Animal and Plant Health Inspection Service
U.S. DEPARTMENT OF AGRICULTURE

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Guide for Requesting a Regulatory Status Review under 7 CFR part 340

The information contained in this document is intended solely as guidance. Except where noted, persons may choose to follow APHIS guidance or follow different procedures, practices, or protocols that meet applicable statutes and regulations.

Language implying that guidance is mandatory (e.g., "shall," "must," "required," or "requirement") should not be construed as binding unless the terms are used to refer to a statutory or regulatory requirement.

Following the guidance contained in this document should not be construed as a guarantee of compliance with applicable statutes and regulations.

Biotechnology Regulatory Services
Animal and Plant Health Inspection Service
United States Department of Agriculture

4700 River Road
Riverdale, MD 20737

GUIDE INFORMATION

ISSUING AGENCY/OFFICE:	Animal and Plant Health Inspection Service (APHIS)/ Biotechnology Regulatory Services (BRS)
TITLE OF DOCUMENT:	GUIDE FOR REQUESTING A REGULATORY STATUS REVIEW (RSR) UNDER 7 CFR PART 340
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SUMMARY:	This document assists with preparing a request for Regulatory Status Review (RSR) of a plant developed using genetic engineering as described in 7 CFR § 340.4. APHIS protects and enhances U.S. agricultural and natural resources using a science-based and risk-basedregulatory framework to ensure the safe movement – including importation, interstate movement, and confined environmental release –of organisms developed using genetic engineering. APHIS receives its regulatory authority from the Plant Protection Act, and oversees organisms developed using genetic engineering in accordance with its regulations under 7 CFR part 340 (Movement of Organisms Modified or Produced Through Genetic Engineering) (85 FR 29790). See https://www.aphis.usda.gov/aphis/ourfocus/biotechnology for more information.
DISCLAIMER:	The contents of this document do not have the force and effect of law and are not meant to bind the public in any way. This document is intended only to provide clarity to the public regarding existing requirements under the law or agency regulations.

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INTRODUCTION TO THE REGULATORY STATUS REVIEW (RSR) PROCESS

APHIS regulations at 7 CFR part 340 govern the movement (importation, interstate movement, and confined environmental release) of certain organisms that are developed (modified or produced) through genetic engineering. A person may request a Regulatory Status Review (RSR) of a plant developed using genetic engineering (also called a modified plant) to determine whether a plant is subject to the regulations, based on the provisions in 7 CFR § 340.4. Until APHIS completes an RSR, any plant not otherwise eligible for exemption pursuant to 7 CFR § 340.1, is subject to the regulations. This document provides guidance on preparing an RSR request. If you have questions or would like to consult with APHIS about the RSR process generally or regarding a specific product, please contact us at RSRrequests@usda.gov.

The RSR process involves two distinct review steps, an initial review step (step 1) and a Plant Pest Risk Assessment (PPRA) step (step 2) (Figure 1). When a requestor initiates an RSR, they must submit information to APHIS describing the plant, the trait developed using genetic engineering, and the Mechanism of Action (MOA). This information is described in greater detail below. APHIS will use this information, publicly available information, and its knowledge and experience with the plant, trait, and MOA to conduct an initial review. APHIS will complete an initial review of the plant within 180 calendar days of receiving an RSR request that meets the information requirements in 7 CFR § 340.4(a)(4), except in circumstances that could not reasonably have been anticipated.

In the initial review, APHIS will consider whether the combination of the plant and the trait's MOA create a plausible pathway to increased plant pest risk relative to the comparator plant. APHIS will identify a plausible pathway to increased plant pest risk when there is a reasonable scientific hypothesis that the plant described in the RSR request, or its sexually compatible relatives that could receive the introduced or modified trait through gene flow, would pose an increased plant pest risk relative to the comparator plant if released into the environment.

- If APHIS does not identify a plausible pathway by which the plant or its sexually compatible relatives would pose an increased plant pest risk relative to appropriate comparator(s) in the initial review, APHIS will issue a response letter concluding the modified plant is not subject to regulation under 7 CFR part 340. APHIS will post the RSR request, the RSR response letter, and the plant, trait, and a general description of the Mechanism of Action (MOA) on the APHIS website[1]. The posting of plant, trait, and Mechanism of Action (MOA) combinations provides a growing range of modifications that are eligible for exemption from regulation under 7 CFR § 340.1(c).

If APHIS identifies one or more plausible pathways by which the plant or its sexually compatible relatives would pose an increased plant pest risk relative to appropriate comparator(s) in the initial review, APHIS will issue a letter to the requestor that describes the factor(s) of concern that require further evaluation. The requestor may choose to: 1) pause the RSR process; or 2) request that APHIS conduct a PPRA (Step 2) to evaluate the factor(s) of concern and determine the likelihood and consequence of the plausible increased plant pest risk; or 3) withdraw the RSR request. A requestor may consult with APHIS on these options when the requestor may need to make decisions about how to navigate the PPRA portion of the RSR process. If the requestor pauses the RSR process, they may subsequently and at any time ask APHIS to complete a PPRA. A requestor may at any time apply for a permit to move a plant, including a plant that is undergoing an RSR or for which they pause the RSR process.

If a requestor elects to proceed with the PPRA, the requestor may submit information related to the factor(s) of concern identified during the initial review. APHIS will use this information, the information from the initial review, publicly available information, and its knowledge of and experience with the plant, trait, and MOA to conduct the PPRA. Except in circumstances that could not reasonably have been anticipated, APHIS will complete both RSR steps within 15 months of receiving the RSR request, excluding any time that the requestor pauses the RSR process.

- If APHIS reaches a preliminary finding that the modified plant and its sexually compatible relatives are

unlikely to pose an increased plant pest risk, APHIS will publish the RSR request and the draft PPRA in the *Federal Register* and will solicit and review comments from the public. After reviewing the comments, if APHIS concludes that the modified plant and its sexually compatible relatives are unlikely to pose an increased plant pest risk relative to their appropriate comparator(s), it will determine that the plant is not subject to regulation under 7 CFR part 340. APHIS will publish its final PPRA in a second *Federal Register* notice. APHIS will also post the final PPRA on the APHIS website along with the original request, any supplemental material voluntarily submitted by the requestor during the PPRA step, and the plant, trait, and a general description of the MOA.

- If while conducting the PPRA, it appears that APHIS has insufficient information to reach a preliminary finding that the modified plant and its sexually compatible relatives are unlikely to pose an increased plant pest risk, APHIS will notify the requestor and the requestor will have the option to withdraw the request prior to APHIS completing its evaluation. When APHIS is unable to find that a modified plant or its sexually compatible relatives are unlikely to pose an increase plant pest risk, the modified plant is subject to regulation under 7 CFR part 340. The requestor may seek a re-review of the modified plant if new, scientifically valid evidence bearing on the plant pest risk associated with movement of the plant becomes available (7 CFR § 340.4(a)(2)).

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[1] APHIS will release such information without revealing CBI. APHIS will evaluate CBI claims, in accordance with applicable laws before releasing information in your submission to the public. If the trait and/or MOA is claimed as CBI, APHIS will propose, and requestors will have the opportunity to review and comment on, general trait and/or MOA descriptions prior to public disclosure. CBI designations expire 10 years after the date of the submission unless the submitter requests and provides justification for a longer designation period. 7 CFR § 1.8(c).

If APHIS previously evaluated a modified plant through the RSR or legacy petition process and determined it is not regulated, a plant with the same plant-trait-MOA combination is exempt from the regulations under 7 CFR part 340. APHIS' determination that a modified plant is not subject to the regulations extends to any progeny of the modified plant that is derived from crosses with other non-modified plants or other modified plants that are also not subject to regulation under 7 CFR part 340. Please see the Guide for Requesting a Confirmation of Exemption from Regulation for more information.

Anyone wishing to move (including importation, interstate transport, or release into the environment) a plant that is not eligible for regulatory exemption or has not been evaluated through the RSR process where APHIS determined the plant is not subject to the regulations may apply for a permit under 7 CFR § 340.5. Please see the Permit User's Guide for more information.

IMPORTANT DEFINITIONS

The definitions below are pertinent to understanding the RSR process. Definitions found in the regulations are referenced as § 340.3.

Comparator plant. A plant used as a baseline for comparison to a modified plant to determine if the modified plant poses an increased plant pest risk. The comparator plant is usually the plant from which the modified plant is derived. The comparator plant can also be a modified plant that was developed using genetic engineering if it: 1) is not subject to the regulations under 7 CFR part 340; and 2) is determined to be the most appropriate baseline for comparison to a plant that is the subject of the RSR request. Use of more than one comparator plant may be appropriate.

Consequence. An outcome that can occur when the plant is present.

Genetic Engineering. Techniques that use recombinant, synthesized, or amplified nucleic acids to modify or create a genome. § 340.3

Mechanism of Action (MOA). The biochemical process(es) through which genetic material determines a trait. § 340.3

Occurrence Pattern. The location, time, and manner in which a plant may be found in the environment including the distribution (the geographic area where a plant is grown with intentional human assistance, the geographic areas and habitat types where the plant occurs without intentional human assistance), density (number of individuals per unit area), and development (the timing of growth and developmental stages).

Person. Any individual, partnership, corporation, company, society, association, or other organized group. § 340.3

Phenotype. A set of observable characteristics of an organism resulting from the interaction of its genotype with the environment. A genetic locus controlling a trait within a species can have

two or more different forms, which result in different phenotypes. For example, flower color is considered a trait, while red and white flower colors are two different phenotypes for the flower color trait.

Plant Pest. Any living stage of a protozoan, 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. § 340.3

Plant Pest Risk. The potential for direct or indirect injury to, damage to, or disease in any plant or plant product resulting from introducing or disseminating a plant pest, or the potential for exacerbating the impact of a plant pest. § 340.3

Trait. An observable (able to be seen or otherwise identified) characteristic of an organism. § 340

The Regulatory Status Review Process

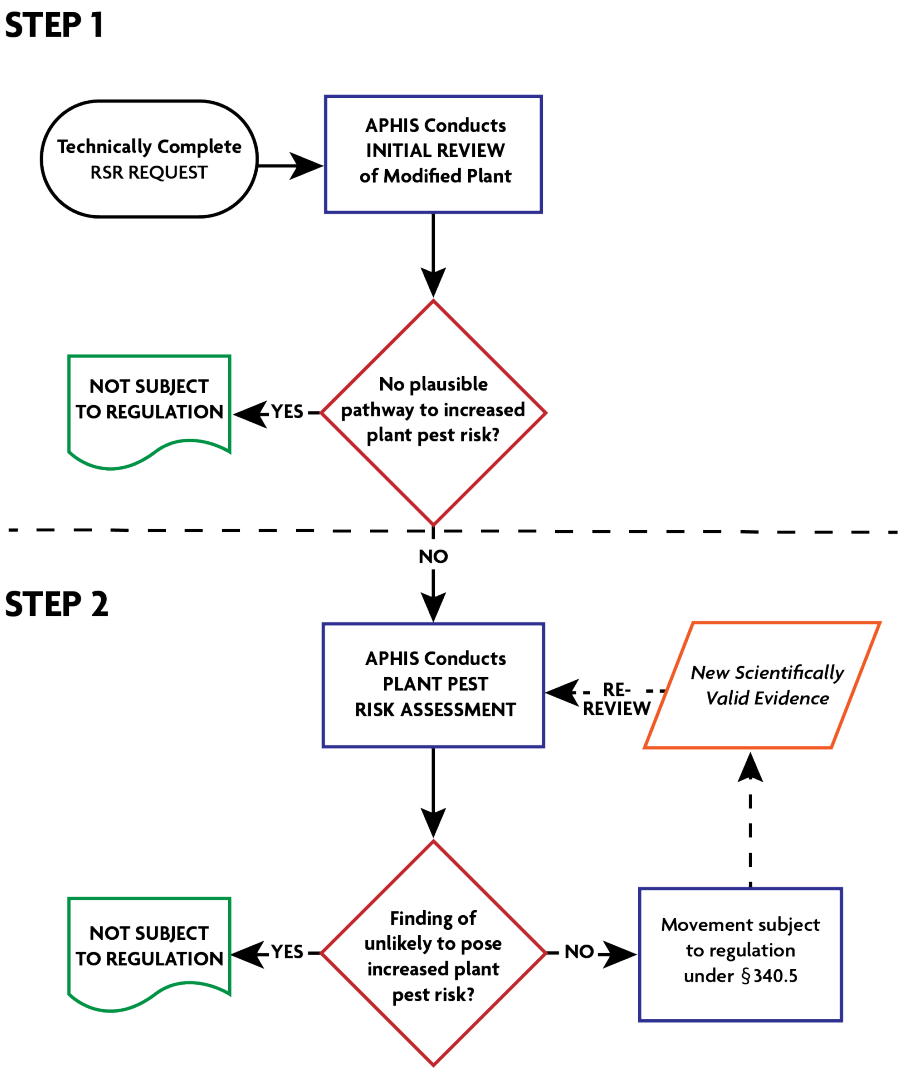

Figure 1. The Regulatory Status Review Process

Figure 1. The two-step Regulatory Status Review (RSR) process. The purpose of the initial review (Step 1) is to determine whether there are any plausible pathway(s) by which the modified plant or any sexually compatible relatives would pose an increased plant pest risk relative to the comparator plant. If APHIS does not identify a plausible pathway(s) to increased plant pest risk, the modified plant is unlikely to pose an increased plant pest risk and is not subject to the regulations and the RSR is complete. Alternatively, if APHIS identifies one or more plausible pathways to increased plant pest risk in the initial review, the requestor may pause the RSR, withdraw the RSR, or ask APHIS to proceed to Step 2, conducting an evaluation of the factor(s) of concern identified in the initial review through a plant pest risk assessment (PPRA), to determine the likelihood and consequence of the plausible increased plant pest risk. Following the PPRA, if APHIS finds the modified plant is unlikely to pose an increased plant pest risk, the modified plant is not subject to the regulations and the RSR is complete. Alternatively, if APHIS does not make such a finding, movement (importation, interstate movement, environmental release) of the modified plant is subject to the regulations. If new, scientifically valid evidence bearing on the plant pest risk associated with movement of the plant becomes available, the modified plant may be eligible for a re-review of the regulatory status found to be subject to the regulation if new, scientifically valid evidence bears on the plant pest risk associated with the movement of the plant.

THE RSR EVALUATION IN DETAIL

Plant pest risk is the potential for direct or indirect injury to, damage to, or disease in any plant or plant product resulting from introducing or disseminating a plant pest, or the potential for exacerbating the impact of a plant pest. In the case of modified plants, increased plant pest risk relative to a comparator plant may result from moving a modified plant into the environment and/or may be the result of direct or indirect effects of the modified plant. If a modified plant has one or more sexually compatible relatives that may receive the modified genetic material through gene flow, the potential for the sexually compatible relative(s) to pose an increased plant pest risk is also considered in the RSR analysis.

The plant pest risk associated with a plant is determined by the plant's occurrence pattern and the plant pest-related adverse consequences that arise when the plant occurs in an environment. Plant pest risk can increase if the plant modification (i) changes the occurrence pattern of the modified plant relative to that of the comparator plant, exposing a new environment to the modified plant and adverse consequences associated with the plant; or (ii) increases plant pest related adverse consequences relative to those of the comparator plant, even if the modification does not change the occurrence pattern of the plant; or (iii) changes both occurrence pattern and adverse consequences relative to the comparator plant. In the firstcase, the plant pest-related adverse consequences associated with the presence of the modified plant are the same as the comparator, but plant pest risk increases because the modified plant occurs (and therefore imparts those consequences) in different locations or situations than the comparator (e.g., plants modified for abiotic stress tolerance). In the second case, the modified plant occurs in the same locations and situations as the comparator, but plant pest risk increases because the plant pest-related consequences associated with the modified plant are different than the comparator (e.g., plants with a significant reduction in lignincontent). In the third case both occurrence pattern and the plant pest-related consequences associated with the modified plant are different than the comparator (e.g., a molecular stack for abiotic stress tolerance and lower lignin content).

- In Step 1 (initial review), APHIS determines whether there are any plausible pathways by which the modified plant (or sexually compatible relatives that could acquire the new trait from the modified plant) would pose an increased plant pest risk relative to the plant pest risk posed by an appropriate comparator. The review considers the biology of the comparator plant (and its sexually compatible relatives, if applicable), the trait and mechanism of action, and the effect of the trait and mechanism of action on:

- The distribution, density, or development of the plant and its sexually compatible relatives;
- The production, creation, or enhancement of a plant pest or a reservoir for a plant pest;
- Harm to non-target organisms beneficial to agriculture; and
- The weedy impacts of the plant and its sexually compatible relatives.

To support this analysis, APHIS relies on two internal reference documents, a Plant Reference Document (PRD), and a Mechanism of Action Description (MOAD).

The PRD documents the following information:

- The taxonomy and sexually compatible relatives of a plant
- Its agroecology including domestication history and use, where it is cultivated in the United States
- The agronomic practices used in cultivation of the plant
- The occurrence pattern of the plant, with and without intentional human assistance
    - A model of the climatic suitability for the plant (i.e., where general climatic conditions (i.e., the average climatic conditions over time) could enable the plant to complete a normal life cycle)
- A synthesis section that concludes which biological properties could change the occurrence of the plant if they were altered by genetic modification

- The following impacts of the plant:
  - Impacts on non-target organisms beneficial to agriculture
  - Impacts mediated by plant pests and pathogens
  - Impacts on agricultural productivity or quality
  - Impacts on agriculturally important natural resources including plant communities and hydrology

MOADs summarize key information about the mechanism of action, including the biochemical action of the introduced or modified genetic material and its metabolic, physiological and/or developmental functions, as well as the intended and any previously observed or plausible changes that could occur as a result of introducing or modifying the genetic material. The MOAD identifies whether there is a linkage between the MOA and any of the biological properties discussed in the PRD or adverse consequence associated with plant pest risk, whether there are potential changes in occurrence of the modified plant relative to the comparator, and whether any identified potential occurrence change or linkage to an adverse consequence justifies a plausible pathway to increased plant pest risk.

If APHIS identifies one or more plausible pathway(s) to increased plant pest risk, APHIS will issue a letter to inform the requestor of the factor(s) of concern and provide the requestor with the following options: withdraw the RSR, pause the RSR process to collect data, or proceed to the PPRA step of the RSR process (a requestor may apply at any time for a permit to move a plant that is undergoing an RSR or for which they pause the RSR process). This letter will not be posted on the APHIS website. Upon request, APHIS will proceed with Step 2 of the RSR process. At this point, the requestor may elect to submit information about the factor(s) of concern identified in the initial review. In Step 2, APHIS will conduct a PPRA to evaluate the factor(s) of concern identified in the initial review (Step 1), including any plausible change in occurrence pattern and/or plant pest-related adverse consequences of the modified plant relativeto the comparator, to assess the likelihood and consequence of the plausible pathway(s) to increased plant pest risk. APHIS will conduct the PPRA based on the best information available, including any information the requestor elected to submit related to the factors of concern identified in the initial review, information from the initial review, publicly available sources and APHIS' knowledge of and experience with the plant, trait, and MOA.

If, while conducting the PPRA, APHIS believes it may be unable to find that a modified plant is unlikely to pose an increased plant pest, APHIS will notify the requestor and the requestor will have the option to withdraw the RSR request prior to APHIS completing its evaluation. After completing its evaluation and preparing a draft PPRA, APHIS will publish the draft PPRA in the *Federal Register* for public review and comment. If, after reviewing public comments, APHIS finds the modified plant is unlikely to pose an increased plant pest risk, the plant is not subject to regulation under 7 CFR part 340, and APHIS will publish the final PPRA in the *Federal Register* and post it along with APHIS' response letter and the plant, trait, and MOA on the APHIS website. If APHIS does not find the modified plant is unlikely to pose an increased plant pest risk, the plant is subject to regulation under 7 CFR part 340, and its movement will be allowed only under permit in accordance with § 340.5.

Demonstrating the two-step RSR process by way of hypothetical example, if the comparator of a modified plant is limited by drought stress, an MOA that increases drought tolerance may generate a plausible hypothesis that increased drought tolerance in the modified plant would alter the occurrence pattern of that plant in a manner that would lead to an increase in plant pest risk relative to the comparator in managed and/or unmanaged ecosystems (e.g., by allowing the modified plant to inflict a plant-pest associated adverse consequence already present in the comparator plant in a new location or context). If APHIS identified such a pathway to increased plant pest risk as plausible for the given plant-trait-MOA combination in the initial review (Step 1), the requestor could ask APHIS to conduct a PPRA to assess the likelihood and consequence of thealtered occurrence pattern in terms of direct or indirect injury, damage or disease from plant pests (Step 2).[1]

[1] This is an illustrative example and does not indicate that all drought tolerance modifications would necessarily result in plausible pathways to increased plant pest risk.

The PPRA would examine the plausible magnitude of the change in drought tolerance, refine the predicted occurrence pattern that would result, and assess the likelihood and consequence of increased plant pest risk given the altered occurrence pattern of the plant that was identified in the initial review as plausibly associated with the modified plant in the new occurrence pattern. If the modified plant has sexually compatible relatives in the United States, the PPRA would assess whether the sexually compatible relatives could receive the MOA via gene flow from the modified plant, and, if so, would conduct the same assessment for the sexually compatible relatives.

The RSR assumes that the characteristics of the modified plant and its comparator will be similar unless there is a justified scientific rationale for a difference. Therefore, only those plant characteristics that may be plausibly predicted to be altered by the MOA will be addressed in the PPRA. As a second hypothetical example, Figure 2 shows the RSR pathway for corn modified to express a pesticidal protein. In this example, the initial review identifies one plausible pathway to increased plant pest risk based on a change in effects on non-target organisms. The requestor elects to proceed with the PPRA and submit information about potential effects on non-target organisms. APHIS conducts a PPRA that analyzes the predicted effects of the modified plant on non-target organisms based on the information about how the pesticidal protein expressed in the plant is expected to affect non-target organisms. The conclusions of the PPRA are based on whether the modified plant has different effects on non-target organisms than the comparator, and whether these differences are associated with increased plant pest risk.

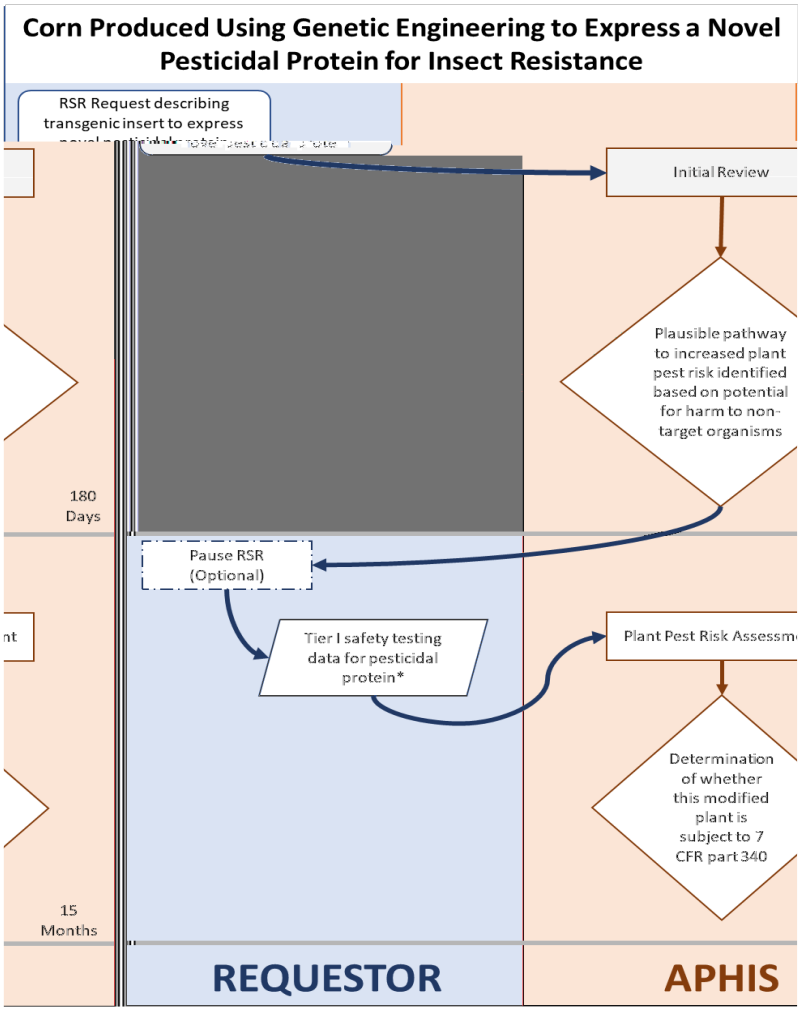

Figure 2. RSR Process for a corn modified to express a novel pesticidal protein for insect resistance. The RSR requestor initiates the RSR by submitting a description of the modified plant to APHIS. Based on known plant biology and the MOA, APHIS identifies a plausible pathway to increased plant pest risk in the modified corn based on the potential for the pesticidal protein to affect beneficial non-target organisms. APHIS communicates these findings to the requestor after completing the initial review. The requestor may choose to pause the RSR process or may instruct APHIS to continue with a PPRA. At this time the requestor may provide information related to the factor of concern identified during the initial review. APHIS conducts the PPRA based on publicly available information and the information supplied by the requestor. Based on the PPRA, APHIS determines whetherthe modified plant is subject to 7 CFR part 340. In the absence of unanticipated circumstances, APHIS will complete the RSR process in 15 months. This timeframe does not include any time the requestor pauses the RSR after being notified of the factor(s) of concern identified in the initial review.

*After BRS identifies plausible pathways to increased plant pest risk, the requestor may submit data related to the factor(s) of concern to support the PPRA. In this example, the requestor used the Tiered testing framework as described in the 2007 APHIS/EPA white paper (USDA-EPA. 2007. White Paper on Tier-Based Testing for the Effects of Proteinaceous Insecticidal Plant-Incorporated Protectantson Non-Target Arthropods for Regulatory Risk Assessments. https://www.epa.gov/sites/production/files/2015- 09/documents/tier-based-testing.pdf). If Tier I testing was not possible or not sufficient to show that increased plant pest risk is not likely, the requestor could submit higher tier testing data, or a different type of experimental data. APHIS will evaluate that information and relevant publicly-available information in the PPRA. The requestor may consult with APHIS regarding relevant types of information for addressing any factors of concern.

REQUEST FOR AN RSR—INITIAL REVIEW STEP

Electronically submit your RSR request to RSRrequests@usda.gov, addressed as follows:

Bernadette Juarez
APHIS Deputy Administrator Biotechnology Regulatory Services

When a new request is received, APHIS will assign it an RSR identification number and provide the number to the requestor. All subsequent communications regarding the request should include the RSR identification number in the subject line. When a requestor submits a modified version of the original RSR request or would like to submit additional information during the RSR review, they should send a single document that includes both the original request and the additional information. The cover letter should state it is an updated submission and indicate, where possible, the location of the new information within the submission.

Requestors may submit RSR requests for modified plants at any stage in the product development process. If a large number of RSR requests are pending requiring APHIS responses, APHIS will prioritize products that have been developed over products that are conceptual in nature. Please let us know if your submission is for a plant that is conceptual or a plant that has already been developed.

In general, RSR requests should be for one modified plant, although several MOAs may be included in the modification. In situations where a requestor has several modified plants of same species, or varieties with similar traits, phenotypes, and MOAs, they may combine multiple plants into a single document. Combined RSRs should have no more than five MOAs submitted and should make clear which MOAs occur in the same modified plant.

When submitting an initial RSR request, the requestor must submit the information required under 7 CFR § 340.4, and may submit additional optional information, as listed below. APHIS will review the information within 30 calendar days and inform the requestor if it is sufficient or whether there is a need for clarification or additional information (technical completeness review). Considering the detailed description of the information we review and assess during the initial review of the RSR process, requestors may voluntarily include publicly available literature related to their plant and MOA that they believe would be helpful to APHIS in conducting the initial review. These should be original sources; please do not prepare and submit summaries of the plant biology. Additionally, do not submit information that directly addresses risk hypotheses or factors of concern that you believe APHIS may identify in the initial review until the request advances to the PPRA step of the RSR (e.g., custom data, propriety information). It is important that APHIS has an opportunity to independently perform problem formulation during the initial review. Information from the requester that directly addresses risk hypotheses or factors of concern are relevant for the risk analysis in the PPRA; they are not helpful for APHIS' initial review.

Submission Information

Requestor

Personal Information (required). You must provide the requestor's **first name**, **last name**, **position** (optional, if any)**, organization name** (if any), and **contact** information (telephone number and/or email address).

Confidential Business Information (CBI) Statement

Does the RSR request contain CBI information? (required). You must indicatewhether the RSR request contains CBI (e.g., "This RSR request contains CBI." or "This RSR request does not contain CBI.")

If CBI information is included, provide a CBI Justification Statement (required). See the instructions at the end of this document regarding the CBIJustification Statement.

Description of Comparator Plant

Scientific Name (required). You must provide the **genus**, **species**, and subspecies (if relevant) for the comparator plant. You may provide the common name and/or the variety/cultivar/breeding line, though this information is optional. This information is used to inform our development of an appropriate PRD.

Biology of the Plant (optional). You may provide publicly available references related to the biology of the plant. However, please do not prepare or submit a review of the biology of the plant. We will contact you if needed to obtain certain specific information about the plant's biology. If an RSR has already been completed for a plant of the same species, this information is not needed.

Genotype of the Modified Plant

Genotype (required). You must provide APHIS with information to understand the genetic differences between the modified plant and the comparator plant, as described below. The information required to describe the genotype depends on whether geneticmaterial is inserted into the plant or endogenous sequences are altered.

If genetic material is inserted
This category captures situations in which genetic material is inserted into and remains in the genome of the modified plant. If this is the case, the requestor mustprovide the following information:

Sequence of the Insertion (required). Provide the nucleotide sequence of theinserted genetic material or the intended insertion in FASTA (FAST-All) format or other (e.g., GFF, MS-Word) format in a single block. Please feel free to pre-consult with APHIS if you wish to submit another sequence format. The sequence of all genetic elements integrated, or intended to be integrated, into the plant genome need to be described; therefore, vector sequence information is not required if vector sequences are not inserted. APHIS uses the specified sequence information to confirm the intended trait(s) at the molecular/genetic level; to understand the MOA for purposes of identifying and, if applicable, assessing plausible plant pest risk(s) of the modified plant; and to assess the similarity of the plant with previously reviewed plants.

Annotation of the Inserted Genetic Material. Provide an annotation in tabular format showing the order of the different genetic components (in 5' to 3' direction) and a description of their function. APHIS uses this information to understand and verify the purpose and function of the inserted genetic material, and to ensure that the complete insertion is reported and described. For each component, include the following five pieces of information:

Nucleotide position (required). Provide the base pair position for each component (e.g., 1-100 or 86-205) in the insertion. If the exact nucleotide number of an introduced border region is unknown, provide a range that you wish BRS toconsider (e.g., a border region of 10-50 nucleotides). All nucleotide positions should be covered in the annotations (e.g., there can be no gaps in the reported positions—components like linker or spacer regions, border regions, etc., should be reported). APHIS uses this information to ensure the entire inserted sequence has been reported.

Name of inserted component (required). Provide a one-to-three-word namebased on the component (e.g., 35S promoter, catalase, extensin, PAT, nos terminator, noncoding spacer). Component names allow APHIS to easily communicate with requestors regarding particular elements included in the insertion.

Construct Component Donor (required). Provide the scientific name (genus and species) of the organism from which the genetic sequence was first described or obtained. This information alerts APHIS of whether there may be additional regulatory obligations regarding the inserted sequence (e.g., for select agent reporting) and contribute to the understanding of the function of a component.

- For viruses, do not use abbreviations; spell out the name (i.e., enter Cauliflower Mosaic Virus, not CaMV).
- For a fusion or chimeric component (e.g., a hybrid gene formed from two ormore genes), all donor organisms corresponding to each fusion partner should be listed with a comma separating the individual donors.
- Most construct components are derived from sequences originally found in a donor organism. If the original sequence has been altered, the requestor should list the original donor organism and briefly describe the nature of the modifications.
- Synthetic sequences that could be considered truly artificial (e.g., linkers, spacers, and tags) do not share significant sequence homology to a native source of sequences. In this case, the requestor can list the donor organism as "synthetic."
- "Unknown" may not be used.

Function (required). Provide a short statement (generally a phrase or a sentence) describing the function of the inserted genetic material. For lesser-known components, the requestor may wish to provide literature references to assist APHIS in conducting the review. Avoid the use of internal codes that are not referenced in publicly available sources. APHIS uses this information to understand how a construct component contributes to the MOA.

Reference Numbers (optional). APHIS requests, but you are not obligated to provide, publicly available nucleotide sequence identification number(s) and protein accession number(s). This information will assist APHIS' review of the inserted genetic material. APHIS uses this information if genomic analysis is needed to confirm the function of a component.

Information about insertion site (when relevant) (optional). For many RSR requests, this information will not affect the conclusions of the RSR. However, in some cases, knowledge of the insertion site may affect the identification of plausible plant pest risks associated with the modified plant. Requestors may wish to provide information on the insertion site when understanding information about the insertionsite (e.g., if the insertion is on the plastid genome or if the insertion is limited to a specific genome of a polyploid plant) may affect the potential for gene flow to a sexually compatible relative.

If genetic material is not inserted

This category captures situations in which the genome is modified with or without a template such that existing endogenous genetic sequence is altered (e.g., the sequence of a gene or regulatory sequence is edited). APHIS uses this information to understand the purpose and function of the alteration, and to ensure the alteration is reported and understood by APHIS. If the endogenous genetic sequence is altered, provide the following information in your RSR request:

Name of the altered genetic component and nature of modification(s) (required). You must identify the genetic component(s) that are modified, designating genetic components by a short (generally one-to-three word) summary based on the component (e.g., catalase, extensin, peroxidase). You must also provide a description of the function of modified sequences. Spell out abbreviations (e.g., alkaline phosphatase). All predictable changes must be provided when the method used may result in more than one modification e.g., for multiple members of a gene family or homeologous genes in a polyploid

species. Component names allow APHIS to easily communicate with requestors regarding particular elements included in the insertion.

Sequence of the Modification (required). Provide the nucleotide sequence of the entire edited region(s) (e.g., the entire edited gene or functional motif of a regulatory region) in FASTA or other formats mentioned above. APHIS uses the specified sequence information to confirm the intended trait(s) at the molecular/genetic level; to understand the targeted sequence modification(s) and MOA for purposes of identifying and, if applicable, assessing plausible plant pest risk(s) of the modified plant; and to assess the similarity of the plant with previously reviewed plants.

Sequence comparison (required). Compare the modified sequence(s) with the unmodified sequence and designate the changes. A figure or graphical representation of sequence alignment using standard software packages is recommended.

Reference Numbers (optional). APHIS requests, but you are not obligated to provide, publicly available nucleotide sequence identification number(s) and protein accession number(s) of the unaltered genetic component. This information will assist APHIS' identification and review of the altered genetic component. APHIS uses this information if genomic analysis is needed to confirm the function of a component.

Description of New Trait

Intended trait(s) (required). Briefly describe the intended trait. If possible, provide a description that does not include CBI. If there are multiple traits, please describe each trait. Selectable and screenable markers are considered traits. APHIS uses this information to understand the intended trait(s) for purposes of identifying and, if applicable, assessing plausible plant pest risk(s) of the modified plant.

Intended phenotype(s) (required). Describe the phenotype associated with each trait. Provide information on the expected difference between the modified plant and the comparator plant (e.g., purple flower color, resistance to *Phytophthora*). APHIS uses this information to understand the intended phenotype(s) for purposes of identifying and, if applicable, assessing plausible plant pest risk(s) of the modified plant.

Description of the Mechanism(s) of Action (MOA) (required). You must describe the MOA by which each intended phenotype will be conferred, to the extent known. Please limit your description to a few paragraphs, and no more than three pages. This could be a biochemical change (e.g., production of a stress hormone that rapidly altersthe osmotic potential of stomatal guard cells, causing them to shrink and stomata to close, or altered induction of an endogenous stress response). The description should include any expected changes in metabolism, physiology, and development due to the trait/genetic modification. The description should be based on publicly available information and should not include experimental data. The requestor is encouraged to cite references in this section. APHIS uses this information to understand the MOA for purposes of identifying and, if applicable, assessing plausible plant pest risk(s) of the modified plant.

Other Information on the MOA(s) (when relevant, optional). The requestor may submit information on the MOA, to the extent that it is known, to aid the analysis. This information could include any publications and other publicly available science-based assessments that may be helpful for APHIS' evaluation of the plant's potential to pose plant pest risks. Such information could include information about any new enzymes or other gene products produced; the biochemical action of the genetic material or its product; a description of the pathway involved; or how the genetic material or its product participates in or interacts with metabolic, physiological, or developmental processes in the engineered plant or in other organisms. In general, information must be publicly available and must not include experimental data other than that needed to describe the MOA, as noted above. Risk assessment conclusions should not be provided. If the same MOA has been previously evaluated for a different plant taxon under either the RSR process or the legacy petition

process, the number of the previous RSR request or petition may also be included. Citations of publicly available literature are particularly useful in this section.

BRS' Plant-Trait-MOA table shows previous RSR and petition submissions that have cleared the review process. Please note that BRS' Plant-Trait-MOA table specifies that the evaluation of some MOAs,such as MOAs for pesticidal products, considers the tissue concentration profile of the pesticidal product. For such traits, requestors may specify the tissue concentration profilethat they wish APHIS to evaluate. The tissue expression profile should be explained in terms of the maximum tissue concentration that may be included under the MOA for the tissues and timepoints specified. Plants developed using genetic engineering that express the same compound at a higher concentration or in new tissues may be considered a different MOA.

APHIS is aware that not all information will be known about every MOA. The optional information described above are examples of the optional information that may be included. APHIS does NOT expect this information will be submitted for every RSR request.

REQUEST FOR AN RSR—PLANT RISK ANALYSIS STEP

When APHIS identifies one or more plausible pathways to increased plant pest risk in the initial review, APHIS will inform the requestor of the factor(s) of concern in a letter. At any point after receiving that letter, the requestor may ask APHIS to proceed with conducting an evaluation of the identified factor(s) of concern to determine the likelihood and consequence of the plausible increased plant pest risk by preparing a PPRA. If they wish, the requestor may provide APHIS with information or data addressing the factor(s) of concern when they ask APHIS to proceed with the PPRA. Submissions should be limited to the factor(s) of concern that APHIS identified in the initial review letter and should not include packages of standard tests or data or information that does not address a factor of concern identified by APHIS. APHIS encourages requestors to contact us prior to submitting additional data or information if they have questions about the types of data or information to include in their submission. The interim time between the date APHIS issues the letter identifying the factor(s) of concern and the date the requestor asks APHIS to proceed with aPPRA will not be counted in the 15-month timeline of the RSR; the process will be paused during this time. The 15-month timeline will include the 30-day public comment period on the draft PPRA.

A requestor may ask APHIS to produce a PPRA for an RSR request by sending a letter to RSRrequests@usda.gov, addressed as follows:

Bernadette Juarez
APHIS Deputy Administrator Biotechnology Regulatory Services

Please reference the RSR identification number in the subject line of the message. The letter should also include the RSR identification number. Requestors who wish to submit optional information to support the PPRA should submit such information and an explanation of how it addresses the factor(s) of concern identified in the initial review as an attachment to their letter asking APHIS to proceed with a PPRA. The PPRA data package should include the exact package submitted at the initial review stage, followed by new information pertinent to the PPRA.

If information to support the PPRA is being submitted, the data and explanation should be submitted as a single file. For large files, APHIS can provide access to a secure Cloud Vault for upload. Send a message to RSRrequests@usda.gov for access to the Cloud Vault.

When a requestor submits information at the same time as requesting that APHIS proceed with a PPRA, APHIS will review the information within 30 calendar days and inform the requestor whether there is a need for clarification related to the data provided. If information is submitted after the requestor asks APHIS to proceed with a PPRA,

APHIS will inform the requestor of the time it will require to review the information, which will not exceed 30 calendar days. When APHIS informs the requestor of the need for clarification about the data provided, the PPRA process will pause until the requestor provides the clarification APHIS requested. Requestors can also pause the RSR process at any time. Please note the data review identifies only whether clarification is needed to understand how the submitted information pertains to plant pest risk. An indication that APHIS has no further questions does not imply that APHIS will reach a particular conclusion in the PPRA.

If a requestor submits additional information after asking that APHIS conduct a PPRA, please include the RSR Identification number in the subject line of the email message and label the attachments in a way that distinguishes them from the original RSR request (e.g., "Supplemental Information for PPRA").

The draft PPRA and all information submitted by the requestor (except for that designated as CBI) will be published in the *Federal Register* for public comment.

APHIS is available for consultation with requestors who are unsure of whether to submit information to support a PPRA, or of the type and format of information that may be useful for the process.

REQUESTING A RE-REVIEW

If a modified plant was found to be subject to regulation under 7 CFR part 340 after going through the RSR[2], and new information becomes available about the plant pest risk associated with the plant, anyone may request that APHIS develop a new PPRA of the plant based on the new information. In this situation, the requestor must submit new, scientifically valid information pertaining to the plant pest risk of the plant. The requestor should also submit a statement explaining how the new information pertains to the outcome of the previous review. If the request for re-review is not submitted by the original requestor, APHIS will make the original requestor aware of the request for re-review. The requestor will be able to provide input if we determine that a PPRA or a new PPRA is required.

To request a re-review, a requestor should send a letter, in accordance with the Guide for Submitting CBI, to RSRrequests@usda.gov. The letter should include:

- The RSR inquiry number associated with the previous submission
- An explanation of how the new information being presented affects the conclusions of the previous review
- An attachment presenting the new information to be considered.

TIMELINE FOR THE RSR PROCESS

Except in circumstances that could not reasonably have been anticipated, APHIS will complete the initial review within 180 calendar days of receiving a complete submission and the entire RSR within 15 months of receiving a request that meets the requirements specified above. If the requestor chooses to pause the RSR prior to development of a PPRA and instructs APHIS to resume development of the PPRA at a later time, the period that the RSR was paused is not included in the 15-month timeline.

RSR REFERENCES

Plant-Trait-MOA table for exemptions

Tiered Testing White Paper

Final Rule

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[2] The regulation states: "Any person may request re-review of a modified plant previously found to be subject to this part after an initial review was conducted, provided that the request is supported by new, scientifically valid evidence..." In this case, the use of "initial review" refers to the first completed regulatory status review of a modified plant. An RSR of a modified plant cannot find that the modified plant is subject to regulation until the PPRA has been completed. A re-review may be requested after the first time the entire RSR, including the PPRA step is completed.

Guidance for Requesting a Confirmation of Exemption from Regulation under 7 CFR part 340

The Revised Rule (previously known as the SECURE Rule)

eFile Permitting System

CONFIDENTIAL BUSINESS INFORMATION

If your RSR request, as well as any follow-up documentation you provide, does not contain Confidential Business Information (CBI), you must mark it "**Does Not Contain CBI**" or "**No CBI.**"

If your RSR request, as well as any documentation you provide, contains CBI, you must mark it **"Contains CBI"** and submita CBI copy, a CBI-deleted copy, and a CBI justification.

BRS will evaluate any CBI claims in accordance with applicable laws and procedures before releasing information in your submission to the public. Our goal is to undertake this review as close in time as possible to any public release of information. The review will include communication with the developer about claims of CBI, if any. 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. CBI designations expire 10 years after the date of the submission unless the submitter requests and provides justification for a longer designation period. 7 CFR 1.8(c).

For further information on submitting RSR requests with or without CBI, see the Guide for Submitting CBI.

SUGGESTED TEMPLATE FOR RSR REQUESTS

INFORMATION MARKED WITH * IS REQUIRED (see above for details)

1. Information about Requestor
   First Name*
   Last Name,* and Position
   Organization Name (if applicable) *

Contact information* (choose one or both)
Telephone Email address

2. Does the request contain Confidential Business Information (CBI)?*
   If yes, CBI Justification Statement.*

3. Description of the comparator plant:
   Scientific name (genus, species)*
   Common Name
   Subspecies / Cultivar / Breeding Line

4. Genotype of the modified plant.
   A. If genetic material is inserted into the genome:

      Sequence of the Insertion*:
         Annotation of the Inserted Genetic Material*
         Nucleotide position*
         Name of inserted component*
         Construct component donor organism*
         Function*
         Sequence ID (e.g., NCBI) (when available)
      Information about insertion site (when relevant)

   B. If genetic material is not inserted into the genome: Nature of modification(s)*
      Sequence of the Modification*
      Sequence comparison*

5. Description of new trait intended trait*
   Intended phenotype*
   Description of the MOA*