Response to Comments
Regulatory Status Review Guide

December 20, 2022

On August 25, 2021, APHIS-BRS published a draft Guide for Submitting Regulatory Status Review (RSR) Requests for public comment. We received comments from 11 individuals and organizations. After considering the comments, we revised and finalized the RSR Guide. This document summarizes and responds to the comments we received related to the RSR Guide, including indicating whether we revised the Guide based on the comment.

We received comments on a range of different issues and grouped the comments into the following categories:

- Procedures, generally
- Initial Review and Plant Pest Risk Assessment (PPRA) processes
- Information and data requirements and submissions
- Treatment of Plant Incorporated Protectants (PIPs)
- Examples provided in the RSR Guide
- Confidential Business Information (CBI)
- National Environmental Policy Act (NEPA)
- Confirmations of Exemption from Regulation in relation to RSRs

We also received comments related to permits, permit reviews, and permit requirements. These comments are out of scope for the RSR Guide and will be considered as we revise our Permit Guide. Comments about exemptions and the confirmation of exemption process, and general comments about communication, outreach, and the BRS website that address issues unrelated to the RSR process are also out of scope and will not be addressed here.

Comments about procedures, generally

1. Commenters requested we consider interim findings that a modified plant poses a plausible pathway to increased plant pest risk at the conclusion of step 1 or initial review, to be confidential communications between the Agency and the developer that APHIS would not publish. They asked APHIS to clarify whether we would publish findings that products are subject to the part 340 regulations if we are unable to conclude in a PPRA that the plant is unlikely to pose an increased plant pest risk.

   Response: We have revised the RSR Guide to clarify that if we identify a plausible pathway to increased plant pest risk (initial review), we will not publish our response letter to the requestor. Similarly, we have revised the RSR Guide to indicate that if, while conducting a PPRA, we believe we may be unable to conclude the plant is unlikely to pose an increased plant pest risk, we will notify the requestor, and the requestor will have the option to withdraw the RSR request prior to APHIS completing and publishing a draft PPRA for public comment. If the requestor withdraws the RSR, APHIS will not publish the draft PPRA.

2. Commenters requested clarification on timelines for the technical review and completeness check of an initial review submission, and on whether developers may request an RSR for products in the early development stage.

   Response: We have revised the RSR Guide to clarify timelines and that we will accept RSR requests for modified plants early in the product development. However, if APHIS has a large number of RSR requests, it intends to prioritize products that have been developed over products that are conceptual in nature.

3. One commenter asked that when APHIS receives an RSR request for a plant with a phenotype or mechanism of action (MOA) observed in the species or its sexually compatible relatives, that APHIS expedite the review and issue a decision on regulatory status in less than 180 days.

   Response: APHIS agrees that initial reviews may often take less than 180 days when there is familiarity with the plant-trait-MOA; in the preamble APHIS states that in such situations we can likely complete the initial review in less than 180 days.

4. Commenters requested that, when APHIS determines a modified plant is not subject to regulation, our response letter succinctly summarize our findings and make clear our determination that the modified plant is not regulated also applies to progeny of the modified plant.

   Response: Our response letters succinctly summarize the basis for our finding, and we will make clear our determination extends to progeny of the modified plant when bred with itself or other plants not subject to 7 CFR part 340. We have revised the RSR Guide to clarify this point.

5. Commenters sought clarification on whether the re-review process allows for requests to be submitted by anyone other than the original requestor and, if so, whether and how the original requestor would have an opportunity to provide input on the re-review process.

   Response: We have revised the RSR Guide to clarify the regulations do allow requests for re-review to be submitted by any person. If the original requestor does not submit the request for re-review, we will make the original requestor aware of the request. The requestor will be able to provide input if we determine a PPRA or a new PPRA is required.

Comments about the Initial Review and PPRA processes

1. We received several comments asking we provide additional information regarding our evaluation in the initial review of whether a plant poses a plausible pathway to increased plant pest risk, regarding the Plant Reference Documents (PRDs) we prepare to inform the initial review, and regarding the PPRA, the types of information we would typically request to support a PPRA, and the basis of decision-making. Commenters stated such information would help developers better understand the kinds of information used by APHIS to complete either stage of the RSR process and could help prevent potential delays in the RSR process that could result if developers have to wait to receive an initial review outcome

before preparing additional information to support a PPRA. Commenters also stated APHIS should retain the authority to choose a different comparator plant than the requestor, and asked we make PRDs publicly available.

Response: We have revised the RSR guide to provide additional information on the factors we consider during the RSR process, and the information we document in the PRDs and in the Mechanisms of Action Descriptions (MOADs). Both PRDs and MOADs are internal reference materials that we do not intend to post on our website. We also clarify information about the PPRA and basis of decision-making. With no prior knowledge of the plant-trait-MOA combinations we will receive, it is difficult to predict the information we might request if a PPRA is required. As examples of PPRAs become available in the Federal Register when posted for public review and comment, requestors will gain knowledge of the types of information APHIS considers in the PPRA process for particular categories of plant-trait-MOA combinations. PRDs are prepared at the species level considering the genetic variation present in the cultivated gene pool. APHIS will choose the most appropriate comparator plant for a given RSR and will provide an opportunity for developers to discuss with the Agency the most appropriate comparator(s) for any agronomic and ecological investigations they undertake to inform a PPRA.

2. Commenters recommended the Initial Review should limit its consideration of plant pest risk to the context of unmanaged, non-agricultural ecosystems, because in a typical or anticipated agricultural environment, modified plants will not present a reasonable hypothesis of increased plant pest risk due to practices that a grower will likely take as part of crop production. Another commenter recommended we assess the modified plant in the context of its agricultural landscape and associated cultivation practices.

   Response: In the initial review we do not limit our consideration of plant pest risk to unmanaged ecosystems. We do include knowledge about standard agronomic practices for the crop when considering whether there is a plausible pathway to increased plant pest risk. For example, increased plant pest abundance in fields of a modified plant may or may not lead to an increase in plant pest risk, depending on the ability of existing management practices to prevent an increase in pest pressure on comparator plants not subject to regulation.

3. A commenter noted the plant pest risk potential of a plant is not merely dependent on exposure, and even when there is a change in occurrence pattern relative to the comparator(s), the overall risk may remain unchanged. The commenter also recommended only changes in characteristics beyond the range of what has previously been observed in the plant species' gene pool should be considered for any possible change in occurrence pattern, and when a change in occurrence pattern of a modified plant provides a new route of exposure, the RSR process should progress to the PPRA only for those modified plants where the expected changes in occurrence pattern would be outside the observed range in the plant species' gene pool and there is a plausible pathway to increased plant pest risk as compared to the comparator(s).

   Response: APHIS agrees the plant pest risk potential of a plant is not merely dependent on exposure, and there may not be an increased plant pest risk simply because of a

change in occurrence pattern. However, we do not agree with the commenter that the identification of plausible pathways to increased plant pest risk should consider whether a change in a characteristic, or a resulting change in an occurrence pattern, is within the range observed in the plant species gene pool. Nor do we agree we should only progress to a PPRA when the expected changes in a characteristic or occurrence pattern are outside the range found in the plant species' gene pool. For RSR, APHIS considers genetic variation present in the species cultivated gene pool and the occurrence pattern in managed and unmanaged ecosystems. If the modified trait and MOA results in a plausible change in a characteristic or occurrence pattern within the range of genetic variation commonly found in cultivated comparator plants, then the RSR will not progress to step 2. However, if the gene pool of the plant being assessed includes other species that do not contain the introduced trait and/or MOA, potentially including wild and weedy relatives or distant species that are rarely cultivated, we will consider effects that could change the characteristics or occurrence patterns of the other species if the introduced or modified genetic sequence were to introgress.

4. A commenter recommended our consideration of whether an introduced trait and MOA could lead to the production, creation, or enhancement of a plant pest or a reservoir for a plant pest should be focused on modified plants with a new trait or characteristic that is *intended* to alter the plant's relationship with plant pests. The commenter similarly recommended evaluation of harm to non-target organisms should be limited to modified plants where the intended trait or characteristic targets a pest via a toxic mechanism of action. In both cases, the commenter recommended that consideration be limited to changes in phenotype that are outside the range observed in the plant species' gene pool.

   Response: APHIS does not agree with the commenter. While knowing the intent of the modification can facilitate our review in the RSR, the RSR must evaluate whether the trait and/or mechanism of action could have plausible yet unintended effects that could result in a plausible pathway to increased plant pest risk regardless of intent. Similarly, APHIS reviews all products subject to the RSR process to assess whether there are any plausible pathways to increased plant pest risk via harm to a beneficial non-target organism, regardless of the toxicity of the MOA. We also do not agree our consideration should be limited to changes in phenotype that are outside the range observed in the species' gene pool for the reasons stated above.

5. A commenter recommended APHIS limit its evaluation of the weedy impacts of the modified plant and its sexually compatible relatives to instances where each of four criteria are met: (1) the modified plants or its wild relative(s) inherently has invasive characteristics, (2) the modification of these characteristics is outside the range observed in the plant species' gene pool, (3) where gene introgression may be likely to occur to the wild relative(s), and (4) where there is exposure to wild relatives in unmanaged ecosystems.

   Response: APHIS does not agree with the commenter. Adopting the commenter's approach would limit the evaluation to only those plants with sexually compatible relatives that already have invasive characteristics, and then only when gene flow to the sexually compatible relative is likely to occur in unmanaged ecosystems. If we identify a plausible pathway to increased plant pest risk via gene introgression to a sexually compatible relative, the PPRA will evaluate, and the findings will reflect, the likelihood

and consequence of gene introgression. Since sexually compatible relatives can occur in both managed and unmanaged ecosystems, as well as on the borders of managed ecosystems, this assessment must include the likelihood of introgression whether that occurs within unmanaged ecosystems, within managed ecosystems, or from a managed to an unmanaged ecosystem. Additionally, limiting the evaluation to those plants which are already invasive would prevent the identification of plausible pathways to increased plant pest risk that could occur due to increasing the range of the modified plant or its sexually compatible relative.

6. A commenter stated our requirement that RSR requests include information on the intended trait and intended phenotype implies our review will be limited to the consideration of the intended change, but that a plant modified for one intended purpose will often exhibit unintended changes that require assessment in the initial review and PPRA. The commenter also recommended APHIS consult available databases and the scientific literature to determine whether a MOA may have multiple functions that could result in unintended phenotypes.

   Response: APHIS requests information on the intended trait and the intended phenotype to inform the initial review. However, the initial review is not limited to the intended changes in the plant. The initial review also considers whether there are plausible pathways to increased plant pest risk based on the plant, the trait, and the function(s) and plausible effects of the mechanism(s) of action on the plant, regardless of whether the plausible effects are intended or unintended. APHIS consults both information provided by the requestor and information APHIS obtains from databases and scientific literature. If one or more plausible pathways to increased plant pest risk are identified, they will be evaluated in the PPRA regardless of whether they are due to intended or unintended changes in the plant. We have revised the RSR Guide to clarify this point.

7. A commenter raised several concerns that the scope of the PPRA is too narrow, especially regarding herbicide resistant crops.

   Response: The comments raise issues outside the scope of the RSR process.

Comments about information and data requirements and submissions

1. A commenter suggested the Guide would be more useful if we described how each of the required pieces of information is used in the initial review to evaluate the regulatory status of a plant.

   Response: We have revised the Guide to provide a brief description of how each piece of requested information will be used.

2. Some commenters did not agree nucleotide sequence information is relevant to evaluation of plant pest risk and should not be required. Commenters also noted if such information is required, the FASTA format for submitting sequence information does not support annotation or redaction of such information as CBI and requested allowing the submission of sequence information in other formats. Another commenter noted that full sequence

information of the inserted or modified DNA, and/or the sequence that bridges gene deletions, would help the agency assess the effects of the genetic modification.

Response: APHIS uses nucleotide sequence information to confirm the intended trait(s) at the molecular/genetic level; to understand the MOA for purposes of assessing the plant pest impact(s), if any, of the modification(s); and to assess similarity with previously reviewed plants. We have revised the RSR Guide to indicate other formats that may be used to submit sequence information.

3. A commenter stated many questions that need answers in the initial review and the PPRA will require empirical data, and APHIS should make clear that no finding regarding plant pest risk will be made until all needed data are collected.

Response: As described in the RSR Guide, empirical data is generally not necessary to conduct an initial review. When the initial review identifies a plausible pathway to plant pest risk, empirical data may be necessary for APHIS to reach a finding. In such instances, APHIS would inform the submitter of the types of data that would be useful. If APHIS has insufficient information to reach a finding that a plant is unlikely to pose an increased plant pest risk, the plant will remain subject to the regulations.

Comments about the treatment of Plant Incorporated Protectants (PIPs)

1. Commenters requested APHIS coordinate with EPA when conducting RSRs on plants modified to contain plant incorporated protectants (PIPs) so that the agencies' assessments and conclusions are consistent and do not result in unnecessary duplication, while noting the two agencies have different assessment endpoints, and thus may have different information and data needs. Commenters also requested clarification about whether plants containing PIPs are required to undergo an RSR if PIP-containing products are registered or exempted under FIFRA.

Response: APHIS agrees with the commenter that the overall assessment endpoints for the two agencies differ and thus the agencies may have related but distinct data needs. APHIS will continue to discuss our analyses of plants containing PIPs with EPA when both agencies receive the same product for review. Commenters correctly noted that plants modified solely to contain PIPs registered with EPA are exempt from the permit requirements under part 340 and thus do not need to undergo an RSR to be moved or planted without a permit. This exemption applies whether the plant is modified to contain a single registered PIP or multiple registered PIPs. A developer may nonetheless request an RSR if they wish to have clarification whether the agency considers the PIP unlikely to pose a plant pest risk, or to add the plant containing the PIP to APHIS' list of plant-trait-MOA combinations that are exempt from the part 340 regulations. If an EPA registration expires or is rescinded, the developer would have to apply for a BRS permit to engage in regulated activities or submit an RSR request to learn whether the modified plant is subject to 7 CFR part 340. APHIS will clarify the status under 7 CFR part 340 of plants containing PIPs exempt from registration requirements once EPA completes rulemaking regarding such PIPs.

Comments about the examples provided in the RSR Guide

1. Commenters requested we indicate the drought tolerance and insect resistance examples provided in the RSR Guide are simply examples and do not necessarily represent conclusions that will apply to all drought tolerant or insect resistant plants.

   Response: The RSR Guide makes clear these are examples only.

2. A commenter requested we clarify the PPRA for the drought tolerance example would focus on whether the drought tolerance is modified so as to result in a plausible pathway to increased plant pest risk in an unmanaged ecosystem, and, if so, whether the trait may increase plant pest risk to such a degree that other species or ecotypes are displaced, or the plant becomes unmanageable.

   Response: As indicated above, we consider both managed and unmanaged ecosystems in the RSR process, including knowledge about standard agricultural production and management practices for the crop, when considering whether there is a plausible pathway to increased plant pest risk. We also consider such practices when conducting a PPRA if we identify a plausible pathway to increased plant pest risk during the initial review. Additionally, the focus of both the initial review and PPRA is on plausible plant pest risks to *other* plants, not to the plant under review, although other plants may include plants of the same species that are not the plant under review. We have revised the RSR Guide to clarify these points. APHIS does not agree the PPRA should focus solely on whether the increase in plant pest risk is to such a degree that other species or ecotypes are displaced or the plant becomes unmanageable. There could be plant pest impacts that have major consequences for other species yet remain short of displacing those species.

3. Commenters requested examples of plant-trait-MOA combinations that would not lead to a plausible pathway to increased plant pest risk relative to the comparator(s) and thus would complete the RSR process after the initial review.

   Response: APHIS posts RSR requests, response letters, and plant-trait-MOA combinations on its website that provide examples where no plausible pathways to plant pest risk were identified. These examples will continue to grow over time.

Comments about Confidential Business Information (CBI)

1. Commenters requested APHIS consider the possibility that RSR requests may be submitted much earlier in the commercial development of a product than when petitions for nonregulated status had historically been submitted and will be more likely to contain CBI that could not be disclosed until a product is closer to commercialization. Commenters also requested we withdraw any suggestions the protection of CBI is subject to a time limitation.

   Response: We understand there may be more CBI claims in RSRs than in petitions submitted under the legacy regulations. BRS will evaluate any CBI claims in accordance with applicable laws and procedures before releasing information in submissions to the public. Our goal is to undertake this CBI review as close in time as possible to any public release of information. The review will include communication with the requestor about any CBI claims. In our experience, minimizing CBI claims in published materials fosters

public acceptance of plant products of biotechnology and is important to enable informed public comment on PPRAs. Regarding time limitations, per 7 CFR 1.8(c), CBI designations expire 10 years after the date of the submission unless the submitter requests and provides justification for a longer designation period. We revised the RSR Guide to clarify these points.

Comments about the National Environmental Policy Act (NEPA)

1. Commenters requested we describe APHIS' expected processes for conducting analyses under NEPA when reviewing an RSR request, clarify whether requestors could provide supplemental information to APHIS which may not relate directly to plant pest risk but could assist in APHIS' preparation of appropriate analyses under NEPA, and develop a mechanism that allows requestors to submit such supplemental information if they wish.

   Response: When APHIS is reviewing an RSR request, it is determining whether a modified plant is unlikely to pose an increased plant pest risk relative to an appropriate comparator (and, thus, is not a plant pest or a plant that requires regulation to prevent introducing or disseminating a plant pest). If APHIS determines the modified plant is unlikely to pose an increased plant pest risk relative to the comparator plant, APHIS has no authority to regulate the modified plant under 7 CFR part 340. In these instances, APHIS is not required to undergo NEPA analysis as it "lacks the power to act on whatever information might be contained in the [NEPA analysis]." *Dep't of Transp. v. Pub. Citizen*, 541 U.S..

Comments about Confirmations of exemption in relation to RSRs

We received multiple comments discussing the regulatory exemptions in 7 CFR 340.1(b). Most of these comments were not directly relevant to the RSR process or the RSR Guide and are not discussed here. Please see our recently updated Guide for Submitting Confirmation Requests, which provides clarity on some of the issues in these comments.