the act of movement into, the territorial limits of the United States.'' This is the definition of ''import'' used in the PPA.

Interstate movement would read ''To move interstate.'' This proposed definition is necessary to clarify the specific type of movement referenced in the regulations.

Noxious weed would read ''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.'' This is the definition for noxious weed found in the PPA.

Nucleic acid would read ''A chain or chains of nucleotides found in either DNA or RNA.'' This proposed definition is necessary to clarify the term ''nucleic acid,'' which is used in reference to ''regulatory sequences'' in the proposed regulations.

Plant pest risk assessment would read ''An assessment evaluating whether a GE organism is a plant pest.''

Plant product would read ''Any flower, fruit, vegetable, root, bulb, seed, or other plant part that is not included in the definition of plant or any manufactured or processed plant or plant part.'' This is the definition of *plant products* found in the PPA. This definition is more precise than the current definition of ''product'' in 7 CFR part 340, which this definition would replace. For example, the current definition of product includes ''anything made by or from, or derived from an organism, living or dead.'' APHIS does not plan to regulate dead organisms as APHIS has found that they do not present plant pest or noxious weed risks.

Regulated organism would read ''Any GE organism that is regulated pursuant to § 340.0.'' This definition would replace the definition of ''regulated article.''

Regulatory sequence would read ''A segment of nucleic acid molecule that is capable of increasing or decreasing the expression of specific genes within an organism.'' This definition would be added to ensure clarity within the

requirements for regulatory status determinations.

Secure shipment would read ''Shipment in a container or a means of conveyance of sufficient strength and integrity to withstand leakage of contents, shocks, pressure changes, and other conditions incident to ordinary handling in transportation.'' This definition would be used to clarify the container requirements in the proposed rule.

Unauthorized release would read: ''The intentional or accidental release of a regulated organism in a manner not authorized by a permit issued pursuant to 7 CFR part 340.''

Weed risk assessment would read ''An assessment of the characteristics of a plant as these relate to weediness.''

APHIS proposes to remove the following definitions from the regulations: *Antecedent organism, courtesy permit, expression vector, introduce or introduction, product, regulated article, Secretary, stably integrated, vector or vector agent,* and *well-characterized and contains only non-coding regulatory regions.*

These definitions would be removed because the terms would no longer be used in the regulations. APHIS proposes to eliminate the term *regulated article* partly because the use of the term ''article'' in current part 340 is not consistent with usage in the PPA, which uses the term article to mean ''any material or tangible object that could harbor plant pests or noxious weeds''—that is, things like packing materials, shipping containers, commodities, etc.—and not a plant pest or noxious weed itself. Under the current regulation, however, *regulated article* refers exclusively to certain genetically engineered organisms. For this reasons, the term ''regulated article'' in the current regulations is both inconsistent with the terminology of the PPA and difficult for the public to comprehend.

APHIS also proposes to remove the definition for *introduction.* APHIS currently uses the term in part 340 to denote certain kinds of activities that fall within the scope of the regulations, namely importation, interstate movement, and release into the environment. The PPA, however, does not specifically define the term *introduction.* Therefore, to avoid confusion, instead of using the term *introduction* to define the different types of regulated activities, APHIS will instead refer to these activities in the regulations as *movement* in accordance with the definition of *move* in the PPA. Additionally, as APHIS mentioned above, the regulations will specify and define the types of movements to which the regulations would apply, namely, importation, interstate movement, and release into the environment.

Finally, based on the terms that APHIS is proposing to add or remove from the regulations, as well as the revised scope of the regulations, the Agency would revise the title of part 340 to ''Movement of organisms altered or produced through genetic engineering that are noxious weeds or plant pests or that there is reason to believe are noxious weeds or plant pests.''

Costs and Charges (§ 340.7)

Section 340.7 would contain APHIS' policy regarding costs and charges for the services of inspector, which are found in the current regulations in § 340.9. Currently, the section provides that the services of an inspector during regularly assigned hours of duty are provided free of charge, but that APHIS will not be responsible for any other costs or charges incident to inspections or compliance, apart from the services of this inspector. These provisions would be unchanged.

Technical Evaluations

APHIS recognizes that many aspects of our proposed rule hinge on a determination by APHIS regarding the plant pest or noxious weed risk posed by a particular GE organism or class of GE organisms. Often, APHIS will be able to make a determination of plant pest or noxious weed risk based on our collective experience regulating genetic engineering and review of relevant scientific literature.

However, as genetic engineering evolves and new genetic engineering techniques are developed, APHIS may lack technical expertise to fully evaluate certain GE organisms or classes of GE organisms. This is particularly likely when new or emerging genetic engineering techniques are applied to recipient organisms that have not previously been subject to genetic engineering.

In such instances, APHIS may rely on researchers or other Federal, State, Tribal, or industry experts to provide information to help APHIS determines the organism's appropriate regulatory status. APHIS may solicit such information through a variety of means, including, but not limited to, working groups, workshops, peer review of documents (particularly risk analyses), or webinars.

National Environmental Policy Act

To provide the public with documentation of APHIS' review and analysis of any potential environmental impacts associated with the revision of our regulations regarding the movement of certain GE organisms, APHIS has prepared a programmatic environmental impact statement (PEIS). The PEIS was prepared in accordance with: (1) The National Environmental Policy Act of 1969 (NEPA), as amended (42 U.S.C. 4321 *et seq.*), (2) regulations of the Council on Environmental Quality for implementing the procedural provisions of NEPA (40 CFR parts 1500–1508), (3) USDA regulations implementing NEPA (7 CFR part 1b), and (4) APHIS' NEPA Implementing Procedures (7 CFR part 372).

The PEIS may be viewed on the *Regulations.gov* Web site or in our reading room. (A link to *Regulations.gov* and information on the location and hours of the reading room are provided under the heading **ADDRESSES** at the beginning of this proposed rule.) In addition, copies may be obtained by calling or writing to the individual listed under **FOR FURTHER INFORMATION CONTACT**.

Executive Orders 12866 and 13563 and Regulatory Flexibility Act

This proposed rule has been determined to be significant for the purposes of Executive Order 12866 and, therefore, has been reviewed by the Office of Management and Budget.

We have prepared an economic analysis for this rule. The economic analysis provides a cost-benefit analysis, as required by Executive Orders 12866 and 13563, which direct agencies to assess all costs and benefits of available regulatory alternatives and, if regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety effects, and equity). Executive Order 13563 emphasizes the importance of quantifying both costs and benefits, of reducing costs, of harmonizing rules, and of promoting flexibility. The economic analysis also provides an initial regulatory flexibility analysis that examines the potential economic effects of this rule on small entities, as required by the Regulatory Flexibility Act. The economic analysis is summarized below. Copies of the full analysis are available by contacting the person listed under **FOR FURTHER INFORMATION CONTACT** or on the *Regulations.gov* Web site (see **ADDRESSES** above for instructions for accessing *Regulations.gov*).

Under the PPA, the Secretary of Agriculture is authorized to regulate the movement into and through the United States of plants, plant products, and other articles to prevent the

introduction or dissemination of plant pests and noxious weeds. As one part of its implementation of the PPA, APHIS regulates the safe introduction (environmental release, interstate movement, and importation) of certain GE organisms that might be plant pests (7 CFR part 340). APHIS is proposing to revise its regulation of GE organisms to respond to emerging trends in genetic engineering, to more efficiently use APHIS resources, and eliminate unnecessary regulatory burdens.

The proposed revisions to 7 CFR part 340 would create the framework for more focused, risk-based regulation of the GE organisms that pose plant pest and/or noxious weed risks. They would establish a regulatory status evaluation process in which risk analysis would be used to assess whether permitting of a GE organism is necessary. Shipping standards would be less prescriptive and more generally applicable, and the rule would provide for the issuance of multi-year permits. The proposed rule would also exclude certain techniques from the definition of genetic engineering and certain organisms from the definition of genetically engineered organism. These changes would improve the efficiency and clarity of the regulations.

The proposed amendments would benefit developers, producers, and consumers of certain GE organisms, public and private research entities, and the Agency. There would not be any decrease in the level of protection provided against plant pest risks, and protection against noxious weed risks would be enhanced. The risk-based process used to determine regulatory status under the proposed rule would provide cost savings to the biotech industry and allow for reallocation of APHIS resources to Biotechnology Regulatory Services (BRS) priorities.

Based on APHIS' experience evaluating field trial data from thousands of permits that authorize environmental release of regulated organisms, as well as more than 150 petitions for non-regulated status, APHIS has determined that most of the GE organisms evaluated by the Agency do not merit regulatory oversight under the PPA. There would be both direct and indirect economic benefits of not subjecting the majority of these organisms to permitting requirements.

Direct regulatory costs to biotech developers would be reduced for those organisms that are not considered to pose plant pest and/or noxious weed risk. Savings to the regulated community would result from a reduced need to collect field data, fewer reporting requirements, and lower management costs. Petitions for non-regulated status—and the petition costs incurred—would be eliminated. There would be some new costs borne by regulated entities under the proposed rule including rule familiarization and recordkeeping. Recordkeeping cost tabulations are based on the information collection categories from the paperwork burden section of the rule, and are estimated to total about $275,000. About 1,100 distinct entities have applied for permits or notifications under part 340. APHIS estimates that those entities would spend about 8 hours becoming familiar with the provisions of this rule at a total cost of about $576,000.

Cost savings for these entities are expected to more than offset the new costs. APHIS estimated the cost savings for two regulatory oversight scenarios, based on a study of the costs encountered by private biotech developers as they pursue regulatory authorization of their innovations. When only USDA has regulatory oversight, compliance cost savings under the proposed rule could range from $1.5 million to $5.4 million for the development of a given GE trait. If EPA and/or FDA also have an oversight role in the development of a given GE trait, compliance cost savings could range from $485,000 to $861,000. Since 1992, between 2 and 14 petitions have been processed (granted non-regulated status or the petition withdrawn) in a given year, with an average of just under 6.

Because the rule is expected to spur innovation, we expect the number of new organisms developed annually to increase over time. In the following discussion, the annual number of new GE organisms developed under the proposed rule would range from 6 (the current annual average), to 12 (twice this average), with 10 as an intermediate number. For GE organisms that would have solely required USDA oversight, the annual savings could range from $8.8 million to $32.4 million (6 new organisms), from $14.7 million to $53.9 million (10 new organisms), and from $17.6 million to $64.7 million (12 new organisms). For organisms that are submitted for multi-agency evaluation, the annual savings could range from $2.9 million to $5.2 million (6 new organisms), from $4.9 million to $8.6 million (10 new organisms), and from $5.8 million to $10.3 million (12 new organisms).

APHIS costs of regulating GE organisms that may pose plant pest or noxious weed risks also are expected to change under the proposed rule. Fewer permits would be issued and notifications and petitions for non-regulated status would be eliminated, but more risk assessments for regulatory determination would be performed. Current annual personnel costs of conducting GE activities (costs of activities that would be affected by the proposed rule) are estimated to total about $5.6 million. With the proposed rule, annual costs are expected to range from $2.5 million to $7.8 million, depending on the volume of permits, weed risk assessments, inspections, and NEPA activities. In addition, costs to APHIS of implementing the proposed rule would include outreach activities, developing guidance documents, training, and adjusting the current permit system. APHIS estimates that the public outreach, guidance and training would cost about $88,000. Requests for regulatory status and response letters under the proposed rule could be handled in a manner similar to the current ''Am I Regulated'' process outside the electronic permitting system without incurring new costs.

A quicker USDA evaluation process and related reduction to firms' regulatory uncertainty may facilitate small companies' ability to raise venture capital. Reduced regulatory requirements may also lead to greater participation by the public sector in GE research. These indirect benefits of the proposed rule may spur GE innovations, particularly in small acreage crops where genetic engineering has not been widely utilized due to the expense of regulation. While the proposed rule may help promote biotech innovations, the pace of commercialization and volume of GE products commercialized are not expected to change dramatically from current levels. Nor is control over the development process expected to be materially altered by the proposed rule. It would be in a biotech developer's own best interest to maintain the same level of supervision and control over the development process as at present to prevent undesired cross-pollination or commingling with non-GE crops.

GE crop varieties, in general, are not required to be reviewed or approved for safety by the FDA before going to market. However, the developer is responsible for ensuring product safety and developers consider voluntary consultations with FDA on food safety to be an absolute necessity for applicable GE products.[11] Developers also have various legal, quality control

[11] Genetically Engineered Crops: Past Experience and Future Prospects. Committee on Genetically Engineered Crops: Past Experience and Future Prospects; Board on Agriculture and Natural Resources; Division on Earth and Life Studies; National Academies of Sciences, Engineering, and Medicine.

and marketing motivations to maintain rigorous voluntary stewardship measures. APHIS therefore believes that developers would continue to utilize such measures for field testing even in cases where USDA would not require a permit.

Certain plants are genetically engineered in order to produce pharmaceutical or industrial compounds (plant-made pharmaceuticals or industrials), or PMPIs. Under the provisions of the proposed rule, there is a possibility that APHIS could reach a determination that a GE plant that produces PMPIs is not a regulated organism. Such a plant would not be subject to field trial oversight by USDA, and could be planted before or without an evaluation by FDA or EPA. Several options have been identified for addressing this potential gap in oversight. APHIS estimates that current PMPI inspections cost roughly $35,000 in total annually or about $800 each on average. Assuming that oversight continues in the same manner as APHIS oversight, a similar government expenditure could be expected under any of the PMPI oversight scenarios.

Certain plants are genetically engineered to produce PIPs. PIPs fall under the regulatory oversight of EPA. However, APHIS exercises regulatory oversight of all PIP plantings on 10 acres or less of land. Under the proposed rule, APHIS would only require permits for PIPs planted on 10 acres or less if they present a plant pest or noxious weed risk or have not yet been evaluated by APHIS for such risk. This proposal would shift Federal oversight of small-scale (10 acres or less) outdoor plantings of PIPs to EPA. EPA may decide to require EUPs for all, some, or none of such PIPs, and may conduct inspections of all, some, or none of those PIPs under permit. EPA would need to develop a program to oversee small-scale testing of PIPs and issue regulations if warranted. APHIS is fully committed to coordinating with EPA in this matter in order to give EPA time to stand up such a program. APHIS understands that a memorandum of understanding (MOU) and services agreement may be necessary to provide personnel and other resources to assist EPA during the interim period while EPA implements its own program of oversight of outdoor planting of PIPs on 10 acres or less. APHIS recognizes that there are challenges associated with such a transition that also would require EPA to incur the costs associated with setting up a revised regulatory program. Further, it would require policies, procedures, and guidance regarding APHIS' interaction with EPA.

Farmers who adopt GE crops also may indirectly benefit from the proposed rule. The adoption of GE crops in the United States has generally reduced costs and improved profitability at the farm level. As mentioned, under the proposed rule, regulatory costs are expected to be lower, thereby potentially spurring developer innovation, especially among small companies and universities. Farmers may benefit by having access to a wider variety of traits as well as a greater number of new GE crop species, affording them a broader selection of crops to suit their particular management needs. Among the types of innovations expected are crops with greater resistance to disease and insect pests, greater tolerance of stress conditions such as drought, high temperature, low temperature, and salt, and more efficient use of fertilizer. These types of traits can lower farmer input costs (water, fertilizer, pesticide) and increase yields during times of adverse growing conditions.

On the other hand, some farmers (*e.g.,* growers of organic and or identity-preserved crops) could be negatively impacted by these same innovations. Some consumers choose not to purchase products derived from GE crops and instead purchase commodities such as those labeled ''non-GMO'' or organic. When crops intended for the non-GE or identity-preserved marketplace contain unintended GE products, the value of the non-GE or identity-preserved product is diminished. Effects of the proposed rule on the variety of GE crop species grown in the United States and their wider adoption may increase risks of cross-pollination or commingling. As more small acreage crops are modified using genetic engineering, the unintended presence of a GE organism becomes increasingly possible. Unauthorized releases of regulated GE crop plants and the entry of regulated plant material in the commercial food and feed supply can have impacts on domestic or international markets. While such releases have occurred and may occur again, such incidents are expected to be rare.

Entities potentially affected by the proposed rule fall under various categories of the North American Industry Classification System. While economic data are not available on business size for some entities, based on industry data obtained from the Economic Census and the Census of Agriculture we can assume that the majority of the businesses affected by the proposed rule would be small. APHIS welcomes public comment on the proposed rule's possible impacts.

The following table provides a summary statement of the expected direct benefits and costs of the proposed rule:

EXPECTED ANNUAL BENEFITS AND COSTS OF THE PROPOSED RULE FOR THE BIOTECHNOLOGY INDUSTRY AND FOR USDA, 2015 DOLLARS

Entity			
Biotechnology Industry	Costs ($1,000)		
Developer costs (recordkeeping and rule familiarization) [1].	851		
	Cost Savings per Trait ($1,000)		
Developer Savings [2]		Proposed rule, lower bound	Proposed rule, upper bound
USDA sole regulatory agency		−1,468	−5,393
USDA with FDA and/or EPA oversight		−485	−861
APHIS Biotechnology Regulatory Services	Costs ($1,000)		

EXPECTED ANNUAL BENEFITS AND COSTS OF THE PROPOSED RULE FOR THE BIOTECHNOLOGY INDUSTRY AND FOR USDA, 2015 DOLLARS—Continued

Costs for public outreach, training, and epermitting [3]	88		
Activities affected by the rule	Current rule	Proposed rule, lower bound	Proposed rule, upper bound
Notifications	203	0	0
Petitions	2,130	0	0
Interstate movement and environmental release permits	239	139	261
Courtesy permits	19	0	0
Letters of No Permit Required	0	3	3
''Am I Regulated'' Process	7	0	0
Weed risk assessments	0	700	1,265
Compliance and Inspections	361	361	1,014
NEPA/ESA	2,648	1,324	5,297
Total [4]	5,607	2,527	7,840

[1] Becoming familiar with the rule are one-time costs.
[2] These savings are shown on a per trait basis. If between 6 and 12 GE organisms are developed each year that would have solely required USDA oversight, annual savings could range from $9 million to $64.8 million. If between 6 and 12 new GE organisms per year are submitted for multi-agency evaluation, the annual savings could be from $2.9 million to $10.3 million.
[3] Requests for regulatory status and response letters under the proposed rule could be handled in a manner similar to the current 'Am I Regulated' process outside the electronic permitting system without new costs.
[4] Annual staffing costs of APHIS Biotechnology Regulatory Services total about $19 million.

Executive Order 12372

This program/activity is listed in the Catalog of Federal Domestic Assistance under No. 10.025 and is subject to Executive Order 12372, which requires intergovernmental consultation with State and local officials. (See 2 CFR chapter IV.)

Executive Order 12988

This proposed rule has been reviewed under Executive Order 12988, Civil Justice Reform. If this proposed rule is adopted: (1) All State and local laws and regulations that are inconsistent with this rule will be preempted; (2) no retroactive effect will be given to this rule; and (3) administrative proceedings will not be required before parties may file suit in court.

Executive Order 13175

This rule has been reviewed in accordance with the requirements of Executive Order 13175, ''Consultation and Coordination with Indian Tribal Governments.'' Executive Order 13175 requires Federal agencies to consult and coordinate with Tribes on a government-to-government basis on policies that have Tribal implications, including regulations, legislative comments or proposed legislation, and other policy statements that have substantial direct effects on one or more Indian Tribes, on the relationship between the Federal Government and Indian Tribes, or on the distribution of power and responsibilities between the Federal Government and Indian Tribes.

The Animal and Plant Health Inspection Service has assessed the impact of this rule on Indian Tribes and determined that this rule does have Tribal implications that require Tribal consultation under E.O. 13175. If a Tribe requests consultation, the Animal and Plant Health Inspection Service will work with the Office of Tribal Relations to ensure meaningful consultation is provided where changes, additions, and modifications identified herein are not expressly mandated by Congress.

Paperwork Reduction Act

In accordance with section 3507(d) of the Paperwork Reduction Act of 1995 (44 U.S.C. 3501 *et seq.*), some of the reporting, recordkeeping, and third party disclosure requirements included in this proposed rule have been approved under 0579–0085. The new reporting, recordkeeping, and third party disclosure requirements proposed by this rule have been submitted as a new information collection package for approval to the Office of Management and Budget (OMB). Upon approval of this new information collection, it will be merged into the existing 0579–0085.

Please send comments on the Information Collection Request (ICR) to OMB's Office of Information and Regulatory Affairs via email to *oira_submissions@omb.eop.gov,* Attention: Desk Officer for APHIS, Washington, DC 20503. Please state that your comments refer to Docket No. APHIS–2015–0057. Please send a copy of your comments to: USDA, using one of the methods described under **ADDRESSES** at the beginning of this document.

APHIS is proposing to revise its regulations governing the importation, interstate movement, and release into the environment of organisms developed using genetic engineering. Organisms would be regulated because APHIS has determined them to present a plant pest or noxious weed risk, or has not yet evaluated them for such risk.

Persons would be able to submit a request for APHIS to evaluate the regulatory status of a GE organism. They would also be able to petition APHIS to add a genus, species, or subspecies to a list of taxa that are or contain plant pests. Finally, permits would be required for the importation, interstate movement, and environmental release of all regulated GE organisms. Responsible persons who are issued permits would be required to retain records, and would have to submit reports if they conduct field testing.

APHIS is soliciting comments from the public (as well as affected agencies) concerning our proposed information collection and recordkeeping requirements. These comments will help APHIS:

(1) Evaluate whether the proposed information collection is necessary for the proper performance of our agency's functions, including whether the information will have practical utility;

(2) Evaluate the accuracy of our estimate of the burden of the proposed information collection, including the validity of the methodology and assumptions used;

(3) Enhance the quality, utility, and clarity of the information to be collected; and

(4) Minimize the burden of the information collection on those who are to respond (such as through the use of appropriate automated, electronic, mechanical, or other technological

collection techniques or other forms of information technology; *e.g.,* permitting electronic submission of responses).

Estimate of burden: Public reporting burden for this collection of information is estimated to average 0.828 hours per response.

Respondents: Developers of organisms regulated under 7 CFR part 340; businesses and individuals associated with such organisms; Tribal governments.

Estimated Annual Number of Respondents: 311.

Estimated Annual Number of Responses per Respondent: 16.

Estimated Annual Number of Responses: 5035.

Estimated Total Annual Burden on Respondents: 4174 hours. (Due to averaging, the total annual burden hours may not equal the product of the annual number of responses multiplied by the reporting burden per response.)

A copy of the information collection may be viewed on the *Regulations.gov* Web site or in our reading room. (A link to *Regulations.gov* and information on the location and hours of the reading room are provided under the heading **ADDRESSES** at the beginning of this proposed rule.) Copies can also be obtained from Ms. Kimberly Hardy, APHIS' Information Collection Coordinator, at (301) 851–2483. APHIS will respond to any ICR-related comments in the final rule. All comments will also become a matter of public record.

E-Government Act Compliance

The Animal and Plant Health Inspection Service is committed to compliance with the E-Government Act to promote the use of the Internet and other information technologies, to provide increased opportunities for citizen access to Government information and services, and for other purposes. For information pertinent to E-Government Act compliance related to this proposed rule, please contact Ms. Kimberly Hardy, APHIS' Information Collection Coordinator, at (301) 851–2483.

List of Subjects in 7 CFR Part 340

Administrative practice and procedure, Biotechnology, Genetic engineering, Imports, Packaging and containers, Plant diseases and pests, Transportation.

Accordingly, we are proposing to revise 7 CFR part 340 to read as follows:

PART 340—MOVEMENT OF ORGANISMS ALTERED OR PRODUCED THROUGH GENETIC ENGINEERING THAT ARE NOXIOUS WEEDS OR PLANT PESTS OR THAT THERE IS REASON TO BELIEVE ARE NOXIOUS WEEDS OR PLANT PESTS

Sec.

Authority: 7 U.S.C. 7701–7772 and 7781–7786; 31 U.S.C. 9701; 7 CFR 2.22, 2.80, and 371.3.

§ 340.0 General restrictions and scope.

(a) No person may move any regulated organism except in accordance with this part.

(b) A regulated organism is any GE organism that either:

(1) Prior to genetic engineering, belonged to any taxon listed in accordance with § 340.2 and met the definition of *plant pest* in § 340.1; or

(2) Has received deoxyribonucleic acid (DNA) from any taxon listed in accordance with § 340.2, the DNA from the donor organism is sufficient to produce an infectious entity capable of causing plant disease or encodes a compound known to be pathogenesis-related that is expected to cause plant disease symptoms, and the organism has not been evaluated by APHIS for plant pest risk in accordance with § 340.4; or

(3) Is a plant that has a plant and trait combination that has not been evaluated by APHIS for plant pest and noxious weed risk in accordance with § 340.4; or

(4) Is any of the foregoing that has been evaluated by APHIS in accordance with § 340.4 and determined to pose a risk as a plant pest and/or noxious weed or is a GE organism that has otherwise been determined by the Administrator to pose a risk as a plant pest or noxious weed.[1]

§ 340.1 Definitions.

Terms used in the singular form in this part shall be construed as the plural, and vice versa, as the case may demand. The following terms, when used in this part, shall be construed, respectively, to mean:

Administrator. The Administrator of the Animal and Plant Health Inspection Service (APHIS) or any other employee of APHIS to whom authority has been or may be delegated to act in the Administrator's stead.

Agent. A person who is authorized to act on behalf of the responsible person to maintain control over a regulated organism during its importation, interstate movement, or environmental release and ensures compliance with all conditions contained in any applicable permit or exemption as well as other requirements in this part. Agents may be, but are not limited to, brokers, farmers, researchers, or site cooperators. An agent must be at least 18 years of age and be a legal resident of the United States.

Animal and Plant Health Inspection Service (APHIS). An agency of the United States Department of Agriculture.

Contained facility. A structure for the storage and/or propagation of living organisms designed with physical barriers capable of preventing the escape of the enclosed organisms. Examples include laboratories, growth chambers, fermenters, and containment greenhouses.

Donor organism. The organism from which genetic material is obtained for transfer to the recipient organism.

Environment. All the land, air, and water; and all living organisms in association with land, air, and water.

Genetic engineering. Techniques that use recombinant or synthetic nucleic acids with the intent to create or alter a genome. Genetic engineering does not include traditional breeding techniques (including, but not limited to, marker-assisted breeding and chemical or radiation-based mutagenesis, as well as tissue culture and protoplast, cell, or embryo fusion).

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:

(1) The genetic modification to the organism is solely a deletion of any size or a single base pair substitution which could otherwise be obtained through the use of chemical- or radiation-based mutagenesis; or

(2) The genetic modification to the organism is solely introducing only naturally occurring nucleic acid sequences from a sexually compatible relative that could otherwise cross with the recipient organism and produce viable progeny through traditional breeding (including, but not limited to, marker-assisted breeding, as well as

[1] The importation, interstate movement, and release into the environment of regulated organisms is subject to any other applicable restrictions of this chapter. For example, in ''Subpart—Plants for Planting'' (§§ 319.37–319.37–14 of this chapter), a permit is required for the importation of certain plants for planting, regardless of whether the plants for planting have been genetically engineered.

tissue culture and protoplast, cell, or embryo fusion); or

(3) The organism is a ''null segregant,'' that is, the progeny of a GE organism where the only genetic modification was the insertion of donor nucleic acid into the recipient's genome, but the donor nucleic acid is not passed to the recipient organism's progeny and the donor nucleic acid has not altered the DNA sequence of the progeny.

Import (importation). To move into, or the act of movement into, the territorial limits of the United States.

Inspector. Any individual authorized by the Administrator of APHIS or the Commissioner of Customs and Border Protection, Department of Homeland Security, to enforce the regulations in this part.

Interstate. From one State into or through any other State or within the District of Columbia, Guam, the Virgin Islands of the United States, or any other territory or possession of the United States.

Interstate movement. To move interstate.

Move (moving, movement). To carry, enter, import, mail, ship, or transport; aid, abet, cause, or induce the carrying, entering, importing, mailing, shipping, or transporting; to offer to carry, enter, import, mail, ship, or transport; to receive to carry, enter, import, mail, ship, or transport; to release into the environment; or to allow any of the above activities to occur.

Noxious weed. 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.

Nucleic acid. A chain or chains of nucleotides found in either DNA or ribonucleic acid.

Organism. Any active, infective, or dormant stage of life form of an entity characterized as living, including vertebrate and invertebrate animals, plants, bacteria, fungi, mycoplasmas, mycoplasma-like organisms, as well as entities such as viroids, viruses, or any entity characterized as living, related to the foregoing.

Permit. A written authorization, including by electronic methods, by the Administrator to move regulated organisms and associated articles under conditions prescribed by the Administrator.

Person. Any individual, partnership, corporation, company, society, association, or other organized group.

Plant. Any plant (including any plant part) for or capable of propagation, including a tree, a tissue culture, a plantlet culture, pollen, a shrub, a vine, a cutting, a graft, a scion, a bud, a bulb, a root, and a seed.

Plant pest. Any living stage of a protozoan, invertebrate nonhuman animal, parasitic plant, bacterium, fungus, virus or viroid, infectious agent or other pathogen, or any article similar to or allied with any of the foregoing, that can directly or indirectly injure, cause damage to, or cause disease in any plant or plant product.

Plant pest risk assessment. An assessment evaluating whether a GE organism is a plant pest.

Plant product. Any flower, fruit, vegetable, root, bulb, seed, or other plant part that is not included in the definition of plant or any manufactured or processed plant or plant part.

Recipient organism. The organism whose nucleic acid sequence will be altered through the use of genetic engineering.

Regulated organism. Any GE organism that is regulated pursuant to § 340.0.

Regulatory sequence. A segment of nucleic acid molecule that is capable of increasing or decreasing the expression of specific genes within an organism.

Release into the environment (environmental release). The use of a regulated organism outside the physical constraints found in a contained facility.

Responsible person. The person who has control and will maintain control over a regulated organism during its movement and ensures compliance with all conditions contained in any applicable permit or exemption as well as other requirements in this part. A responsible person must be at least 18 years of age and be a legal resident of the United States.

Secure shipment. Shipment in a container or a means of conveyance of sufficient strength and integrity to withstand leakage of contents, shocks, pressure changes, and other conditions incident to ordinary handling in transportation.

State. Any of the several States of the United States, the Commonwealth of the Northern Mariana Islands, the Commonwealth of Puerto Rico, the District of Columbia, the Virgin Islands of the United States, or other Territories or possessions of the United States.

State or Tribal regulatory official. State or Tribal official with responsibilities for plant health, or any other duly designated State or tribal official, in the State or on the Tribal lands where the movement is to take place.

Unauthorized release. The intentional or accidental release of a regulated organism in a manner that is not authorized by a permit issued pursuant to this part.

Weed risk assessment. An assessment of the characteristics of a plant as these relate to weediness.

§ 340.2 Taxa that are or contain plant pests.

(a) Taxa that are or contain plant pests are listed on the APHIS Web site at *http://www.aphis.usda.gov/biotechnology/2016-340-proposed-rule.* Within any taxonomic group included on the list, the lowest unit of classification actually listed is the taxon or group which may contain organisms that are regulated. Organisms belonging to all lower taxa contained within the group listed are included as organisms that may be or may contain plant pests, and are regulated if they meet the definition of a plant pest in § 340.1.

(b) *APHIS-initiated changes to listed taxa.* APHIS may propose to add or remove a taxon from the list referred to in paragraph (a) of this section through a notice published in the **Federal Register**. The notice will state why APHIS has determined it necessary to add or remove the taxon, and will request public comment. If no comments are received on the notice, or the comments received do not affect APHIS' determination, APHIS will publish a subsequent notice in the **Federal Register** stating that the taxon has been added or removed from the list referred to in paragraph (a) of this section.

(c) *Petitions to amend the list of taxa.* Any person may submit to the Administrator a petition to amend the list of taxa referred to in paragraph (a) of this section by adding or removing any taxon. The petitioner may supplement, amend, or withdraw a petition in writing without prior approval of the Administrator and without prejudice to resubmission at any time until the Administrator rules on the request. A petition to amend the list of taxa must be submitted in accordance with the procedures and format provided on the APHIS Web site at *http://www.aphis.usda.gov/biotechnology/2016-340-proposed-rule.*

(d) *Administrative action on a petition.* (1) A petition to amend the list of taxa that meets the requirements of paragraph (b) of this section as well as the date of the petition will be acknowledged by APHIS. If a request does not meet the requirements of paragraph (b) of this section, the requester will be sent a notice indicating how the request is deficient.

(2) APHIS will publish in the **Federal Register**, for 60 days public comment, a notice announcing the availability of a petition to amend the list of organisms. Following the close of the comment period, APHIS will review the comments received and publish its final decision in the **Federal Register**.

(e) *Appeal of denial.* Any person whose petition has been denied may appeal the decision in writing to the Administrator within 30 days after receiving the written notification of the denial. The appeal must state all of the facts and reasons upon which the person relies to assert that the petition was wrongfully denied. The Administrator will grant or deny the appeal, in writing, stating the reasons for the decision as promptly as circumstances allow.

§ 340.3 Permits.

(a)(1) Except as provided in paragraph (a)(2) of this section, APHIS must have evaluated a regulated organism in accordance with § 340.4 before it will issue permits for importation, interstate movement, or release into the environment of the organism pursuant to this section.

(2) APHIS may issue a permit pursuant to this section for the importation or interstate movement of a regulated organism that has not been evaluated in accordance with § 340.4, at the request of an applicant. For the purposes of permitting conditions, APHIS will assume the regulated organism presents a risk as a plant pest and/or noxious weed. If the regulatory status of the organism is evaluated in accordance with § 340.4 during the duration of the permit, APHIS may amend or terminate the permit accordingly.

(3) Except as provided in paragraph (c) of this section, a permit must be issued by APHIS for the importation, interstate movement, or release into the environment of all regulated organisms.

(b) A responsible person must apply for and obtain a permit through a method listed at *http://www.aphis.usda.gov/biotechnology/2016-340-proposed-rule.* The application must also contain all the categories of information listed at that Web site for the type of permit being requested.

(c) A permit for interstate movement is not required for genetically engineered *Arabidopsis thaliana,* provided that it is moved as a secure shipment, the cloned genetic material is stably integrated into the plant genome, and the cloned material does not include the complete infectious genome of a plant pest.

(d) *Administrative actions.* (1) APHIS will review the application to determine if it is complete. APHIS will notify the applicant in writing if the application is incomplete, and the applicant will be provided the opportunity to revise the application. If the applicant does not respond to the request for additional information within 30 days of receipt of APHIS's request, APHIS will deem the application withdrawn. Once an application is complete, APHIS will review it to determine whether to approve or deny the application.

(2) *APHIS assignment of permit conditions.* If a permit application is approved, the Administrator will assign permit conditions to each permit commensurate with the risk of the regulated organism and activity. General conditions assigned to all permits are located in paragraph (e) of this section. The Administrator may assign additional or expanded permit conditions commensurate with the risk that the activities listed on the permit application present of disseminating the regulated organism, or other plant pests or noxious weeds.

(3) *Inspections.* All premises associated with the permit are subject to inspection before and after permit issuance. The responsible person must provide APHIS inspectors access to inspect any relevant premises, facility, release location, storage area, waypoint, materials, equipment, means of conveyance, and other articles related to the proposed movement of organisms regulated under this part. Failure to allow the inspection of a premises prior to the issuance of a permit will be grounds for the denial of a permit application. Failure to allow the inspection of a premises following permit issuance will be grounds for revocation of the permit.

(4) *State or Tribal review and comment.* The Administrator will submit for notice and review a copy of the permit application and any permit conditions to the appropriate State or Tribal regulatory official. Comments received from the State or Tribal regulatory official may be considered by the Administrator prior to permit issuance.

(5) *Agreement with permit conditions.* Prior to issuance of a permit, the responsible person must agree in writing, in a manner prescribed by the Administrator, that the responsible person and all agents of the responsible person are aware of, understand, and will comply with the permit conditions. Failure to comply with this provision will be grounds for the denial of a permit.

(e) *General permit conditions.* The following conditions will be assigned to all permits issued under this section. A responsible person, and his/her agents, must ensure compliance with these conditions, as well as any additional or expanded conditions listed on the permit:

(1) The regulated organism must be maintained and disposed of in a manner so as to prevent the unauthorized release of the regulated organism.

(2) The regulated organism must be kept separate from other organisms, except as specifically allowed in the permit.

(3) The regulated organism must be maintained only in areas and premises specified in the permit.

(4) The regulated organism's identity must be maintained at all times.

(5) In the event of an unauthorized release:

(i) The regulated organism must undergo the application of remedial measures determined by the Administrator to be necessary to prevent the spread of regulated organism;

(ii) The responsible person must contact APHIS as described in the permit within 24 hours of discovery, and subsequently supply a statement of facts in writing no later than 5 business days after discovery.

(6) The duration that the permit is valid will be listed on the permit itself. During such time, the responsible person must maintain records related to permitted activities of sufficient quality and completeness to demonstrate compliance with all permit conditions and requirements under this part. The responsible person must submit reports and notices to APHIS at the times specified in the permit and containing the information specified within the permit. Inspectors must be allowed access, during regular business hours, to the place where the regulated organism is located and to any records relating to the movement of a regulated organism. APHIS' access to records includes visual inspection and reproduction (photocopying, digital reproduction, etc.) of all records required to be maintained under this part, as requested by APHIS.

(7) The responsible person must notify APHIS in writing if any permitted activity associated with environmental release will not be conducted.

(8) Within 28 days after the initiation of any permitted activity related to environmental release, the responsible person must report to APHIS in writing the actual release site coordinates and details of the release, such as how many acres planted, how many organisms released, etc., based on permit

conditions, as well as every 28 days thereafter until all releases are completed.

(9) A person who has been issued a permit must submit to APHIS an environmental release report within 6 months after the termination of any release into the environment. The report must include the APHIS reference number, methods of observation, resulting data, and analysis regarding all deleterious effects on plants, nontarget organisms, or the environment.

(f) *Denial or revocation of a permit.* Permit applications may be denied, or permits revoked, in accordance with this paragraph.

(1) *Denial.* The Administrator may deny, either orally or in writing, any application for a permit. If the denial is oral, the Administrator will communicate the denial and the reasons for it in writing as promptly as circumstances allow. The Administrator may deny a permit application if:

(i) The Administrator concludes that, based on the application or on additional information, the actions proposed under the permit may result in the unauthorized release of the regulated organism, or another plant pest or noxious weed; or

(ii) The Administrator determines that the responsible person or any agent of the responsible person has failed to comply at any time with any provision of this part or any other part of the regulations, or any permit that has previously been issued in accordance with this part.

(2) *Revocation.* The Administrator may revoke, either orally or in writing, any permit which has been issued. If the revocation is oral, the Administrator will communicate the revocation and the reasons for it in writing as promptly as circumstances allow. The Administrator may revoke a permit if:

(i) Following issuance of the permit, the Administrator receives information that would otherwise have provided grounds for APHIS to deny the permit application;

(ii) The Administrator determines that actions taken under the permit have resulted in the unauthorized release of the regulated organism, or another plant pest or noxious weed; or

(iii) The Administrator determines that the responsible person or any agent of the responsible person has failed to comply at any time with any provision of this part or any other part of the regulations. This includes failure to comply with the conditions of any permit issued.

(g) *Appeal of denial or revocation of permit.* Any person whose permit application has been denied or whose permit has been or revoked may appeal the decision in writing to the Administrator. Any appeal must occur within 10 days after receiving the written notification of the denial or revocation. The appeal must state all of the facts and reasons upon which the person relies to assert that the permit was wrongfully denied or revoked. The Administrator will grant or deny the appeal, in writing, stating the reasons for the decision as promptly as circumstances allow. If there is a conflict as to any material fact, a hearing shall be held to resolve such conflict. Rules of practice concerning such a hearing will be adopted by the Administrator.

(h) *Amendment of permits.*

(1) *Amendment at responsible person's request.* If a responsible person determines that circumstances have changed since the permit was initially issued and wishes the permit to be amended accordingly, he or she must request the amendment by contacting APHIS directly. The responsible person may have to provide supporting information justifying the amendment. APHIS will review the amendment request, and may amend the permit if only minor changes are necessary. Requests for more substantive changes may require a new permit application. Prior to issuance of an amended permit, the responsible person may be required to agree in writing that he or she, and his or her agents, will comply with the amended permit and conditions.

(2) *Amendment initiated by APHIS.* APHIS may amend any permit and its conditions at any time, upon determining that the amendment is needed to address newly identified considerations concerning the risks presented by the organism or the activities being conducted under the permit. APHIS may also amend a permit at any time to ensure that the permit conditions are consistent with all of the requirements of this part. As soon as circumstances allow, APHIS will notify the responsible person of the amendment to the permit and the reason(s) for it. Depending on the nature of the amendment, the responsible person may have to agree in writing or electronically that he or she, and his or her agents, will comply with the permit and conditions as amended before APHIS will issue the amended permit. If APHIS requests such an agreement, and the responsible person does not so agree, the existing permit will be revoked.

(i) *Shipping under a permit.* All shipments of regulated organisms must be secure shipments. Regulated organisms must also be shipped in accordance with the regulations in 49 CFR part 178. The container must be accompanied by a document that includes the names and contact details for the sender and recipient. Following the completion of the shipment, all packing material, shipping containers, and any other material accompanying the regulated organism must be treated or disposed of in such a manner so as to prevent the unauthorized dissemination and establishment of regulated organisms. Additionally, for any regulated organism to be imported into the United States, the outmost container must bear the nature and quantity of the contents; the country and locality where collected, developed, manufactured, reared, cultivated, or cultured; the name and address of the shipper, owner, or person shipping or forwarding the organism; the name, address, and telephone number of the consignee; the identifying shipper's mark and number; and the number of written permit authorizing the importation. For regulated organisms imported by mail, the container must also be addressed to a plant inspection station listed in § 319.37–14 of this chapter. All imported containers of regulated organisms must be accompanied by an invoice or packing list indicating the contents of the shipment.

§ 340.4 Regulatory status evaluation.

(a) Any person may submit a request to APHIS to have a GE organism's regulatory status evaluated, or to request the reevaluation of the regulatory status of a previously evaluated regulated organism. Information needed for such a request is found on the Internet, at *http://www.aphis.usda.gov/biotechnology/2016-340-proposed-rule.*

(b) *Administrative action.* (1) Upon receiving or initiating a regulatory status request, APHIS will evaluate the request for completeness, and may contact the person submitting the request for additional information.

(2) If the request is complete, APHIS will conduct an analysis of plant pest and/or weed risks of the GE organism.

(c)(1) APHIS will make both the request and the risk analysis available for public review through a notice published in the **Federal Register**. The notice will request public comment, and will propose a regulatory status for the organism.

(2) If no comments are received on the notice, or if the comments do not affect the conclusions of the risk analysis or the proposed regulatory status of the organism, APHIS will provide notification through the APHIS stakeholder registry at the end of the

comment period announcing that the proposed regulatory status has been finalized. APHIS will subsequently publish a notice in the **Federal Register** compiling these determinations.

(3) If comments lead APHIS to change its proposed regulatory status for the organism, APHIS will publish a subsequent notice in the **Federal Register** characterizing these comments and announcing the new regulatory status.

§ 340.5 Record retention, compliance, and enforcement.

(a) *Record retention.* Responsible persons or their agents are required to establish and keep the following records and reports:

(1) All records and reports required as a condition of a permit;

(2) Addresses and any other information needed to identify all contained facilities where the regulated organism was stored or utilized, and all locations where the regulated organism was used in an environmental release;

(3) A record identifying which APHIS permit, if any, authorized the permitted activity; and

(4) Copies of contracts between the responsible person and all agents that conduct activities subject to this part for the responsible person, and copies and documents relating to agreements made without a written contract.

(b) *Record retention.* Records indicating that a regulated organism that was imported or moved interstate reached its intended destination must be retained for at least 2 years. All other records must be retained for 10 years following permit expiration, unless determined otherwise by the Administrator and documented in the supplemental permit conditions or other regulatory requirements.

(c) *Compliance and enforcement.* (1) Responsible persons and their agents must comply with all of the requirements of this part. Failure to comply with any of the requirements of this part may result in any or all of the following:

(i) Denial of a permit application or revocation of a permit;

(ii) Application of remedial measures in accordance the Plant Protection Act, 7 U.S.C. 7701 *et seq.;* and/or

(iii) Criminal and/or civil penalties.

(2) Prior to the issuance of a complaint seeking a civil penalty, the Administrator may enter into a stipulation, in accordance with § 380.10 of this chapter.

(d) *Liability for acts of an agent.* For purposes of enforcing this part, the act, omission, or failure of any agent for a responsible person may be deemed also to be the act, omission, or failure of the responsible person.

§ 340.6 Confidential business information.

Persons submitting confidential business information in any document submitted to APHIS under this part should do so in the following manner. If there are portions of a document deemed to contain confidential business information, those portions must be identified, and each page containing such information must be marked ''CBI Copy.'' A second copy of each such document must be submitted with all such CBI deleted and marked on each page where the CBI was deleted: ''CBI Deleted.'' In addition, any person submitting CBI must justify how each piece of information requested to be treated as CBI is a trade secret or is commercial or financial information and is privileged or confidential.

§ 340.7 Costs and charges.

The services of the inspector related to carrying out this part and provided during regularly assigned hours of duty and at the usual places of duty will be furnished without cost.[2] The U.S. Department of Agriculture will not be responsible for any costs or charges incident to inspections or compliance with the provisions of this part, other than for the services of the inspector.

Done in Washington, DC, this 10th day of January 2017.

Ben Thomas,

Deputy Under Secretary for Marketing and Regulatory Programs.

[FR Doc. 2017–00858 Filed 1–18–17; 8:45 am]

BILLING CODE 3410–34–P

[2] The Department's provisions relating to overtime charges for an inspector's services are set forth in part 354 of this chapter.

Proposed Rules

Federal Register
Vol. 82, No. 214
Tuesday, November 7, 2017

This section of the FEDERAL REGISTER contains notices to the public of the proposed issuance of rules and regulations. The purpose of these notices is to give interested persons an opportunity to participate in the rule making prior to the adoption of the final rules.

DEPARTMENT OF AGRICULTURE

Animal and Plant Health Inspection Service

7 CFR Part 340

[Docket No. APHIS–2015–0057]

RIN 0579–AE15

Importation, Interstate Movement, and Environmental Release of Certain Genetically Engineered Organisms

AGENCY: Animal and Plant Health Inspection Service, USDA.

ACTION: Proposed rule; withdrawal.

SUMMARY: We are withdrawing a proposed rule that would have revised our regulations regarding the importation, interstate movement, and environmental release of certain genetically engineered organisms. We are taking this action after considering the comments we received following the publication of the proposed rule.

DATES: We are withdrawing the proposed rule published January 19, 2017 (82 FR 7008) as of November 7, 2017.

FOR FURTHER INFORMATION CONTACT: Mr. Sidney Abel, Assistant Deputy Administrator, Biotechnology Regulatory Services, APHIS, 4700 River Road Unit 147, Riverdale, MD 20737–1238; (301) 851–3896.

SUPPLEMENTARY INFORMATION: On January 19, 2017, we published in the **Federal Register** (82 FR 7008–7039, Docket No. APHIS–2015–0057) a proposal [1] to amend the regulations in 7 CFR part 340 regarding the importation, interstate movement, and environmental release of certain genetically engineered (GE) organisms.

We solicited comments concerning our proposal for 120 days ending May 19, 2017. We extended the deadline for comments until June 19, 2017, in a document published in the **Federal Register** on February 10, 2017 (Docket No. APHIS–2015–0057, 82 FR 10312–10313). We received 203 comments by that date. They were from GE developers, growers of GE crops, GE industry and agricultural trade associations, universities and academic researchers, organic producers and trade associations, consumer safety and environmental advocacy groups, a Federal agency, and private citizens.

Many commenters objected to the scope of the proposed rule. Some thought that our criteria for designating GE organisms as regulated organisms were too expansive, potentially resulting in our regulating a wider range of GE organisms than necessary and thereby increasing, rather than reducing, the regulatory burden for the biotechnology industry. Other commenters, however, thought that certain exemptions and exclusions contained in the proposed rule would effectively narrow the scope of our regulatory authority over GE organisms and increase the risk of the unintended presence of GE crops in organic and other non-GE crops.

The January 2017 proposed rule represented a major change from our existing ''regulate first/analyze later'' approach to one that entailed assessing new GE organisms to determine if they posed plant pest or noxious weed risks and then regulating only organisms that did present risks. Some commenters expressed concern that the proposed risk assessment process could prove lengthy, cumbersome, and confusing, thereby hindering innovation and preventing GE products from getting to market in a timely manner. Though we did provide exclusions that would have allowed GE organisms with certain plant/trait combinations to bypass the risk assessment process, these commenters viewed the exclusions as too narrow. Other commenters, however, took the opposite view. These commenters objected to our proposed exemption from the risk assessment process of products having plant/trait combinations corresponding to specific organisms that had been granted nonregulated status based on previous risk assessments. A number of these commenters also thought the proposed process as a whole would be insufficiently rigorous, with some objecting specifically to our proposal to no longer require the submission of field test data as part of the assessment process.

Another issue that drew many comments was our proposal to incorporate our noxious weed authority into the biotechnology regulations in part 340. Noting that noxious weeds are also regulated under the Plant Protection and Quarantine regulations in 7 CFR part 360, commenters expressed concern that this proposal could result in the creation of two parallel but inconsistent regulatory systems and thus more regulatory uncertainty.

Finally, many commenters expressed opposition to genetic engineering in general, as well as concerns about a wide range of issues, many of which were outside the scope of the proposed rule. For example, commenters stated that the Animal and Plant Health Inspection Service (APHIS) should consider non-safety-based risks, such as economic and social impacts, including impacts on the marketability of non-GE products. Other commenters requested that APHIS regulations include provisions related to the labeling of GE products and raised concerns regarding health effects of GE products and increased pesticide use.

Based on the scope of comments received on the January 2017 proposed rule, we have decided to withdraw the rule and to begin a fresh stakeholder engagement aimed at exploring alternative policy approaches. Because of rules limiting *ex parte* communications with respect to active rulemakings, publication of the 2017 proposed rule has constrained our ability to talk about alternatives with stakeholders. Withdrawing the proposed rule will lift this constraint and provide for a more open and robust policy dialogue.

Therefore, we are withdrawing the January 19, 2017, proposed rule referenced above. As we explore a full range of policy alternatives, we will consider the comments we received on the proposed rule, as well as new scientific knowledge, and continue to seek the active and open input of stakeholders.

Authority: 7 U.S.C. 7701–7772 and 7781–7786; 31 U.S.C. 9701; 7 CFR 2.22, 2.80, and 371.3.

[1] To view the proposed rule, supporting documents, and the comments we received, go to *http://www.regulations.gov/#!docketDetail;D=APHIS-2015-0057*.

Done in Washington, DC, this 1st day of November 2017.

Michael C. Gregoire,

Acting Administrator, Animal and Plant Health Inspection Service.

[FR Doc. 2017–24202 Filed 11–6–17; 8:45 am]

BILLING CODE 3410–34–P

DEPARTMENT OF TRANSPORTATION

Federal Aviation Administration

14 CFR Part 39

[Docket No. FAA–2017–1059; Product Identifier 2017–CE–035–AD]

RIN 2120–AA64

Airworthiness Directives; Piper Aircraft, Inc. Airplanes

AGENCY: Federal Aviation Administration (FAA), DOT.

ACTION: Notice of proposed rulemaking (NPRM).

SUMMARY: We propose to adopt a new airworthiness directive (AD) for certain Piper Aircraft, Inc. Models PA–28–140, PA–28–150, PA–28–160, PA–28–180, PA–28–235, PA–32–260, and PA–32–300 airplanes. This proposed AD was prompted by reports of corrosion found in an area of the main wing spar not easily accessible for inspection. This proposed AD would require installing an inspection access panel in the lower wing skin near the left and the right main wing spars if not already there, inspecting the left and the right main wing spars for corrosion, and taking all necessary corrective actions. We are proposing this AD to address the unsafe condition on these products.

DATES: We must receive comments on this proposed AD by December 22, 2017.

ADDRESSES: You may send comments, using the procedures found in 14 CFR 11.43 and 11.45, by any of the following methods:

- *Federal eRulemaking Portal:* Go to *http://www.regulations.gov*. Follow the instructions for submitting comments.
- *Fax:* 202–493–2251.
- *Mail:* U.S. Department of Transportation, Docket Operations, M–30, West Building Ground Floor, Room W12–140, 1200 New Jersey Avenue SE., Washington, DC 20590.
- *Hand Delivery:* Deliver to Mail address above between 9 a.m. and 5 p.m., Monday through Friday, except Federal holidays.

For service information identified in this NPRM, contact Piper Aircraft, Inc., 2926 Piper Drive, Vero Beach, Florida 32960; telephone: (772) 567–4361; Internet: *www.piper.com*. You may review this referenced service information at the FAA, Policy and Innovation Division, 901 Locust, Kansas City, Missouri 64106. For information on the availability of this material at the FAA, call (816) 329–4148.

Examining the AD Docket

You may examine the AD docket on the Internet at *http://www.regulations.gov* by searching for and locating Docket No. FAA–2017–1059 or in person at the Docket Management Facility between 9 a.m. and 5 p.m., Monday through Friday, except Federal holidays. The AD docket contains this NPRM, the regulatory evaluation, any comments received, and other information. The street address for the Docket Office (phone: 800–647–5527) is in the **ADDRESSES** section. Comments will be available in the AD docket shortly after receipt.

FOR FURTHER INFORMATION CONTACT: Dan McCully, Aerospace Engineer, FAA, Atlanta ACO Branch, 1701 Columbia Avenue, College Park, Georgia 30337; telephone: (404) 474–5548; fax: (404) 474–5606; email: *william.mccully@faa.gov*.

SUPPLEMENTARY INFORMATION:

Comments Invited

We invite you to send any written relevant data, views, or arguments about this proposal. Send your comments to an address listed under the **ADDRESSES** section. Include ''Docket No. FAA–2017–1059; Product Identifier 2017–CE–035–AD'' at the beginning of your comments. We specifically invite comments on the overall regulatory, economic, environmental, and energy aspects of this NPRM. We will consider all comments received by the closing date and may amend this NPRM because of those comments.

We will post all comments we receive, without change, to *http://www.regulations.gov,* including any personal information you provide. We will also post a report summarizing each substantive verbal contact we receive about this NPRM.

Discussion

We received two reports of significant corrosion found on the main wing spars on certain Piper Aircraft, Inc. Models PA–28–140, PA–28–150, PA–28–160, PA–28–180, PA–28–235, PA–32–260, and PA–32–300 airplanes. The corrosion was found during maintenance in an area that is not easily accessible for inspection. This condition, if not detected and corrected, could cause the main wing spar to fail. This failure could result in loss of control.

Related Service Information Under 1 CFR Part 51

We reviewed Piper Aircraft, Inc. Service Bulletin No. 1304, dated August 23, 2017. The service bulletin describes procedures for installing an inspection access panel in the lower wing skin near the left and the right main wing spars, if not already there, inspect for corrosion, and, if corrosion is found, taking all necessary corrective actions. This service information is reasonably available because the interested parties have access to it through their normal course of business or by the means identified in the **ADDRESSES** section.

FAA's Determination

We are proposing this AD because we evaluated all the relevant information and determined the unsafe condition described previously is likely to exist or develop in other products of the same type design.

Proposed AD Requirements

This proposed AD would require accomplishing the actions specified in the service information described previously.

Costs of Compliance

We estimate that this proposed AD affects 11,476 airplanes of U.S. registry.

We estimate the following costs to comply with this proposed AD:

ESTIMATED COSTS

Action	Labor cost	Parts cost	Cost per product	Cost on U.S. operators
Main wing spar inspection	2 work-hours × $85 per hour = $170 to inspect both wings.	Not Applicable	$170	$1,950,920