BILLING CODE 3410-34-P

DEPARTMENT OF AGRICULTURE

Animal and Plant Health Inspection Service

[Docket No. APHIS-2024-0002]

RIN 0579-AE81

Exploring Pathways to Commercialization for Modified Microbes

AGENCY: Animal and Plant Health Inspection Service, USDA.

ACTION: Notice; request for information.

SUMMARY: We are notifying the public that the Animal and Plant Health Inspection Service (APHIS) is soliciting the public to respond to this Request for Information (RFI) as part of our stakeholder engagement to explore pathways to commercialization for modified microbes subject to APHIS jurisdiction, consistent with the APHIS regulations for the movement of organisms modified or produced through genetic engineering. In response to the Office of Science and Technology Policy's (OSTP's) RFI "Identifying Ambiguities, Gaps, Inefficiencies, and Uncertainties in the Coordinated Framework for the Regulation of Biotechnology" issued in December 2022 pursuant to Executive Order 14081, multiple commenters expressed a need for clear regulatory pathways to commercialization for modified microbes. Therefore, we are requesting comments from the public regarding pathways to commercialization, including needs, ideas, and concerns, regarding possible APHIS risk-based deregulation of modified microbes and other potential regulatory and non-regulatory pathways to commercialization. The information provided will help to identify potential criteria and mechanisms for risk-based deregulation,

develop a regulatory framework that could inform future rulemaking, and identify potential non-regulatory solutions.

DATES: We will consider all comments that we receive on or before [Insert date 60 days after date of publication in the Federal Register].

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

- Federal eRulemaking Portal: Go to www.regulations.gov. Enter APHIS-2024-0002 in the Search field. Select the Documents tab, then select the Comment button in the list of documents.
- Postal Mail/Commercial Delivery: Send your comment to Docket No. APHIS-2024-0002, 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 Regulations.gov or in our reading room, which is located in room 1620 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.

Response to this RFI is voluntary. Each individual or institution is requested to submit only one response. Responses should include the name of the person(s) or organization(s) filing the response. Please identify your answers by referring to a specific question number within the response.

Comments submitted in response to this notice are subject to the Freedom of Information Act (FOIA). Responses to this RFI may be posted without change online. No proprietary

information, copyrighted information, or personally identifiable information should be submitted in response to this RFI.

FOR FURTHER INFORMATION CONTACT: Mrs. Chessa Huff-Woodard, Esq., Branch Chief, Policy, Program, and International Collaborations, Biotechnology Regulatory Services, APHIS, 4700 River Road Unit 146, Riverdale, MD 20737; (301) 851-3943; chessa.d.huff-woodard@usda.gov.

SUPPLEMENTARY INFORMATION:

Background

Coordinated Framework

Along with the Environmental Protection Agency (EPA) and the Food and Drug Administration (FDA), the United States Department of Agriculture's (USDA's) Animal and Plant Health Inspection Service (APHIS) and the Food Safety and Inspection Service (FSIS) are responsible for the oversight and review of organisms modified or developed using genetic engineering and the foods derived from them. In 1986, the Coordinated Framework for the Regulation of Biotechnology (Coordinated Framework) was published by the Office of Science and Technology Policy (OSTP). The Coordinated Framework explains the regulatory roles for EPA, FDA, and the USDA (APHIS and FSIS), and how Federal agencies use existing Federal statutes to ensure public health and environmental safety while maintaining regulatory flexibility to avoid impeding innovation. The Coordinated Framework was subsequently updated in 1992 (see 57 FR 6753) and 2017 (see 2017_coordinated_framework_update.pdf) taking into account advances that had occurred in the field of biotechnology.

APHIS Biotechnology Regulations

The regulations in 7 CFR part 340 govern the movement (importation, interstate movement, and release into the environment) of certain organisms, to include plants, plant pests, and biocontrol organisms, modified or produced through genetic engineering. APHIS first issued these regulations in 1987 under the authority of the Federal Plant Pest Act of 1957 and the Plant Quarantine Act of 1912, 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 seven times, in 1988, 1990, 1993, 1994, 1997, 2005, and 2020.

The most recent update was on May 18, 2020, when we published in the *Federal Register* (85 FR 29790-29838, Docket No. APHIS-2018-0034) a final rule that marked the first comprehensive revision of the regulations since they were established in 1987. The May 2020 final rule provided clear, predictable, and efficient regulatory pathways for innovators, facilitating the development of plants developed using genetic engineering that are unlikely to pose plant pest risks.

The May 2020 final rule included regulatory exemptions for certain categories of modified plants. Plants are exempt from regulation in accordance with paragraphs (b), (c), and (d) of § 340.1. Additionally, § 340.4 of the 2020 final rule included a regulatory status review (RSR) process for APHIS to determine if a plant developed or modified using genetic engineering is unlikely to pose an increased plant pest risk relative to the plant pest risk posed by the respective non-modified or other appropriate comparator(s) and therefore is not subject to the

regulations. Because most microbes[1] are not "plants," they do not qualify for an exemption under § 340.1 and are not eligible for an RSR under § 340.4.

Under the May 2020 final rule, modified[2] microbes that are plant pests (as the term is defined in § 340.3); or have received deoxyribonucleic acid (DNA) from a plant pest and the DNA from the donor organism either is capable of producing an infectious agent that causes plant disease or encodes a compound that is capable of causing plant disease; or are used to control plant pests and could pose a plant pest risk, are subject to the regulations.[3]

The May 2020 final rule included permitting exemptions for some microorganisms. A permit for interstate movement is not required for disarmed *Agrobacterium tumefaciens*, provided that it is moved as a secure shipment, the cloned genetic material is stably integrated into the genome, and the cloned material does not include the complete infectious genome of a plant pest. In response to comments on the proposed rule about interagency coordination, in the May 2020 final rule, we also added paragraph (f) to § 340.5, which contains an exemption from permitting requirements for any modified microorganism that is currently registered with the EPA as a microbial pesticide, so long as the microorganism is not a *plant pest* as the term is defined in § 340.3.

However, the May 2020 rule did not include up-front regulatory exemptions or a regulatory review process for modified microorganisms. While several commenters on the proposed rule requested that APHIS develop a process to evaluate the regulatory status of non-

---

[1] The terms "microbes" and "microorganisms" are used interchangeably throughout the document because they are synonymous term; a microbe is a common shortform and colloquial reference.

[2] When we use the term "modified "in this this notice, we are referring to genetic engineering (GE) as defined in the regulations.

[3] 7 CFR part 340.2(b)-(d).

plant modified organisms, based on the subject organism's potential plant pest risk, the commenters did not provide specifics on what factors APHIS should consider in such a process. At the time, APHIS stated that further discussion and outreach with impacted developers and other stakeholders would be required before pursuing rulemaking.

Executive Order 14081 and Subsequent RFI

On September 12, 2022, President Biden issued Executive Order (EO) 14081[4], "Advancing Biotechnology and Biomanufacturing Innovation for a Sustainable, Safe, and Secure American Bioeconomy," with the goal of accelerating biotechnology innovation and growing America's bioeconomy across multiple sectors, including health, agriculture, and energy. Among other objectives, EO 14081 aims to support the safe use of biotechnology by clarifying and streamlining regulations in service of a science- and risk-based, predictable, efficient, and transparent regulatory system to support the safe use of products of biotechnology. Among other things, EO 14081 directs the EPA, the FDA, and USDA to identify any regulatory ambiguities, gaps, or uncertainties in the January 2017 update to the Coordinated Framework for the Regulation of Biotechnology or subsequent policy changes made by the agencies, through engaging with developers and stakeholders and horizon scanning for novel biotechnology products, and to provide a plan with processes and timelines to implement regulatory reform.

On December 20, 2022, in connection with EO 14081, the White House Office of Science and Technology Policy (OSTP)—on behalf of the primary agencies that regulate the products of biotechnology (EPA, FDA, and USDA), issued a request for information[5], or RFI.

---

[4]https://www.federalregister.gov/documents/2022/09/15/2022-20167/advancing-biotechnology-and-biomanufacturing-innovation-for-a-sustainable-safe-and-secure-american.

[5] https://www.federalregister.gov/documents/2023/04/27/2023-08841/executive-order-14081-advancing-biotechnology-and-biomanufacturing-innovation-for-a-sustainable-safe.

The RFI requested relevant data and information, including case studies, that may assist in identifying any regulatory ambiguities, gaps, inefficiencies, or uncertainties in the Coordinated Framework for the Regulation of Biotechnology, particularly regarding new and emerging biotechnology products. The RFI indicated that the information provided would inform regulatory agency efforts to improve the clarity and efficiency of the regulatory processes for biotechnology products.

There has been significant investment and growth over the last few years in the development of modified microbes for agricultural and industrial uses, including for use as biopesticides, fertilizers, biofuel production, and the manufacture of chemicals and other materials. A number of comments were received that discussed APHIS' regulation of modified microbes. Commenters expressed various concerns including the lack of clarity regarding the regulation of modified microbes generally, a lack of a clear and predictable pathway to commercialization, and what were perceived as onerous regulatory requirements. Commenters suggested APHIS develop regulatory pathways for commercialization for modified microbes, including exemptions and a process similar to the RSR process described in § 340.4 for modified plants. Suggestions for exemptions included exemptions based on the modification similar to exemptions provided for modified plants listed in § 340.1, exemptions based on the species of microbe, and exemptions based on the trait (e.g., barcoding traits). Suggestions were also made to improve the efficiency of the permitting system for modified microbes by reducing information requirements for certain movement permits (approved under OMB control number 0579-0471) and to set permit conditions that are risk-based and in alignment with agricultural practices.

Draft Microbial Permits Guide

On March 23, 2023, APHIS made available for review a draft *Guide for Submitting Permit Applications for Microorganisms Developed using Genetic Engineering Under 7 CFR part 340* on its website at https://www.aphis.usda.gov/aphis/newsroom/stakeholder-info/sa_by_date/sa-2023/microorganism-guide. We indicated that comments should be submitted to Regulations.gov and received by May 22, 2023. Comments received within that 60-day comment period were similar to those received to the RFI related to potential pathways to commercialization for modified microbes. For example, commenters expressed concern that there were no processes for modified microbes similar to the up-front exemptions at § 340.1 and the Regulatory Status Review process at § 340.4 for modified plants.

Based on this background information, we are soliciting public comments regarding the following questions:

RFI Questions

1. Describe new or emerging categories of biotechnology products that are relevant to the development and use of modified microorganisms. To assess new and emerging technologies with modified microbes, what expertise and resources are needed in the government to evaluate the overall plant pest risk of modified microbes?
2. Describe areas where the clarity and/or efficiency of regulations governing modified microorganisms could be improved (e.g. definitions that need to be provided or revised, barriers to obtaining the data necessary to achieve commercialization).

3. Describe key elements of a regulatory framework that would enable a scientifically sound assessment of a modified microorganism's plant pest risk, in order to inform regulatory decision-making by APHIS.
    a. Describe any biological features of microorganisms that APHIS should consider when determining whether a modification changes the plant pest risk, and thus the regulatory status of a modified microorganism (e.g., the potential for horizontal gene transfer, the production of airborne spores, its ecological role, or the ability to remain dormant for long periods of time).
    b. What criteria, data, and information should be considered when assessing a modified microorganism's plant pest risk?
    c. What should APHIS consider when determining whether modification of a biocontrol organism could result in it posing a plant pest risk? Provide scientific evidence to support which types of biocontrol organisms and methods could or could not pose a plant pest risk.
4. How should modified microorganisms with multiple uses (e.g., developed for both biomedical or pharmaceutical purposes and agricultural purposes) be regulated and evaluated by APHIS? What steps should APHIS take to ensure efficient and appropriate oversight and evaluation when a product is subject to regulation and review by both USDA and another Federal agency?
5. Should APHIS consider risk-based exemptions for certain types of microorganisms, or for certain modifications in microorganisms? If so, please provide examples of the types of modified microorganisms that should be exempt from regulation and provide scientific

evidence to support which modifications and types of microorganisms should or should not be exempt.

6. Are there any other specific issues or topics APHIS should consider in developing a regulatory framework for assessing the plant pest risk of modified microorganisms, or possible pathways to commercialization for modified microorganisms?

We welcome all comments on the issues outlined above.

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

Done in Washington, DC, this _____ day of _____ .

Under Secretary for Marketing and Regulatory Programs.